Analysis of Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH) II Trial by As Treated Groups

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Primary hypothesis

- Intensive treatment of elevated systolic blood pressure (≥180 mm Hg) reduces the likelihood of death or disability (modified Rankin scale 4-6) at 3 months after intracerebral hemorrhage, by at least 10 % absolute difference compared with standard treatment.
- Standard treatment goals: 140-179 mm Hg
- Intensive treatment goals: 110-139 mm Hg
- Target recruitment: 1280 subjects
- Presumed mechanism of therapeutic benefit: reduction in rate of hematoma expansion

Qureshi AI, Palesch YY. Neurocrit Care. 2011;15(3):559-76

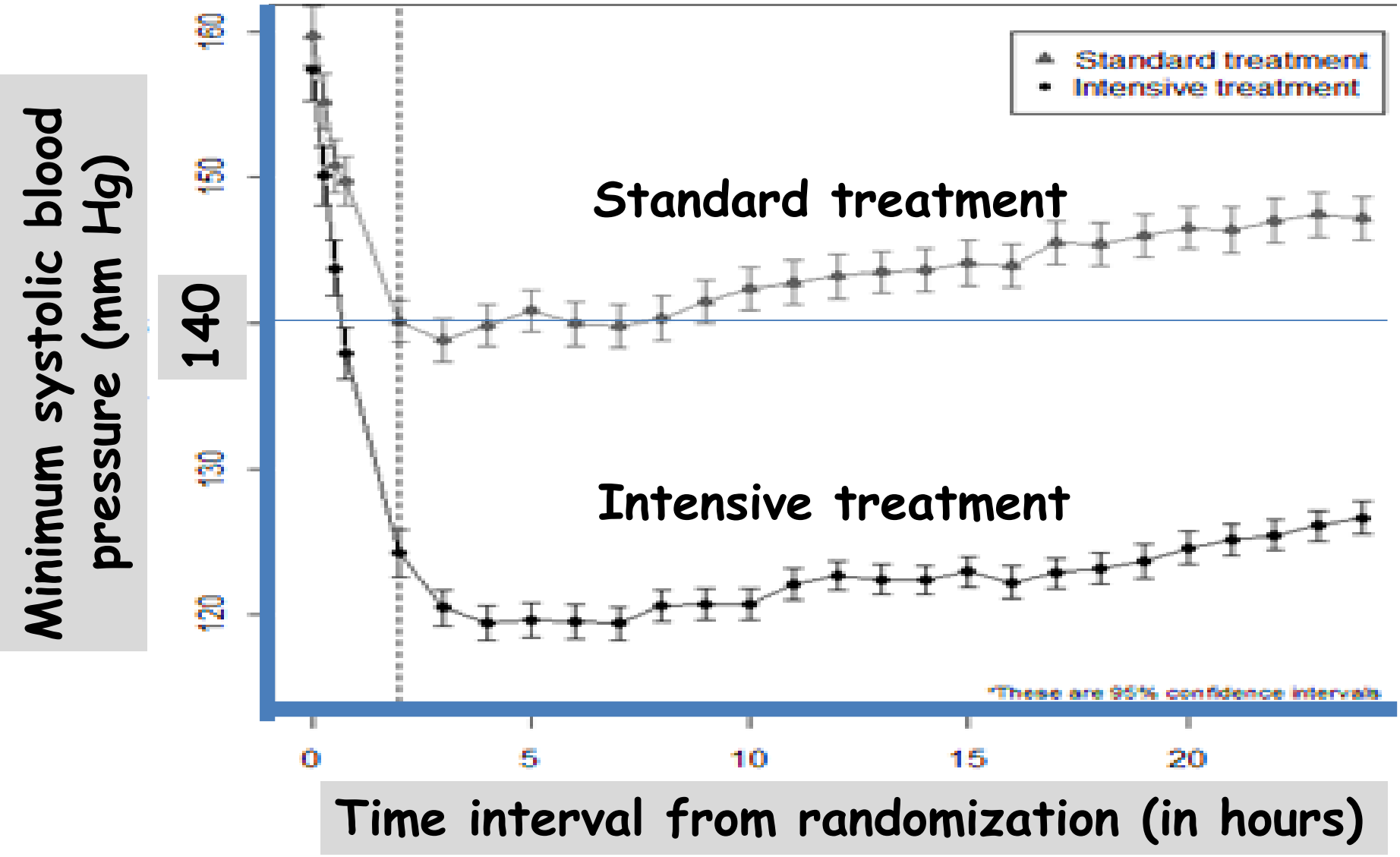
Death or disability (modified Rankin scale 4-6) at 90 days post-randomization- INTENT TO TREAT ANALYSIS

