Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Bivariate analysis comparing good versus poor one-year outcome groups in the combined cohort of CLEAR-III and MISTIE-III Patients

Characteristic [a]	Good One-Year Outcome (N=308)	Poor One-Year Outcome (N=407)	p-value
Demographics			
Age, mean (SD), y	56.53 (11.58)	63.13 (10.99)	<0.001
Male Gender, n (%)	182 (59.1)	235 (57.7)	0.72
Medical Co-morbidities, n (%)			
Hypertension	291 (94.5)	387 (95.1)	0.72
Congestive Heart Failure	8 (2.6)	15 (3.7)	0.41
Atrial Fibrillation	18 (5.8)	33 (8.1)	0.24
Coronary Artery Disease	16 (5.2)	37 (9.1)	0.05
Type 2 diabetes	43 (14.0)	103 (25.3)	<0.001
Hyperlipidemia	89 (28.9)	126 (31.0)	0.55
Anticoagulation	20 (6.5)	32 (7.9)	0.49
Chronic Kidney Disease	15 (4.9)	26 (6.4)	0.39
Chronic Obstructive Pulmonary Disease	10 (3.2)	25 (6.1)	0.08
Premorbid mRS [b], n (%)			
mRS 0	292 (94.8)	352 (86.5)	0.001
mRS 1	16 (5.2)	55 (13.5)	
Clinical severity			
Enrollment NIHSS [c], median (IQR)	18 (13-22)	21 (17-28)	<0.001
Enrollment GCS [d], median (IQR)	10 (8-13)	9 (7-11)	0.05
Radiologic Characteristics			
Admission Imaging Characteristics [e]			
Thalamic location of hematoma	85 (27.6)	137 (33.7)	0.08
Basal ganglia location of hematoma	136 (44.2)	195 (47.9)	0.32
Deep location of hematoma	221 (71.8)	332 (81.6)	0.002
Hemispheric Side of Lesion [f]			
Right Hemisphere	139 (45.1)	199 (48.9)	0.23
Left Hemisphere	155 (50.3)	198 (48.6)	
ICH volume, mean (SD), mL	24.47 (20.26)	30.33 (22.34)	<0.001
IVH volume, mean (SD), mL	14.08 (17.94)	16.13 (20.88)	<0.001
Obstructive Hydrocephalus	128 (41.6)	186 (45.7)	0.27
Septum pellucidum shift, mean (SD), mm [g]	4.09 (2.43)	4.6 (2.92)	0.03
Pineal gland shift, mean (SD), mm [g]	1.85 (2.01)	2.24 (2.15)	0.03
Severe Leukoariosis [h]	29 (9.4)	108 (26.5)	<0.001
Stability Imaging Characteristics			
ICH volume, mean (SD), mL	27.48 (21.55)	33.08 (24.01)	0.001
IVH volume, mean (SD), mL	12.91 (16.71)	14.79 (18.56)	0.16

Characteristic [a]	Good One-Year Outcome (N=308)	Poor One-Year Outcome (N=407)	p-value
End-of-Treatment (EOT) Imaging Characteristics			
ICH volume, mean (SD), mL	17.58 (17.30)	22.60 (19.99)	<0.001
IVH volume, mean (SD), mL	5.94 (9.98)	7.93 (12.41)	0.02
EOT ICH volume < 15 mL	123 (39.9)	110 (27.0)	<0.001
Day 30 Imaging Characteristics [i]			
ICH volume, mean (SD), mL [i]	3.93 (8.40)	5.40 (9.92)	0.037
Resolution of ICH [i,j]	168 (56.6)	159 (42.3)	<0.001
Resolution of IVH [i,j]	229 (35.5)	257 (39.8)	0.001
Persistent Hydrocephalus [i]	18 (6.1)	46 (12.2)	0.007
ICU and Physiologic Variables			
Admission systolic BP, mean (SD), mm Hg	187.09 (34.73)	189.54 (37.27)	0.38
Admission diastolic BP, mean (SD), mm Hg	106.25 (24.97)	103.83 (23.99)	0.2
Mechanical Ventilation Duration, mean (SD), days	5.19 (6.59)	9.21 (9.84)	<0.001
Number of ICU days, mean (SD), days	13.86 (7.32)	17.57 (7.67)	<0.001
Adverse Events			
Ischemic stroke	31 (10.1)	61 (15.0)	0.05
Symptomatic hemorrhage	6 (1.9)	8 (2.0)	0.99
Any cardiac adverse events [k]	28 (9.1)	44 (10.8)	0.45
Cardiac arrest	0 (0.0)	3 (0.7)	0.13
Acute Respiratory Distress Syndrome	4 (1.3)	7 (1.7)	0.65
Pulmonary edema	9 (2.9)	19 (4.7)	0.23
Any Pulmonary adverse events [k]	95 (30.8)	162 (39.8)	0.01
Acute kidney injury	16 (5.2)	29 (7.1)	0.29
Venous thromboembolism	28 (9.1)	43 (10.6)	0.51
Any infection	119 (38.6)	188 (46.2)	0.04
Urinary Tract Infection	39 (12.7)	45 (11.1)	0.51
Central Nervous System infection	15 (4.9)	26 (6.4)	0.39
Sepsis	6 (1.9)	10 (2.5)	0.65
Pneumonia	74 (24.0)	122 (30.0)	0.08
Procedures and Interventions in the first 30 days			
Ventriculo-peritoneal Shunt	27 (8.8)	37 (9.1)	0.88
Gastrostomy Tube placement	66 (21.4)	204 (50.1)	<0.001
Trial treatment assignment [l]	148 (48.1)	214 (52.6)	0.23
Quality of Life (EQ-VAS), mean (SD) [m]			
Day-30	44.9 (24.3)	30.4 (22.3)	<0.001
Day-180	66.9 (19.8)	48.2 (23.9)	<0.001
Day-365	70.7 (18.2)	53.9 (21.7)	<0.001

Characteristic [a]	Good One-Year Outcome (N=308)	Poor One-Year Outcome (N=407)	p-value
Discharge Disposition			
Home	20 (6.5)	9 (2.2)	<0.001
Rehabilitation facility	161 (52.3)	128 (31.7)	
Acute Care Facility	100 (32.5)	175 (43.3)	
Long-term care facility	27 (8.8)	92 (22.8)	
Number of Patients Eventually Discharged Home	294 (95.4)	168 (41.3)	<0.001
Median Time to Home, days (IQR)	60 (43-100)	100 (61-161)	<0.001
Median Time Spent at Home, days (IQR)	303.5 (264-323)	233 (147-293)	<0.001

Abbreviations: CLEAR III, Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage phase 3 trial; MISTIE III, Minimally Invasive Surgery Plus Alteplase for Intracerebral Hemorrhage Evacuation phase 3 trial; ICH, Intracerebral Hemorrhage; IVH, Intraventricular Hemorrhage; mRS, modified Rankin Score; NIHSS, National Institute of Health Stroke Scale; BP, Blood Pressure; CPP, Cerebral Perfusion Pressure; ICP, Intracranial Pressure; ICU, Intensive Care Unit; SD, Standard Deviation; IQR, Interquartile Range

[a] All variables are represented as n and %, unless otherwise specified

[b] Scores range from 0 to 6, with higher scores indicating severe disability and death

[c] Scores range from 0 to 42, higher scores correlate with higher stroke severity; NIHSS was recorded at study enrollment and was not available for 27 CLEAR III patients

[d] Scores range from 3 to 15, with lower scores indicating coma; Glasgow Coma scale readings were recorded at study enrollment

[e] ICH and IVH volume on admission were not available in 14 patients in MISTIE III and 2 patients in CLEAR III

[f] Hemispheric side of lesion was missing in 24 CLEAR-III patients because 17 patients had a primary IVH/periventricular bleed, 1 had infratentorial bleed; thus only 6 with a hemispheric basal ganglia hemorrhage had missing documentation on side of lesion

[g] Midline shift parameters were not available in 79 patients in CLEAR III and 85 patients in MISTIE III

[h] Defined as a combined periventricular and deep white matter score of greater than 2 on Van Sweiten Score for CLEAR III and greater than 3 on Fazekas score for MISTIE III; White matter disease severity was not available in 45 patients in MISTIE III

[i] Day-30 CT IVH resolution data was missing in 13 CLEAR-III and 70 MISTIE-III patients; day-30 CT ICH volumes, ICH resolution and hydrocephalus data was missing in 16 CLEAR-III and 26 MISTIE-III patients

[j] Resolution of IVH defined as modified Graeb Score of 0/IVH volume 0-mL and resolution of ICH defined as ICH volume of 0 mL on day 30 CT scan

[k] These were defined as any serious adverse events (SAR) involving the “respiratory system” and “cardiovascular system” in the prospectively adjudicated events reports of the two trials

[l] Defined as Intraventricular thrombolysis with tissue plasminogen activator in CLEAR III and MISTIE surgery in MISTIE III

[m] In addition to 129 patients that died by one-year, EQ-VAS was also not reported by 70 CLEAR-III and 74 MISTIE-III patients at either day-30 and/or day-365

SI conversion factors: to convert mm to meters multiply by 10^{-3}, to convert mL to Liters multiply by 10^{-3}

eTable 2. Differences between patients included in the analysis versus those excluded due to missing mRS at day-30 and/or day-365

Characteristic	Patients included in analysis (n=715)	Patients excluded due to missing mRS (n=22)	*p*-value
Demographics			
Age, mean (SD), y	60.3 (11.7)	54.2 (10.5)	0.02
Male Gender, n (%)	417 (58.3)	13 (59.1)	0.94
Medical Co-morbidities, n (%)			
Hypertension	678 (94.8)	21 (95.5)	0.90
Congestive Heart Failure	23 (3.2)	1 (4.6)	0.73
Atrial Fibrillation	51 (7.1)	0 (0.0)	0.19
Coronary Artery Disease	53 (7.4)	3 (13.6)	0.28
Type 2 diabetes	146 (20.4)	0 (0.0)	0.02
Hyperlipidemia	215 (30.1)	0 (0.0)	0.002
Chronic Anticoagulation Use	52 (7.3)	0 (0.0)	0.19
Chronic Kidney Disease	41 (5.7)	2 (9.1)	0.51
Chronic Obstructive Pulmonary Disease	35 (4.9)	2 (9.1)	0.38
Clinical severity			
Premorbid mRS[b], median (IQR)	0 (0)	0 (0)	0.47
Enrollment NIHSS[c], median (IQR)	20 (15-25)	20 (18-26)	0.22
Enrollment GCS[d], median (IQR)	10 (8-12)	10 (7-13)	0.99
Radiological Characteristics			
Admission Imaging Characteristics			
Thalamic Location of ICH	226 (31.6)	11 (50.0)	0.07
Deep ICH location	578 (80.8)	18 (81.8)	0.91
Left Hemispheric Location of ICH [e]	353 (49.4)	11 (50.0)	0.95
ICH volume, mean (SD), mL [f]	27.8 (21.7)	20.7 (16.8)	0.13
IVH volume, mean (SD), mL [f]	15.2 (19.7)	15.0 (21.4)	0.95
Pineal midline shift, mean (SD), mm [g]	2.1 (2.1)	1.8 (2.04)	0.58
Severe Leukoariosis [h]	221 (33.0)	6 (28.6)	0.67
Stability imaging characteristics			
ICH volume, mean (SD), mL	30.6 (23.2)	18.6 (15.8)	0.66
IVH volume, mean (SD), mL	14.0 (17.8)	14.6 (20.4)	0.88
End-of-treatment (EOT) imaging			
ICH volume, mean (SD), mL	20.4 (19.0)	17.8 (15.7)	0.48
IVH volume , mean (SD), mL	7.1 (11.5)	8.7 (16.4)	0.52
Removal of > 85% IVH by EOT	87 (14.8)	3 (20.0)	0.58
Day 30 imaging characteristics			
ICH volume, mean (SD), mL [i]	4.7 (9.3)	1.8 (4.4)	0.30
Resolution of IVH [i]	502 (79.4)	12 (80.0)	0.96

Characteristic[a]	Patients included in analysis (n = 715)	Patients excluded due to missing mRS (n = 22)	*p*-value
Resolution of ICH [i]	327 (48.6)	8 (72.7)	0.11
Persistent Obstructive Hydrocephalus [i]	64 (9.3)	0 (0.0)	<0.001
In-hospital Events in first 30 days			
ICU and Physiologic Variables			
Admission Systolic BP, mean (SD), mm Hg	188.5 (36.2)	195.1 (34.0)	0.40
Admission Diastolic BP, mean (SD), mm Hg	105.0 (24.4)	112.2 (27.3)	0.17
Mechanical ventilation duration, mean (SD), days	7.5 (8.8)	7.2 (8.0)	0.88
ICU duration, mean (SD), days	16.5 (9.8)	14.2 (11.2)	0.27
Adverse events			
Ischemic Stroke	92 (12.9)	3 (13.6)	0.92
New symptomatic intracranial hemorrhage	14 (2.0)	2 (9.1)	0.02
Cardiac adverse events [j]	72 (10.1)	3 (10.7)	0.59
Acute respiratory distress syndrome	11 (1.5)	0 (0.0)	0.56
Pulmonary edema	28 (3.9)	1 (4.6)	0.88
Pulmonary adverse events [j]	267 (37.3)	7 (31.8)	0.60
Acute Kidney Injury	45 (6.3)	0 (0.0)	0.23
Venous Thromboembolism	71 (9.9)	2 (9.1)	0.90
Any infection	307 (42.9)	5 (22.7)	0.06
Urinary tract infection	84 (11.7)	1 (4.6)	0.30
Central Nervous system infection	41 (5.7)	0 (0.0)	0.25
Pneumonia	196 (27.4)	4 (18.2)	0.34
Sepsis	16 (2.2)	0 (0.0)	0.48
Interventions and Surgical Procedures in first 30 days			
Treatment assignment [k]	362 (50.6)	10 (45.5)	0.63
Ventriculo-peritoneal shunt placement	64 (9.0)	2 (7.1)	0.74
Gastrostomy tube placement	270 (37.8)	6 (27.3)	0.32
Withdrawal of Life Support	40 (5.6)	1 (4.6)	0.83

Abbreviations: ICH, Intracerebral Hemorrhage; IVH, Intraventricular Hemorrhage; mRS, modified Rankin Score; NIHSS, National Institute of Health Stroke Scale; BP, Blood Pressure; CPP, Cerebral Perfusion Pressure; ICP, Intracranial Pressure; ICU, Intensive Care Unit; SD, Standard Deviation; IQR, Interquartile Range;

[a] Unless otherwise indicated, data are expressed as number (percentage) of patients

[b] Scores range from 0 to 6, with higher scores indicating severe disability and death

[c] Scores range from 0 to 42, higher scores correlate with higher stroke severity; NIHSS was recorded at study enrollment and was not available for 27 CLEAR III patients

[d] Scores range from 3 to 15, with lower scores indicating coma; Glasgow Coma scale readings were recorded at study enrollment and were missing in 1 patient

[e] Hemispheric side of lesion was missing in 24 CLEAR-III patients because 17 patients had a primary IVH/periventricular bleed, 1 had infratentorial bleed; thus only 6 with a hemispheric basal ganglia hemorrhage had missing documentation on side of lesion

[f] ICH and IVH volume on admission were not available in 14 patients in MISTIE-III and 2 patients in CLEAR-III

[g] Midline shift parameters were not available in 79 patients in CLEAR-III and 85 patients in MISTIE-III

[h] Defined as a combined periventricular and deep white matter score of greater than 2 on Van Sweiten Score for CLEAR III and greater than 3 on Fazekas score for MISTIE III; White matter disease severity was not available in 45 patients in MISTIE III

[i] Resolution of IVH defined as modified Graeb Score of 0/IVH volume 0-mL and resolution of ICH defined as ICH volume of 0 mL on day 30 CT scan; IVH resolution data was missing in 83 patients; ICH resolution and day-30 hydrocephalus data was missing in 42 patients
[j] These were defined as any serious adverse events (SAR) involving the “respiratory system” and “cardiovascular system” in the prospectively adjudicated event reporting of the two trials
[k] Defined as Intraventricular thrombolysis with tissue plasminogen activator in CLEAR III and MISTIE surgery in MISTIE III
SI conversion factors: to convert mm to meters multiply by 10-3, to convert mL to Liters multiply by 10-3

eTable 3. Differences between patients that reported EQ-VAS versus those that did not report EQ-VAS

Characteristic[a]	EQ-VAS reported at day-30 (544)	EQ-VAS unreported at day-30 (171)	p-value	EQ-VAS reported at follow-up (only survivors)[a] (509)	EQ-VAS unreported at follow-up (only survivors)[a] (77)	p-value
Demographics						
Age, mean (SD), y	59.9 (11.7)	61.6 (11.6)	0.10	59.0 (11.4)	59.0 (10.7)	0.99
Male Sex, n (%)	319 (58.6)	98 (57.3)	0.76	307 (60.3)	48 (62.3)	0.74
Race						
Black	121 (22.3)	53 (31.0)	0.02	120 (23.6)	27 (35.5)	0.07
White	379 (69.8)	112 (65.5)		349 (68.6)	45 (59.2)	
Others [b]	43 (7.9)	6 (3.5)		40 (7.9)	4 (5.3)	
Hispanic Ethnicity	72 (13.2)	26 (15.2)	0.51	67 (13.2)	14 (18.2)	0.23
Trial						
CLEAR-III	241 (44.3)	98 (57.3)	0.003	227 (44.6)	35 (45.5)	0.89
MISTIE-III	303 (55.7)	73 (42.7)		282 (55.4)	42 (54.5)	
Medical Comorbidities, n (%)						
Hypertension	522 (96.0)	156 (91.2)	0.02	485 (95.3)	72 (93.5)	0.50
Congestive Heart Failure	17 (3.1)	6 (3.5)	0.80	17 (3.3)	0 (0.0)	0.10
Atrial Fibrillation	37 (6.8)	14 (8.2)	0.54	35 (6.9)	1 (1.3)	0.06
Coronary Artery Disease	35 (6.4)	18 (10.5)	0.08	36 (7.1)	0 (0.0)	0.02
Type 2 diabetes	117 (21.5)	29 (17.0)	0.20	98 (19.3)	12 (15.6)	0.44
Hyperlipidemia	173 (31.8)	42 (24.6)	0.07	156 (30.6)	13 (16.9)	0.01
Anticoagulation	36 (6.6)	16 (9.4)	0.23	34 (6.7)	3 (3.9)	0.35
Chronic Kidney Disease	32 (5.9)	9 (5.3)	0.76	28 (5.5)	3 (3.9)	0.56
Chronic Obstructive Pulmonary Disease	28 (5.1)	7 (4.1)	0.58	21 (4.1)	3 (3.9)	0.93
Clinical severity						
Enrollment NIHSS[c], median (IQR)	19 (15-24)	23.5 (18-35)	<0.001	19 (15-24)	25 (19-34)	<0.001
Enrollment GCS[d], median (IQR)	10 (8-13)	9 (7-11)	0.002	10 (8-13)	9 (7-10.5)	0.002
Radiologic Characteristics						
Admission Imaging Characteristics [e]						
Deep location of hematoma	436 (80.1)	142 (83.0)	0.40	409 (80.4)	67 (87.0)	0.16
Left Hemispheric lesion	268 (49.7)	85 (50.0)	0.95	240 (47.5)	47 (61.0)	0.03
ICH volume, mean (SD), mL [e]	28.2 (21.4)	26.5 (22.5)	0.37	27.9 (21.0)	30.3 (21.3)	0.35

Characteristic[a]	EQ-VAS reported at day-30 (544)	EQ-VAS unreported at day-30 (171)	p-value	EQ-VAS reported at follow-up (only survivors)[a] (509)	EQ-VAS unreported at follow-up (only survivors)[a] (77)	p-value
IVH volume, mean (SD), mL [e]	13.5 (18.5)	20.8 (22.2)	<0.001	13.9 (19.0)	13.5 (17.3)	0.88
Obstructive Hydrocephalus	191 (79.3)	88 (89.8)	0.02	181 (81.1)	27 (77.1)	0.59
Pineal gland shift, mean (SD), mm[f]	2.1 (2.02)	2.1 (2.31)	0.71	2.1 (2.1)	2.3 (2.4)	0.58
Severe Leukoariosis[g]	147 (29.0)	57 (35.0)	0.15	121 (25.5)	26 (36.6)	0.04
Stability Imaging Characteristics						
ICH volume, mean (SD), mL	31.2 (23.0)	28.7 (23.7)	0.22	30.9 (22.7)	31.9 (21.5)	0.71
IVH volume, mean (SD), mL	12.1 (16.0)	20.4 (21.7)	<0.001	12.5 (17.0)	12.8 (13.8)	0.91
End-of-Treatment (EOT) Imaging Characteristics						
ICH volume, mean (SD), mL	20.3 (18.4)	21.0 (20.8)	0.66	20.1 (18.5)	21.8 (18.6)	0.44
IVH volume, mean (SD), mL	6.0 (10.4)	10.6 (13.8)	<0.001	6.03 (10.3)	7.3 (14.8)	0.37
>85% IVH removal by EOT	53 (12.4)	19 (12.0)	0.91	62 (12.2)	10 (13.0)	0.84
Day 30 Imaging Characteristics[h]						
ICH volume, mean (SD), mL	4.7 (9.4)	4.8 (9.2)	0.91	4.7 (9.0)	5.0 (9.4)	0.75
Resolution of IVH [h]	404 (84.0)	98 (64.9)	<0.001	376 (83.6)	50 (74.6)	0.07
Resolution of ICH [h]	263 (50.7)	64 (41.6)	0.05	235 (48.0)	32 (47.8)	0.98
Persistent Hydrocephalus [h]	38 (7.3)	26 (16.9)	<0.001	40 (8.2)	8 (11.9)	0.30
Adverse Events						
Acute Ischemic stroke	68 (12.5)	24 (14.0)	0.60	61 (12.0)	10 (13.0)	0.80
New Symptomatic hemorrhage	10 (1.8)	4 (2.3)	0.68	8 (1.6)	3 (3.9)	0.16
Any cardiac adverse event [i]	52 (9.6)	20 (11.7)	0.42	48 (9.4)	8 (10.4)	0.79
Acute Respiratory Distress Syndrome	6 (1.1)	5 (2.9)	0.09	7 (1.4)	1 (1.3)	0.96
Pulmonary edema	19 (3.5)	9 (5.3)	0.30	17 (3.3)	3 (3.9)	0.80
Any Pulmonary adverse event [i]	198 (36.4)	69 (40.4)	0.35	186 (36.5)	23 (29.9)	0.26
Acute kidney injury	30 (5.5)	15 (8.8)	0.13	31 (6.1)	4 (5.2)	0.76
Venous thromboembolism	54 (9.9)	17 (9.9)	0.99	52 (10.2)	7 (9.1)	0.76
Any infection	216 (39.7)	91 (53.2)	0.002	213 (41.8)	29 (37.7)	0.49
Urinary Tract Infection	56 (10.3)	28 (16.4)	0.03	55 (10.8)	11 (14.3)	0.37
Central Nervous System infection	32 (5.9)	9 (5.3)	0.76	26 (5.1)	4 (5.2)	0.97

Characteristic[a]	EQ-VAS reported at day-30 (544)	EQ-VAS unreported at day-30 (171)	p-value	EQ-VAS reported at follow-up (only survivors)[a] (509)	EQ-VAS unreported at follow-up (only survivors)[a] (77)	p-value
Sepsis	12 (2.2)	4 (2.3)	0.92	11 (2.2)	0 (0.0)	0.19
Pneumonia	135 (24.8)	61 (35.7)	0.006	137 (26.9)	16 (20.8)	0.25
Procedures and Interventions in the first 30 days						
Ventriculo-peritoneal Shunt	45 (8.3)	19 (11.1)	0.26	44 (8.6)	4 (5.2)	0.30
Gastrostomy Tube placement	172 (31.6)	98 (57.3)	<0.001	167 (32.8)	38 (49.4)	0.005
Trial treatment assignment [j]	282 (51.8)	80 (46.8)	0.25	261 (51.3)	44 (57.1)	0.34
Mechanical Ventilation Duration, mean (SD), days	6.5 (8.0)	10.7 (10.4)	<0.001	6.6 (8.0)	8.6 (9.5)	0.05
Number of ICU days, mean (SD), days	15.7 (9.7)	19.1 (9.7)	<0.001	15.3 (8.2)	17.0 (8.5)	0.10
Modified Rankin Scores						
Day-0 mRS, median (IQR)	0 (0)	0 (0)	0.19	0 (0)	0 (0)	0.14
Day-30 mRS, median (IQR)	5 (4-5)	5 (5-5)	..	5 (4-5)	5 (5-5)	..
Day-180 mRS, median (IQR)	4 (3-5)	5 (4-5)	<0.001	4 (3-4)	4 (4-5)	<0.001
Day-365 mRS, median (IQR)	4 (3-4)	4 (4-6)	<0.001	3 (3-4)	4 (3-5)	<0.001

Abbreviations: CLEAR III, Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage phase 3 trial; MISTIE III, Minimally Invasive Surgery Plus Alteplase for Intracerebral Hemorrhage Evacuation phase 3 trial; ICH, Intracerebral Hemorrhage; IVH, Intraventricular Hemorrhage; mRS, modified Rankin Score; NIHSS, National Institute of Health Stroke Scale; BP, Blood Pressure; CPP, Cerebral Perfusion Pressure; ICP, Intracranial Pressure; ICU, Intensive Care Unit; SD, Standard Deviation; IQR, Interquartile Range

[a] All variables are represented as n and %, unless otherwise specified; Follow-up refers to day-180 and/or day-365; We included only survivors as patients that died by one-year were unable to report EQ-VAS due to their demise

[b] Asian, Native American, Pacific Islander

[c] Scores range from 0 to 42, higher scores correlate with higher stroke severity; NIHSS was recorded at study enrollment and was not available for 27 CLEAR III patients

[d] Scores range from 3 to 15, with lower scores indicating coma; Glasgow Coma scale readings were recorded at study enrollment

[e] ICH and IVH volume on admission were not available in 14 patients in MISTIE III and 2 patients in CLEAR III

[f] Midline shift parameters were not available in 79 patients in CLEAR III and 85 patients in MISTIE III

[g] Defined as a combined periventricular and deep white matter score of greater than 2 on Van Sweiten Score for CLEAR III and greater than 3 on Fazekas score for MISTIE III; White matter disease severity was not available in 45 patients in MISTIE III

[h] Day-30 CT IVH resolution defined as modified Graeb Score of 0 or IVH volume 0-mL and ICH resolution defined as ICH volume of 0 mL on day-30 CT scan; Day-30 CT IVH resolution data was missing in 13 CLEAR-III and 70 MISTIE-III patients; day-30 CT ICH volumes, ICH resolution and hydrocephalus data was missing in 16 CLEAR-III and 26 MISTIE-III patients

[i] These were defined as any serious adverse events (SAR) involving the “respiratory system” and “cardiovascular system” in the prospectively adjudicated event reporting of the two trials

[j] Defined as Intraventricular thrombolysis with tissue plasminogen activator in CLEAR III and MISTIE surgery in MISTIE III

SI conversion factors: to convert mm to meters multiply by 10^{-3}, to convert mL to Liters multiply by 10^{-3}

Discussion on missing EQ-VAS

There were several differences between patients that reported and did not report EQ-VAS scores as noted in the table above.

EQ-VAS reporting was much lower at day-30, and 171 (24%) patients had missing EQ-VAS at day-30. Patients that could not report EQ-VAS at day 30 were more likely to belong to the black race, had higher NIHSS, lower GCS and larger IVH volumes upon admission. In addition, these patients had lower likelihood of hematoma and IVH resolution by day-30, more likely to have a prolonged ICU stay, longer ventilator duration, hospital infections and need gastrostomy placement, indicating that their disease severity and complicated hospital course likely impeded their ability to report EQ-VAS scores at day-30.

However, many of these patients were eventually able to report EQ-VAS scores at a follow-up time-point (day-180 and/or day-365). After excluding 129 patients that died by one-year and thus could not report EQ-VAS, 77/586 (13.1%) survivors could not report EQ-VAS. Surviving patients that did not report EQ-VAS scores at a follow-up timepoint were more likely to have higher NIHSS, lower GCS, severe leukoariosis, left hemispheric lesions, longer ventilator support, gastrostomy and worse mRS. Baseline hematoma volumes did not seem to impact ability to report EQ-VAS at follow-up. Thus, in addition to higher clinical severity at baseline, poor cognitive and functional recovery, and aphasia may have contributed to inability to report EQ-VAS.

eTable 4. Differences between patients included and excluded from combined multivariable logistic regression model for primary outcome (mRS 0-3) due to missing data

Characteristic[a]	Patients included in MV model (n = 429)	Patients excluded in MV model due to missing data (n = 286)	*p*-value
Demographics			
Age, mean (SD), y	59.1 (11.5)	62.1 (11.8)	0.0008
Male Gender, n (%)	243 (56.6)	174 (60.8)	0.27
Medical Co-morbidities, n (%)			
Hypertension	414 (96.5)	264 (92.3)	0.01
Congestive Heart Failure	16 (3.7)	7 (2.5)	0.34
Atrial Fibrillation	28 (6.5)	23 (8.0)	0.44
Coronary Artery Disease	25 (5.8)	28 (9.8)	0.05
Type 2 diabetes	82 (19.11)	64 (22.4)	0.29
Hyperlipidemia	115 (26.8)	100 (35.0)	0.02
Chronic Anticoagulation Use	29 (6.8)	23 (8.0)	0.52
Chronic Kidney Disease	28 (6.5)	13 (4.6)	0.26
Chronic Obstructive Pulmonary Disease	15 (3.5)	20 (7.0)	0.03
Clinical severity			
Premorbid mRS[b], median (IQR)	0 (0)	0 (0)	0.50
Enrollment NIHSS[c], median (IQR)	20 (16-26)	19 (15-24)	0.55
Enrollment GCS[d], median (IQR)	10 (8-12)	10 (8-13)	0.45
Radiological Characteristics			
Baseline Imaging Characteristics			
Thalamic Location of ICH	144 (33.6)	82 (28.7)	0.17
Basal Ganglia location of ICH	192 (44.8)	127 (44.4)	0.93
Deep ICH location	361 (84.2)	217 (75.9)	0.006
Stability ICH volume, mean (SD), mL	29.2 (23.2)	32.8 (23.1)	0.04
Admission IVH-volume, mean(SD), mL[e] (n=270)	17.4 (20.9)	11.9 (17.2)	0.0003
Pineal shift, mean (SD), mm [f] (n=122)	2.1 (2.1)	2.2 (2.2)	0.53
Severe Leukoariosis [g] (n=241)	128 (29.8)	76 (31.5)	0.65
End-of-treatment (EOT) imaging characteristics			
ICH volume, mean (SD), mL	18.8 (18.8)	22.9 (19.1)	0.005
IVH volume , mean (SD), mL	8.2 (12.8)	5.3 (8.8)	0.0009
Removal of > 85% IVH by EOT	50 (11.7)	37 (12.9)	0.61
Day 30 imaging characteristics			
ICH volume, mean (SD), mL	4.6 (9.4)	4.9 (9.1)	0.30
Resolution of IVH [f]	340 (79.3)	162 (79.8)	0.87
Resolution of ICH [f]	219 (51.1)	108 (44.3)	0.09
Persistent Obstructive Hydrocephalus [f]	43 (10.0)	21 (8.6)	0.55

Characteristic[a]	Patients included in MV model (n = 429)	Patients excluded in MV model due to missing data (n = 286)	*p*-value
In-hospital Events in first 30 days			
ICU and Physiologic Variables			
Admission Systolic BP, mean (SD), mm Hg	191.96 (35.8)	183.2 (36.1)	0.002
Admission Diastolic BP, mean (SD), mm Hg	106.9 (24.6)	102.0 (23.8)	0.01
Mechanical ventilation duration, mean (SD), days	7.5 (8.8)	7.2 (8.0)	0.88
ICU duration, mean (SD), days	16.5 (9.8)	14.2 (11.2)	0.27
Adverse events			
Ischemic Stroke	58 (13.5)	34 (11.9)	0.52
New symptomatic intracranial hemorrhage	8 (1.9)	6 (2.1)	0.83
Cardiac adverse events [g]	35 (8.2)	37 (12.9)	0.04
Acute respiratory distress syndrome	5 (1.2)	6 (2.1)	0.32
Pulmonary edema	17 (3.96)	11 (3.9)	0.94
Pulmonary adverse events [g]	160 (37.3)	107 (37.4)	0.98
Acute Kidney Injury	32 (7.5)	13 (4.6)	0.12
Venous Thromboembolism	42 (9.8)	29 (10.1)	0.88
Any infection	192 (44.8)	115 (40.2)	0.23
Urinary tract infection	52 (12.1)	32 (11.2)	0.70
Central Nervous system infection	25 (5.8)	15 (5.6)	0.90
Pneumonia	119 (27.7)	77 (26.9)	0.81
Sepsis	11 (2.6)	5 (1.8)	0.47
Interventions and Surgical Procedures in first 30 days			
Treatment assignment [h]	211 (49.2)	144 (50.4)	0.90
Ventriculo-peritoneal shunt placement	44 (10.3)	220 (7.0)	0.13
Gastrostomy tube placement	174 (40.6)	96 (33.6)	0.06
Withdrawal of Life Support	17 (3.96)	23 (8.0)	0.02

Abbreviations: ICH, Intracerebral Hemorrhage; IVH, Intraventricular Hemorrhage; mRS, modified Rankin Score; NIHSS, National Institute of Health Stroke Scale; BP, Blood Pressure; CPP, Cerebral Perfusion Pressure; ICP, Intracranial Pressure; ICU, Intensive Care Unit; SD, Standard Deviation; IQR, Interquartile Range;

[a] Unless otherwise indicated, data are expressed as number (percentage) of patients

[b] Scores range from 0 to 6, with higher scores indicating severe disability and death

[c] Scores range from 0 to 42, higher scores correlate with higher stroke severity; NIHSS was recorded at study enrollment and was not available for 27 CLEAR III patients

[d] Scores range from 3 to 15, with lower scores indicating coma; Glasgow Coma scale readings were recorded at study enrollment and missing in 1 patient

[e] Admission IVH volume on admission were not available in 14 patients in MISTIE III and 2 patients in CLEAR III

[f] Pineal shift was not available in 79 CLEAR-III and 85 MISTIE-III patients

[g] Defined as a combined periventricular and deep white matter score of greater than 2 on Van Sweiten Score for CLEAR III and greater than 3 on Fazekas score for MISTIE III; White matter disease severity was not available in 45 patients in MISTIE III

[f] Resolution of IVH defined as modified Graeb Score of 0/IVH-volume of 0-mL and resolution of ICH defined as ICH volume of 0 mL on day 30 CT scan; Day-30 CT IVH resolution data was missing in 13 CLEAR-III and 70 MISTIE-III patients; day-30 CT ICH volumes, ICH resolution and hydrocephalus data was missing in 16 CLEAR-III and 26 MISTIE-III patients

[g] These were defined as any serious adverse events (SAR) involving the “respiratory system” and “cardiovascular system” in the prospectively adjudicated event reporting of the two trials

[h] Defined as Intraventricular thrombolysis with tissue plasminogen activator in CLEAR III and MISTIE surgery in MISTIE III
SI conversion factors: to convert mm to meters multiply by 10-3, to convert mL to Liters multiply by 10-3

eTable 5. Multivariable Logistic Regression Model for Factors Associated with Recovery to mRS 0-2 among Patients with mRS 3-5 at day-30

801 patients had mRS 3-5 at day-30; 167 (21%) recovered to mRS 0-2 by one-year.

Characteristics	Adjusted OR (95% CI)	P value
Factors predicting recovery to mRS 0-2 (n=646)		
Age, per y	0.93 (0.91-0.96)	<0.001
Male Sex	0.70 (0.43-1.14)	0.15
Race (Reference Group: White)		
Black	0.62 (0.33-1.14)	0.12
Others [a]	1.02 (0.41-2.57)	0.97
Hispanic Ethnicity	0.77 (0.37-1.61)	0.49
Type 2 diabetes	0.33 (0.15-0.71)	0.005
NIHSS (per 1-point increase) [b]	0.96 (0.93-0.99)	0.005
Severe Leukoariosis [c]	0.44 (0.24-0.81)	0.008
Deep Location of hematoma	0.28 (0.14-0.54)	<0.001
Left Hemispheric Lesion	0.49 (0.40-0.79)	0.004
ICH volume (per 1-mL increase)	0.96 (0.93-0.98)	<0.001
IVH volume (per 1-mL increase)	1.00 (0.98-1.02)	0.91
Acute Ischemic Stroke	0.08 (0.02-0.35)	0.001
Resolution of IVH by day-30 [d]	2.52 (1.11-5.74)	0.03
Mechanical Ventilator Duration (per day)	0.96 (0.92-1.00)	0.05
Need for Gastrostomy	0.49 (0.25-0.96)	0.04
Need for Ventriculoperitoneal Shunt	0.27 (0.10-0.75)	0.01
MISTIE vs. CLEAR-III trial group	1.55 (0.56-4.24)	0.40

[a] Asian, Native American, Pacific Islander

[b] NIHSS was missing in 31 patients

[c] van Swieten scale (vSS): CT grading scale for leukoariosis severity ranging from 0 to 4 (used in CLEAR-III); Fazekas scale (FS): MRI grading scale from leukoariosis severity ranging from 0 to 6, combining deep and periventricular regions (used in MISTIE-III); Severe Leukoariosis defined as total FS>3 and/or deep FS 2-3 for MISTIE-III and vSS $\geq$ 3 for CLEAR-III; FS was missing in 49 MISTIE-III patients

[d] Day-30 CT IVH resolution data was missing in 90 patients

eTable 6. Multivariable Logistic Regression Model for Factors Associated with Recovery of at least 1-point in mRS among Patients with mRS 1-5 at day-30

850 patients in the combined CLEAR-III and MISTIE-III cohorts survived with an mRS 1-5 at day-30. Of these, a total of 549 (64.5%) patients showed an improvement in mRS by one-year. 250 (29.4%) patients had a 2 or more point improvement in mRS, and 299 (35.2%) had a 1 point improvement in mRS. The median improvement in mRS between day-30 and day-365 (detla-mRS) for all patients with mRS 1-5 at day-30, was 1 (IQR, 0-2).

Characteristics	Adjusted OR (95% CI)	P value
Factors predicting any improvement in mRS (≥1-point) (n=693)		
Age, per y	0.95 (0.93-0.96)	<0.001
Male Sex	1.08 (0.75-1.53)	0.68
Race (Reference Group: White)		
Black	0.61 (0.40-0.94)	0.02
Others [a]	0.93 (0.46-1.88)	0.84
Hispanic Ethnicity	0.75 (0.44-1.28)	0.30
Type 2 diabetes	0.56 (0.36-0.87)	0.01
GCS (per 1-point increase) [b]	1.07 (1.01-1.13)	0.03
Severe Leukoariosis [c]	0.56 (0.40-0.85)	0.005
Thalamic Location of hematoma	0.76 (0.47-1.23)	0.27
Stability ICH volume (per 1-mL increase)	0.98 (0.97-0.99)	0.03
Acute Ischemic Stroke	0.66 (0.41-1.08)	0.09
Resolution of IVH by day-30 [d]	1.67 (1.03-2.71)	0.04
Resolution of ICH by day-30 [d]	0.67 (0.46-0.98)	0.04
Pulmonary Edema	0.47 (0.20-1.08)	0.07
MISTIE vs. CLEAR-III trial group	1.26 (0.58-2.76)	0.56

[a] Asian, Pacific Islander, Native American and others

[b] GCS was missing in 1 patient

[c] van Swieten scale (vSS): CT grading scale for leukoariosis severity ranging from 0 to 4 (used in CLEAR-III); Fazekas scale (FS): MRI grading scale from leukoariosis severity ranging from 0 to 6, combining deep and periventricular regions (used in MISTIE-III). Severe Leukoariosis defined as total FS>3 and/or deep FS 2-3 for MISTIE-III and vSS ≥ 3 for CLEAR-III FS was missing in 46 MISTIE-III patients

[d] Day-30 CT IVH resolution data was missing in 97 patients and day-30 CT ICH resolution data was missing in additional 25 patients

eTable 7. Multivariable Logistic Regression Models Using Other mRS-Dichotomizations for ICH/IVH survivors with mRS 4-5 at day-30

Characteristics	Adjusted OR (95% CI)	P value
A. Recovery to mRS 0-2 (n=568)		
Age, per y	0.94 (0.92-0.97)	<0.001
Male Sex	0.87 (0.51-1.46)	0.59
Race (Reference Group: White)		
Black	0.44 (0.22-0.90)	0.02
Others [a]	1.50 (0.58-3.90)	0.41
Hispanic Ethnicity	0.75 (0.35-1.63)	0.47
Deep Location of hematoma	0.31 (0.15-0.67)	0.003
Type 2 diabetes	0.34 (0.13-0.86)	0.02
GCS (per 1-point increase) [b]	0.98 (0.89-1.08)	0.65
Severe Leukoariosis [c]	0.40 (0.20-0.81)	0.01
Admission IVH volume (per 1-mL increase) [d]	1.00 (0.98-1.02)	0.95
Stability ICH volume (per 1-mL increase)	0.97 (0.95-0.98)	<0.001
Acute Ischemic Stroke	1.28 (0.60-2.73)	0.54
Resolution of IVH by day-30 [e]	2.55 (1.16-5.63)	0.02
Resolution of ICH by day-30 [e]	1.17 (0.67-2.05)	0.59
Persistent Hydrocephalus on day-30 [e]	1.24 (0.50-3.06)	0.70
Gastrostomy placement	0.50 (0.26-0.95)	0.03
Mechanical Ventilation Duration (per 1-day increase)	0.95 (0.91-0.99)	0.04
MISTIE vs. CLEAR-III trial group	1.05 (0.34-3.31)	0.93
B. mRS improvement ≥2-points (n=450)		
Age, per y	0.94 (0.92-0.97)	<0.001
Male Sex	1.17 (0.74-1.88)	0.49
Race (Reference Group: White)		
Black	0.57 (0.31-1.02)	0.06
Others [a]	1.09 (0.43-2.78)	0.86
Hispanic Ethnicity	0.59 (0.30-1.17)	0.13
Deep Location of hematoma	0.28 (0.13-0.58)	0.001
Type 2 diabetes	0.51 (0.26-1.00)	0.05
GCS (per 1-point increase) [b]	1.03 (0.95-1.13)	0.45
Severe Leukoariosis [c]	0.41 (0.23-0.73)	0.01
Stability ICH volume (per 1-mL increase)	0.97 (0.95-0.99)	0.006

Characteristics	Adjusted OR (95% CI)	P value
Admission IVH volume (per 1-mL increase) [d]	0.99 (0.97-1.01)	0.25
Pineal Gland Shift (per 1-mm increase) [f]	0.85 (0.75-0.97)	0.01
Acute Ischemic Stroke	0.77 (0.35-1.66)	0.50
Resolution of IVH by day-30 [e]	2.44 (1.23-4.86)	0.01
Resolution of ICH by day-30 [e]	1.07 (0.65-1.76)	0.78
Persistent Hydrocephalus on day-30 [e]	0.49 (0.20-1.18)	0.11
Gastrostomy Placement	0.61 (0.37-1.00)	0.05
Mechanical Ventilation Duration	1.00 (0.97-1.03)	0.78
MISTIE vs. CLEAR-III trial group	0.78 (0.29-2.08)	0.62
C. Any improvement in mRS (≥1-point) (n=568)		
Age, per y	0.93 (0.91-0.95)	<0.001
Male Sex	1.37 (0.91-2.06)	0.13
Race (reference group: White)		
Black	0.57 (0.34-0.93)	0.03
Others [a]	1.28 (0.53-3.04)	0.58
Hispanic Ethnicity	0.60 (0.33-1.09)	0.09
Type 2 Diabetes Mellitus	0.63 (0.38-1.03)	0.07
GCS (per 1-point increase) [b]	1.09 (1.02-1.17)	0.01
Severe Leukoariosis [c]	0.46 (0.30-0.71)	<0.001
Admission IVH volume (per 1-mL increase) [d]	0.99 (0.98-1.00)	0.11
Stability ICH volume (per 1-mL increase)	0.97 (0.96-0.99)	0.001
Deep ICH location	0.60 (0.33-1.09)	0.09
Acute Ischemic Stroke	0.62 (0.35-1.08)	0.09
Resolution of IVH by day-30 [e]	1.72 (1.00-2.99)	0.05
Resolution of ICH by day-30 [e]	0.79 (0.52-1.21)	0.27
Gastrostomy Placement	0.68 (0.45-1.03)	0.07

[a] Asian, Native American, Pacific Islander

[b] GCS was missing in 1 CLEAR-III patient

[c] van Swieten scale (vSS): CT grading scale for leukoariosis severity ranging from 0 to 4 (used in CLEAR-III); Fazekas scale (FS): MRI grading scale from leukoariosis severity ranging from 0 to 6, combining deep and periventricular regions (used in MISTIE-III). Severe Leukoariosis defined as total FS>3 and/or deep FS 2-3 for MISTIE-III and vSS ≥ 3 for CLEAR-III; FS was missing in 45 MISTIE-III patients

[d] Admission IVH volume was not available in 2 CLEAR-III and 13 MISTIE-III patients

[e] Day-30 CT IVH resolution data was missing in 83 patients, and other day-30 CT ICH resolution was missing in 42 patients
[f] Pineal Gland Shift data was missing 79 CLEAR-III and 85 MISTIE-III patients

eTable 8. Cox Proportional Hazards Regression Models Predicting One-Year All-Cause Mortality Among ICH/IVH survivors with Poor Day-30 Outcome

Characteristic [a]	**HR (95% CI)**	***p*-value**
One-Year Mortality (n = 587, no. of failures = 129 [b])		
Age, per y	1.05 (1.03-1.08)	<0.001
Male Sex	0.63 (0.43-0.94)	0.02
Race (Reference group: White)		
Black	0.97 (0.58-1.61)	0.90
Others [c]	0.60 (0.24-1.53)	0.23
Hispanic Ethnicity	1.42 (0.79-2.58)	0.25
Glasgow Coma Scale, per 1-point	0.89 (0.83-0.95)	<0.001
ICH volume, per 1-mL	1.00 (0.99-1.01)	0.91
Deep ICH location	0.76 (0.43-1.31)	0.32
Type-2 Diabetes	1.75 (1.09-2.79)	0.02
Severe Leukoariosis [d]	1.94 (1.30-2.92)	0.001
Pulmonary edema	3.04 (1.44-6.42)	0.004
Sepsis	2.88 (1.02-8.09)	0.04
Resolution of IVH by day-30 [e]	0.43 (0.27-0.69)	0.001

Abbreviations: ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage

[a] Test for proportional hazards assumption was not significant for the full model (p=0.06)

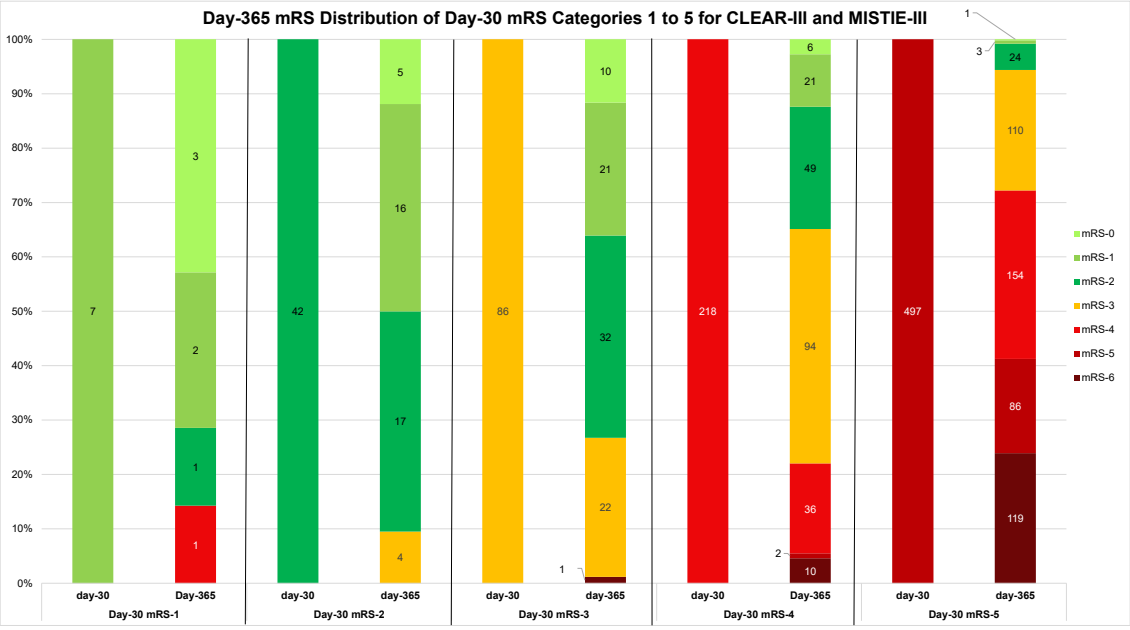
[b] 40 patients died due to WLST. 45 patients had missing leukoariosis data. 83 patients had missing day-30 CT IVH resolution data, 16 patients had missing ICH volumes and 1 had missing GCS.

[c] Asian, Native American, Pacific Islander

[d] Defined as a combined periventricular and deep white matter score of greater than 2 on Van Sweiten Score for CLEAR III and greater than 3 on Fazekas score for MISTIE III; White matter disease severity was not available in 45 patients in MISTIE III

[e] Day-30 CT IVH resolution data was missing in 83 patients

eFigure 1. Distribution of patients in each day-365 mRS category for all CLEAR-III and MISTIE-III Survivors at day-30

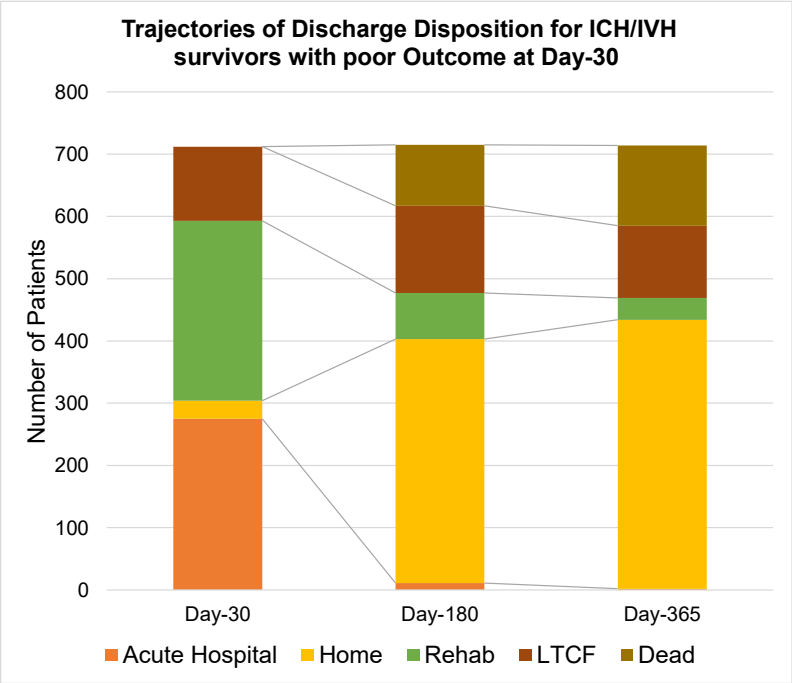


Legend:
Above figure shows how all the day-30 survivors (mRS 1-5) in the combined CLEAR-III and MISTIE-III cohort changed their mRS by day-365. In each panel, the left column shows the number of patients in each day-30 mRS category and the right column shows their mRS distribution at day-365. Green bars represent patients with mRS 0-2, yellow bar represents patients with mRS-3, red bars represent mRS 4-6.

Abbreviations:
mRS, modified Rankin score

eFigure 2. Home Discharge and Discharge Disposition Over One-Year

By one-year, 201/339 (59.2%) CLEAR-III patients and 261/376 (69.4%) MISTIE-III patients returned home at a median of 75 (IQR, 50-134) and 69 (IQR, 46-122) days post-ictus, respectively *(Figure-3)*. Among 308 patients with good-outcome at one-year, 294 (95.4%) returned home, as did 168/407 (41.2%) with poor one-year mRS (mRS-4, 119/190 [62.6%]; mRS-5, 29/88 [33%]). In time-to-event analysis, median time-to-home for the full cohort of patients was 98 (IQR, 52-302) days, for good one-year outcome group was 63 (IQR, 43-108) days, and for poor one-year outcome group was 214 days (IQR, 25th: 86; 75th: could not be computed as <75% returned home). Good one-year outcome patients spent a median of 303.5 (IQR, 264-323) days at home, whereas those with poor one-year outcome spent a median of 233 (IQR, 147-293) days at home. After home-discharge, five patients returned to an acute hospital-setting, six returned to a long-term care facility (LTCF), two to a rehabilitation facility and 19 died within the first-year post-ictus. All but one of these patients had poor mRS at one-year. Discharge disposition trajectories are shown in the figure below.

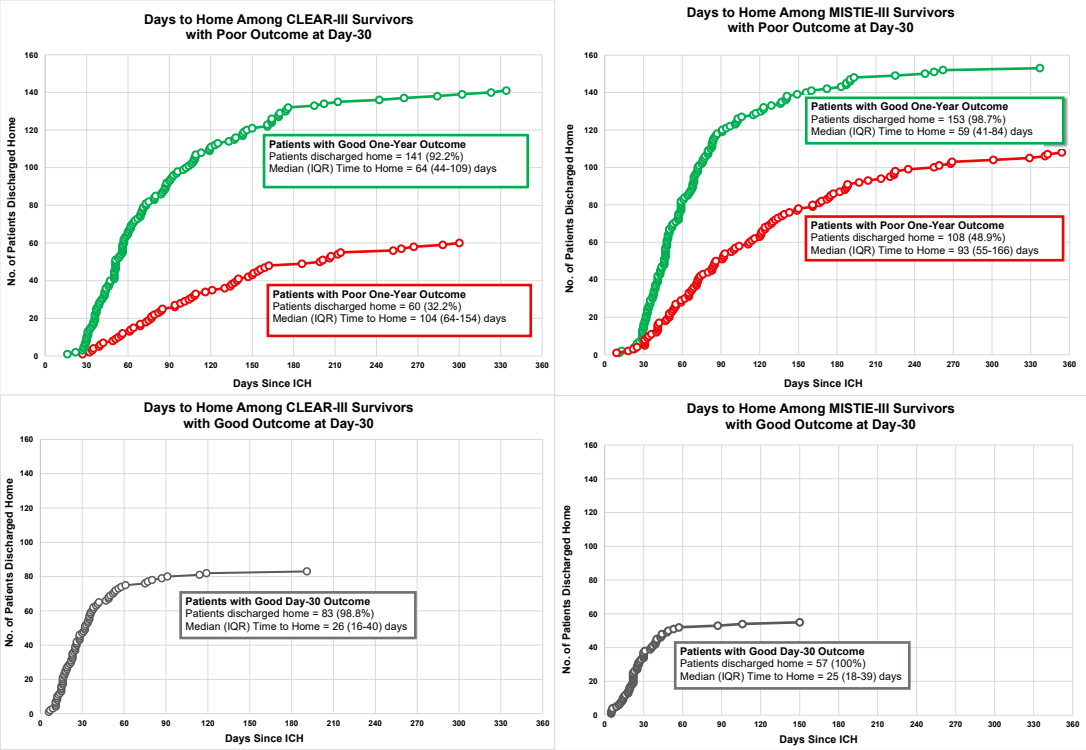


Legend:

This figure shows distribution of patient dispositions at Day-30, 180 and 365 from ictus among CLEAR-III and MISTIE-III subjects.

Abbreviations: IVH, Intraventricular Hemorrhage; ICH, Intracerebral Hemorrhage; CLEAR-III, Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage phase 3 trial; MISTIE-III, Minimally Invasive Surgery Plus Alteplase for Intracerebral Hemorrhage Evacuation phase 3 trial; Rehab, Rehabilitation facility; LTCF, Long Term Care Facility.

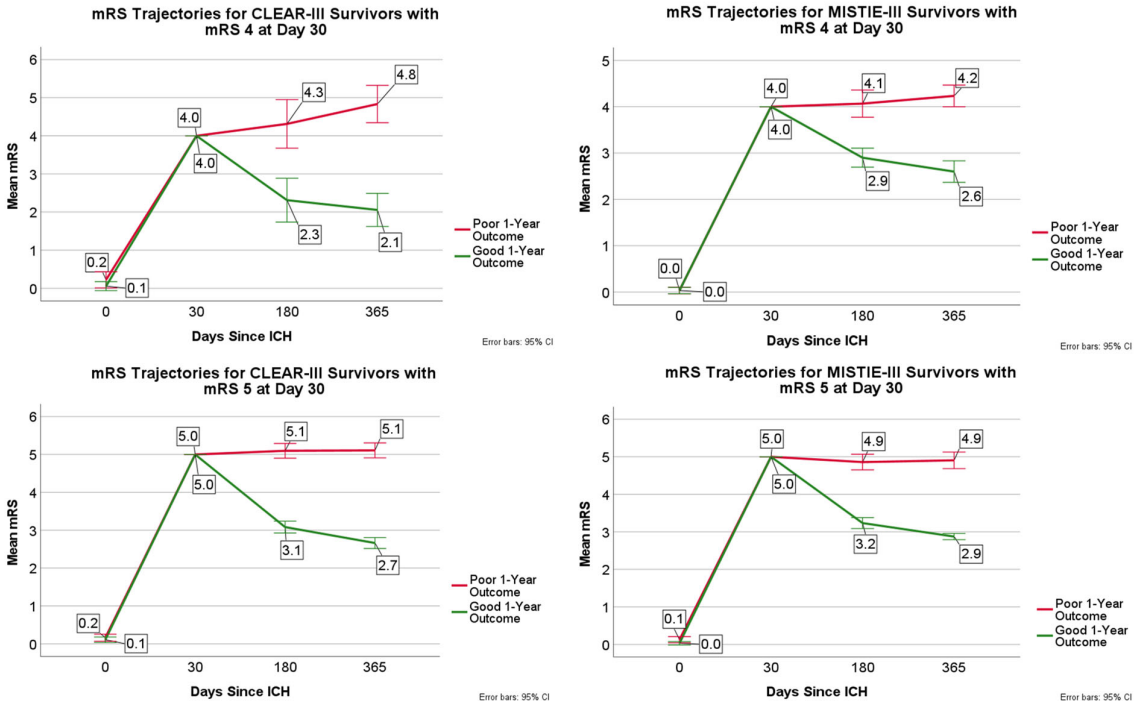
eFigure 3. Time to Home among CLEAR-III and MISTIE-III Patients with Poor-Outcome at Day-30



Legend:
Top two panels show the cumulative number of patients discharged home over the course of 1-year for CLEAR-III (left) and MISTIE-III (right) patients; Green-lines denote patients with good-outcome at one-year and red-lines denote patients with persistent poor-outcome at one-year. Bottom two-panels show the cumulative number of patients with good outcome at day-30 discharged home over the course of 1-year in CLEAR-III and MISTIE-III.

Abbreviations: mRS, modified Rankin Score; EQ-VAS, EuroQol Visual Analog Scale; IVH, Intraventricular Hemorrhage; ICH, Intracerebral Hemorrhage; CLEAR-III, Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage phase 3 trial; MISTIE-III, Minimally Invasive Surgery Plus Alteplase for Intracerebral Hemorrhage Evacuation phase 3 trial.

eFigure 4. Modified Rankin Scale (mRS) trajectories among patients with mRS 4 versus mRS 5 at day-30

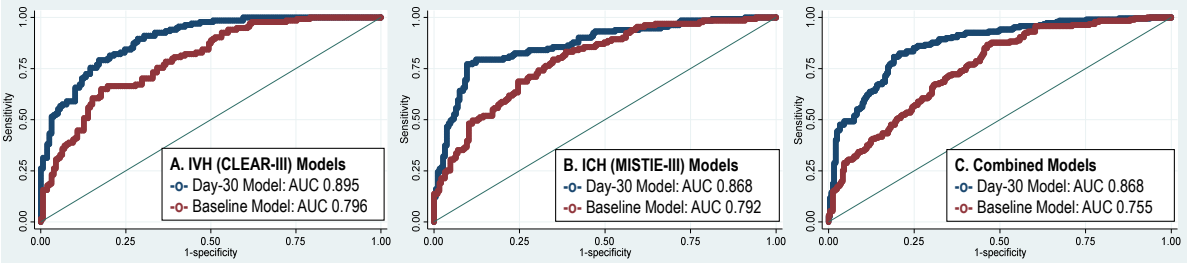


Legend:

Panel a shows mRS Trajectories for mRS 4 patients in CLEAR-III and MISTIE-III trials over the course of 1-year; Panel b shows mRS Trajectories for mRS 5 patients in CLEAR-III and MISTIE-III trials over the course of 1-year; Panel c and d show number of patients shifting their mRS upwards or downwards between day-30 and day-365 in CLEAR-III and MISTIEIII trials respectively (higher thickness of arrows indicates higher number of patients).

Abbreviations: mRS, modified Rankin Score; IVH, Intraventricular Hemorrhage; ICH, Intracerebral Hemorrhage; CLEAR-III, Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage phase 3 trial; MISTIE-III, Minimally Invasive Surgery Plus Alteplase for Intracerebral Hemorrhage Evacuation phase 3 trial.

eFigure 5. Receiver Operator Curves (ROC) and Area-Under-the-Curve (AUC) for day-30 models versus baseline models



Legend:

Panel A shows ROC and AUC for CLEAR-III models; Panel B shows ROC and AUC for MISTIE-III models and Panel C shows ROC and AUC for combined models

Sensitivity Analysis: missing Day-30 mRS

Thirteen patients had missing a mRS outcome at day-30. We conducted sensitivity analyses to assess the impact of missing day-30 mRS on our multivariable regression models. In these analyses, we assumed that at least some of these patients would have an mRS of 4-5 at day-30, and based our assumptions on their final one-year outcome. Five patients had missing a mRS value at one-year, thus we could not make any assumptions about their baseline mRS and we therefore excluded these patients from sensitivity analyses. Three patients had an mRS outcome of 1 or 2 at one-year; therefore, we did not think it appropriate to assume these patients had an mRS of 4-5 at day-30. Five remaining patients had mRS outcome of 3-6 at day-30; we therefore assumed these patients had an mRS of 4-5 at day-30 in our sensitivity analyses. Our regression models did not change significantly after inclusion of these patients in the sensitivity analysis.

eTable 9. Sensitivity Analysis for missing Day-30 mRS

Characteristics	Adjusted OR (95% CI)	P value
One-Year Good Outcome (mRS0-3) (n=431)		
Age, per y	0.92 (0.90-0.95)	<0.001
Male Sex	1.26 (0.76-2.11)	0.37
Race (Reference Group: White)		
Black	0.69 (0.37-1.30)	0.25
Others [a]	1.18 (0.41-3.40)	0.75
Hispanic Ethnicity	0.74 (0.37-1.47)	0.39
Deep Location of hematoma	0.10 (0.04-0.23)	<0.001
Type 2 diabetes	0.50 (0.26-0.96)	0.04
NIHSS (per 1-point increase) [b]	0.94 (0.91-0.96)	<0.001
Severe Leukoariosis [c]	0.36 (0.20-0.63)	<0.001
Admission IVH volume (per 1-mL increase) [d]	0.98 (0.96-0.99)	0.04
Stability ICH volume (per 1-mL increase)	0.96 (0.94-0.98)	<0.001
Pineal gland shift (per 1-mm increase) [e]	0.88 (0.77-0.99)	0.05
Acute Ischemic Stroke	0.44 (0.20-0.93)	0.03
Resolution of IVH by day-30 [f]	2.11 (1.00-4.49)	0.05
Resolution of ICH by day-30 [f]	1.85 (1.10-3.10)	0.02
Persistent Hydrocephalus on day-30 [f]	0.37 (0.14-0.98)	0.04
Gastrostomy placement	0.29 (0.17-0.49)	<0.001
MISTIE vs. CLEAR-III trial group	0.86 (0.31-2.38)	0.77

[a] Asian, Native American, Pacific Islander

[b] NIHSS was missing 27 CLEAR-III patients

[c] van Swieten scale (vSS): CT grading scale for leukoariosis severity ranging from 0 to 4 (used in CLEAR-III); Fazekas scale (FS): MRI grading scale from leukoariosis severity ranging from 0 to 6, combining deep and periventricular regions (used in MISTIE-III). Severe Leukoariosis defined as total FS>3 and/or deep FS 2-3 for MISTIE-III and vSS $\geq$ 3 for CLEAR-III; FS was missing in 45 MISTIE-III patients

[d] Admission IVH volume was not available in 2 CLEAR-III and 14 MISTIE-III patients

[e] Pineal Gland Shift data was missing 79 CLEAR-III and 85 MISTIE-III patients

[f] Day-30 CT IVH resolution data was missing in 86 patients, and other day-30 CT ICH resolution was missing in 45 patients

Sensitivity Analysis: missing mRS at One-Year

Nine patients had missing outcome data at one-year. We conducted two sensitivity analyses to assess impact of missing one-year outcome data. In the first model **(eTable 10-A)** we assumed that all 9 patients had good-outcome at one-year. Resolution of IVH by day-30 continued to demonstrate a trend towards recovery to good outcome, but was no longer statistically significant (p=0.09). The significance of the adjusted odds ratios for all other variables remained essentially unchanged under the assumptions of this sensitivity analysis. In the second model **(eTable 10-B)** we assumed that all 9 patients had a poor-outcome at one-year. Resolution of IVH/ICH on day-30 imaging continued to show a trend towards recovery to good outcome, but was no longer statistically significant under this sensitivity analysis (p=0.07); pineal shift and persistent hydrocephalus on day-30 imaging showed trend towards lack of recovery, but were no longer statistically significant in this sensitivity analysis (p=0.07-0.08).

eTable 10. Sensitivity Analysis for missing One-Year mRS
(Models predicting good One-Year Outcome [mRS 0-3])

Characteristics	Adjusted OR (95% CI)	P value
A. Assuming all patients with missing one-year mRS had good one-year outcome (n=435)		
Age, per y	0.92 (0.89-0.94)	<0.001
Male Sex	1.33 (0.80-2.23)	0.27
Race (Reference Group: White)		
Black	0.69 (0.37-1.28)	0.24
Others [a]	1.16 (0.40-3.36)	0.78
Hispanic Ethnicity	0.73 (0.36-1.45)	0.36
Deep Location of hematoma	0.09 (0.04-0.21)	<0.001
Type 2 diabetes	0.49 (0.25-0.96)	0.03
NIHSS (per 1-point increase) [b]	0.93 (0.91-0.96)	<0.001
Severe Leukoariosis [c]	0.33 (0.20-0.63)	<0.001
Admission IVH volume (per 1-mL increase) [d]	0.98 (0.96-0.99)	0.05
Stability ICH volume (per 1-mL increase)	0.96 (0.94-0.98)	0.001
Pineal gland shift (per 1-mm increase) [e]	0.86 (0.75-0.98)	0.02
Acute Ischemic Stroke	0.45 (0.21-0.95)	0.04
Resolution of IVH by day-30 [f]	1.93 (0.91-4.06)	0.09
Resolution of ICH by day-30 [f]	1.87 (1.11-3.13)	0.04
Persistent Hydrocephalus on day-30 [f]	0.35 (0.13-0.94)	0.04
Gastrostomy placement	0.30 (0.18-0.51)	<0.001
MISTIE vs. CLEAR-III trial group	0.88 (0.32-2.44)	0.80
B. Assuming all patients with missing one-year mRS had poor one-year outcome (n=435)		
Age, per y	0.93 (0.91-0.96)	<0.001
Male Sex	1.27 (0.77-2.08)	0.35
Race (Reference Group: White)		
Black	0.66 (0.35-1.21)	0.18

Characteristics	Adjusted OR (95% CI)	P value
Others [a]	1.28 (0.46-3.56)	0.64
Hispanic Ethnicity	0.80 (0.40-1.57)	0.51
Deep Location of hematoma	0.11 (0.05-0.26)	<0.001
Type 2 diabetes	0.54 (0.28-1.03)	0.06
NIHSS (per 1-point increase) [b]	0.94 (0.91-0.96)	<0.001
Severe Leukoariosis [c]	0.37 (0.21-0.65)	<0.001
Admission IVH volume (per 1-mL increase) [d]	0.98 (0.96-1.00)	0.10
Stability ICH volume (per 1-mL increase)	0.96 (0.94-0.99)	0.001
Pineal gland shift (per 1-mm increase) [e]	0.89 (0.78-1.00)	0.07
Acute Ischemic Stroke	0.42 (0.20-0.89)	0.02
Resolution of IVH by day-30 [f]	1.98 (0.95-4.13)	0.07
Resolution of ICH by day-30 [f]	1.60 (0.96-2.64)	0.07
Persistent Hydrocephalus on day-30 [f]	0.43 (0.17-1.10)	0.08
Gastrostomy placement	0.29 (0.17-0.48)	<0.001
MISTIE vs. CLEAR-III trial group	1.09 (0.40-2.95)	0.97

[a] Asian, Native American, Pacific Islander

[b] NIHSS was missing 27 CLEAR-III patients

[c] van Swieten scale (vSS): CT grading scale for leukoariosis severity ranging from 0 to 4 (used in CLEAR-III); Fazekas scale (FS): MRI grading scale from leukoariosis severity ranging from 0 to 6, combining deep and periventricular regions (used in MISTIE-III). Severe Leukoariosis defined as total FS>3 and/or deep FS 2-3 for MISTIE-III and vSS $\geq$ 3 for CLEAR-III; FS was missing in 44 MISTIE-III patients

[d] Admission IVH volume was not available in 2 CLEAR-III and 14 MISTIE-III patients

[e] Day-30 CT IVH resolution data was missing in 83 patients, and other day-30 CT ICH resolution was missing in 45 patients

[f] Pineal Gland Shift data was missing 79 CLEAR-III and 86 MISTIE-III patients

Sensitivity Analysis: Missing Data-Points

286 patients were initially excluded from multivariable logistic regression analysis for the combined CLEAR-III and MISTIE-III cohort due to missing data-points. We conducted a sensitivity analysis to assess the impact of missing data-points on the combined multivariable model for primary outcome (mRS 0-3). To include all patients in the models, we created an additional category for missing data for the categorical variables that had missing data-points (severe leukoariosis, resolution of IVH/ICH and persistent hydrocephalus at day-30). For continuous variables with missing data-points (NIHSS, admission IVH volume, pineal shift), we first converted them into categorical variables by dichotomizing them by the median value and subsequently created an additional category for missing data. In the final model that included all patients (1 excluded due to missing race), admission IVH volume and pineal shift were no longer significant; but all other variables remained independently associated with outcome. In addition, mechanical ventilation was an additional variable that was now independently associated with poor one-year outcome in the combined model.

eTable 11. Sensitivity Analysis for Missing Data-Points in Combined Model for Good One-Year Outcome

Characteristics	Adjusted OR (95% CI)	P value
One-Year Good Outcome (mRS0-3) (n=714)		
Age, per y	0.93 (0.91-0.95)	<0.001
Male Sex	1.39 (0.94-2.06)	0.09
Race (Reference Group: White)		
Black	0.97 (0.60-1.58)	0.91
Others [a]	1.73 (0.73-4.12)	0.21
Hispanic Ethnicity	0.78 (0.45-1.36)	0.38
Deep Location of hematoma	0.20 (0.11-0.36)	<0.001
Type 2 diabetes	0.55 (0.34-0.89)	0.02
NIHSS ≥ 20 [b]	0.47 (0.32-0.70)	<0.001
Severe Leukoariosis [c]	0.29 (0.19-0.46)	<0.001
Admission IVH volume ≥ 6.5 mL [d]	0.99 (0.51-1.93)	0.99
Stability ICH volume (per 1-mL increase)	0.97 (0.95-0.98)	<0.001
Pineal gland shift ≥ 2.01 mm [e]	0.75 (0.48-1.15)	0.19
Acute Ischemic Stroke	0.58 (0.33-1.03)	0.06
Resolution of IVH by day-30 [f]	2.45 (1.37-4.38)	0.003
Resolution of ICH by day-30 [f]	1.76 (1.18-2.64)	0.006
Persistent Hydrocephalus on day-30 [f]	0.46 (0.21-0.99)	0.05
Gastrostomy placement	0.45 (0.30-0.67)	<0.001
Mechanical Ventilator Duration (per day)	0.94 (0.92-0.97)	<0.001
MISTIE vs. CLEAR-III trial group	1.30 (0.55-3.06)	0.55

[a] Asian, Native American, Pacific Islander

[b] NIHSS missing in 27 patients; It was dichotomized based on median value of 20; patients were divided into 3 categories: <20, ≥20, and patients with missing NIHSS

[c] van Swieten scale (vSS): CT grading scale for leukoariosis severity ranging from 0 to 4 (used in CLEAR-III); Fazekas scale (FS): MRI grading scale from leukoariosis severity ranging from 0 to 6, combining deep and periventricular regions (used in

MISTIE-III). Severe Leukoariosis defined as total FS>3 and/or deep FS 2-3 for MISTIE-III and vSS ≥ 3 for CLEAR-III; FS was missing in 45 MISTIE-III patients
[d] Admission IVH volume was not available in 2 CLEAR-III and 13 MISTIE-III patients; thus admission IVH volume was dichotomized based on median value of 6.50 mL into 3 categories: <6.50 mL, ≥6.50 mL and missing adm IVH volume
[e] Pineal Gland Shift data was missing 79 CLEAR-III and 85 MISTIE-III patients; thus patients were dichotomized based on median pineal gland shift of 2.01 mm; <2.01, ≥2.01, missing pineal shift
[f] Day-30 CT IVH resolution data was missing in 83 patients, and other day-30 CT ICH resolution was missing in 45 patients

eTable 12. Sensitivity Analysis for Missing Data-Points in Cox Regression Models for One-Year Mortality

Characteristic [a]	HR (95% CI)	*p*-value
One-Year Mortality (n = 713, no. of failures = 129[b])		
Age, per y	1.05 (1.03-1.07)	<0.001
Male Sex	0.60 (0.42-0.87)	0.006
Race (Reference group: White)		
Black	0.74 (0.46-1.18)	0.21
Others [c]	0.48 (0.19-1.21)	0.12
Hispanic Ethnicity	1.17 (0.69-2.01)	0.56
Glasgow Coma Scale, per 1-point	0.91 (0.86-0.97)	0.002
ICH volume, per 1-mL	1.01 (0.99-1.02)	0.12
Admission IVH volume $\geq$ 6.5 mL [d]	2.64 (1.54-4.52)	<0.001
Deep ICH location	0.80 (0.49-1.32)	0.39
Type-2 Diabetes	1.86 (1.21-2.86)	0.004
Severe Leukoariosis [e]	1.87 (1.28-2.75)	0.001
Pulmonary edema	2.26 (1.08-4.74)	0.03
Sepsis	2.83 (1.13-7.10)	0.03
Resolution of IVH by day-30 [f]	0.63 (0.39-0.99)	0.05

Abbreviations: ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage

[a] Test for proportional hazards assumption was not significant for the full model (p=0.06)

[b] 40 patients died due to WLST. 45 patients had missing leukoariosis data. 83 patients had missing day-30 CT IVH resolution data, 16 patients had missing ICH volumes and 1 had missing GCS.

[c] Asian, Native American, Pacific Islander

[d] admission IVH volume was not available in 15 patients; all patients were included by dichotomizing by median IVH volume of 6.5 mL and an additional category for missing data was created

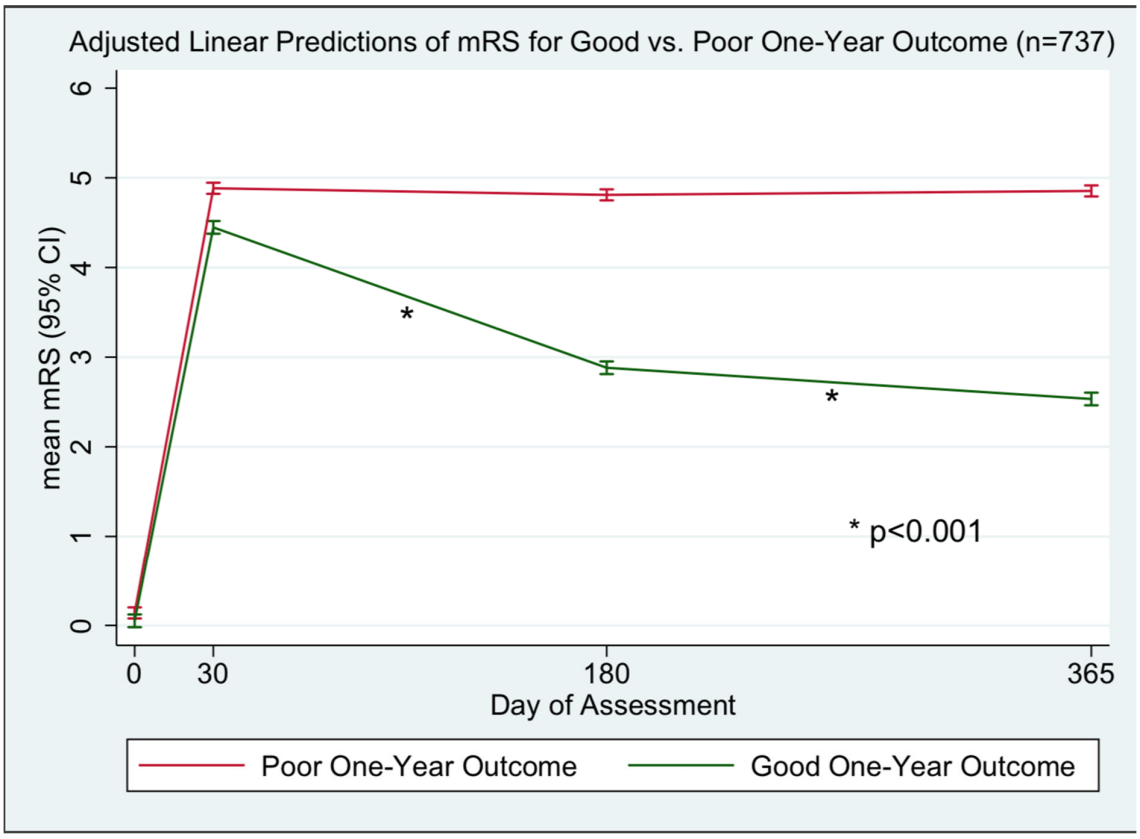
[e] Defined as a combined periventricular and deep white matter score of greater than 2 on Van Sweiten Score for CLEAR III and greater than 3 on Fazekas score for MISTIE III; White matter disease severity was not available in 45 patients in MISTIE III; all patients were included by creating a category for missing data

[f] Day-30 CT IVH resolution data was missing in 83 patients; all patients were included by creating a category for missing data

eFigure 6. Sensitivity Analysis for mRS Trajectories

The day-30 mRS endpoint was missing for 13 patients in combined MISTIE-III and CLEAR-III cohort. Additionally, among patients with mRS 4-5 or missing mRS at day-30 (n=737), mRS was missing for 13 patients at day-180 and for 14 patients at day-365. We conducted sensitivity analysis to assess the impact of missing mRS data at various time-points on the predicted trajectories of mRS over one-year. In this analysis, we included all patients with mRS 4-5 at day-30 as well as those with missing mRS at day-30 (n=737). Mixed effects linear regression models were used to obtain adjusted linear predictions of mRS over one-year, treating mRS as the outcome, day-of-assessment (day-30, 180, 365) as a fixed effect, and study subjects as random effects. Mixed linear models would account for missing mRS data due to lost to follow-up that is missing at random. In addition, to account for intermittently missing mRS data, i.e. patients with mRS recorded at day-30 and day-365, but not at day-180 (n=4), we assumed that day-180 mRS was the same as day-30 mRS (i.e., last observation carried forward), and re-computed the models. There was no significant change in mean mRS at serial time-points after the imputation using last observation carried forward of these missing data-points.

Day of Assessment	Mean mRS (95% CI)		*p*-value
	Good Outcome	Poor Outcome	
Day-30	4.5 (4.4-4.5)	4.9 (4.8-5.0)	<0.001
Day-180	2.9 (2.8-3.0)	4.8 (4.7-4.9)	<0.001
Day-365	2.5 (2.4-2.6)	4.9 (4.8-4.9)	<0.001



eFigure 7. Sensitivity Analysis for EQ-VAS Trajectories

As discussed, EQ-VAS was missing in multiple patients at various time-points. These patients with missing EQ-VAS data had an overall worse clinical trajectory, suggesting that these patients may not have reported EQ-VAS due to their poor clinical status. We conducted a sensitivity analysis to assess the impact of missing data on the predicted EQ-VAS trajectories over one-year. In this analysis, we included all patients with mRS 4-5 at day-30 as well as those with missing mRS data at day-30 and one-year. Mixed effects linear regression models were used to obtain adjusted linear predictions of EQ-VAS over one-year, treating EQ-VAS as the outcome, day-of-assessment (day-30, 180, 365) as a fixed effect, and study subjects as random effects. In these models, all patients with at least one EQ-VAS score recorded at any of the time-points were included (n=669/737). Mixed linear models should account for missing EQ-VAS due to above discussed reasons and due to lost to follow-up (e.g. we assume that missing at random produced the observed missing patterns in our data set). In addition, to account for intermittently missing EQ-VAS data, i.e. EQ-VAS recorded at day-30 and day-365, but missing at day-180 (n=14), we assumed that day-180 EQ-VAS was the same as day-30 EQ-VAS (last observation carried forward) and re-computed the models under this assumption. There was no significant change in mean EQ-VAS at serial time-points after including these data-points under this sensitivity analysis.

Day of Assessment	Mean EQ-VAS (95% CI)		p-value
	Good Outcome	Poor Outcome	
Day-30	44.9 (42.3-47.5)	30.3 (27.7-32.8)	<0.001
Day-180	66.0 (63.5-68.4)	47.1 (44.6-49.7)	<0.001
Day-365	70.9 (68.4-73.4)	53.2 (50.4-55.9)	<0.001