Outcome	Intensive treatment n=500	Standard treatment n=500	Unadjusted Relative Risk (95% CI)[1]	Adjusted Relative Risk (95% CI)[1,2]
Death or disability - number/total number observed (%)	186/481 (38.7)	181/480 (37.7)	1.02 (0.83, 1.25) p=0.84	1.04 (0.85,1.27) p=0.72

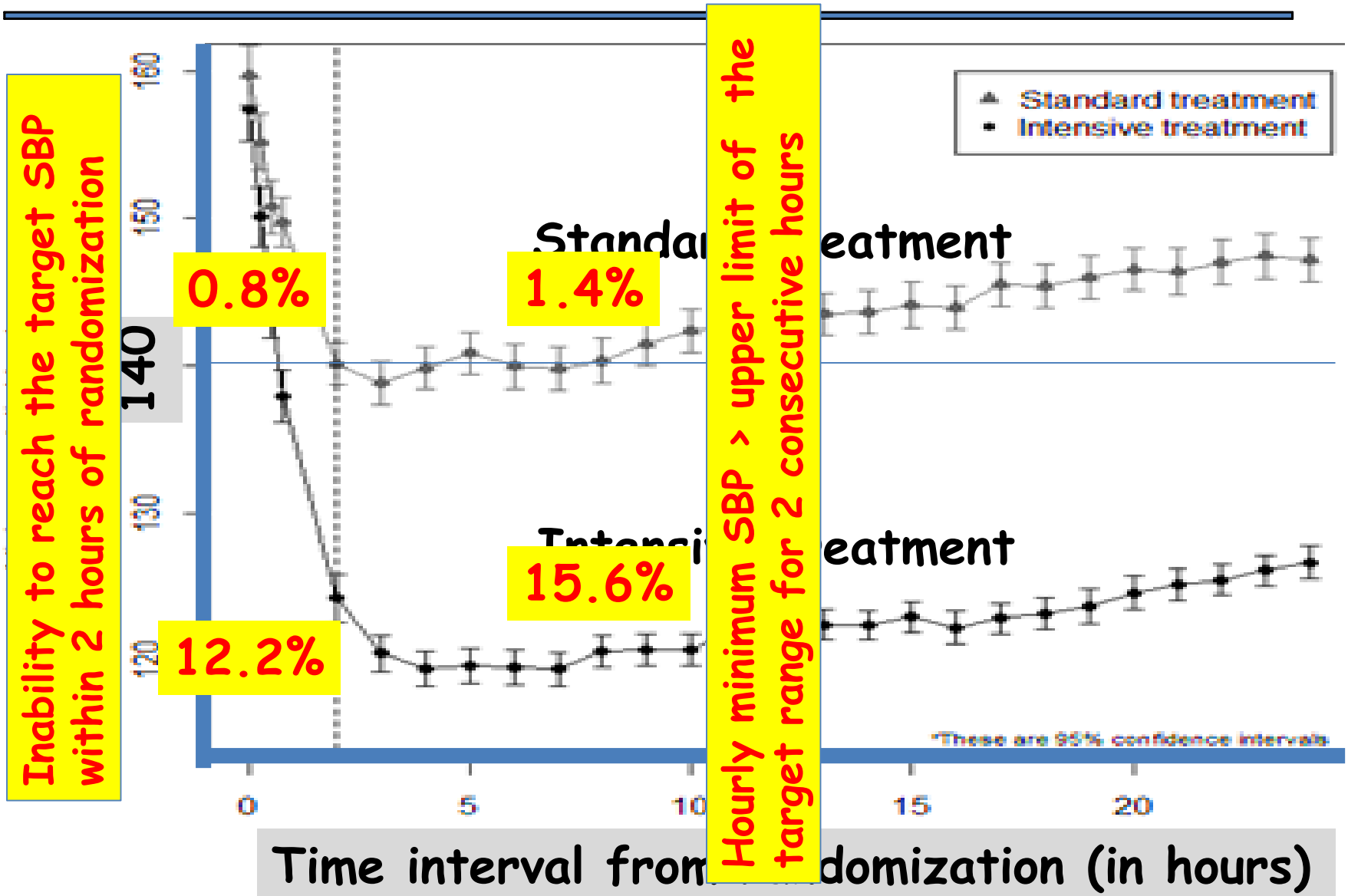
[1]Relative risk for modified Rankin Scale are based on multiple imputation analysis and [2] adjusting for the effects of age, GCS and presence/absence of intraventricular hemorrhage

Re: Qureshi AI. N Engl J Med 2016; 375 (11):1033-43

The mean values of hourly minimum systolic blood pressure (with model based 95% CI) for first 24 hours post randomization by treatment group



Primary and secondary treatment failures



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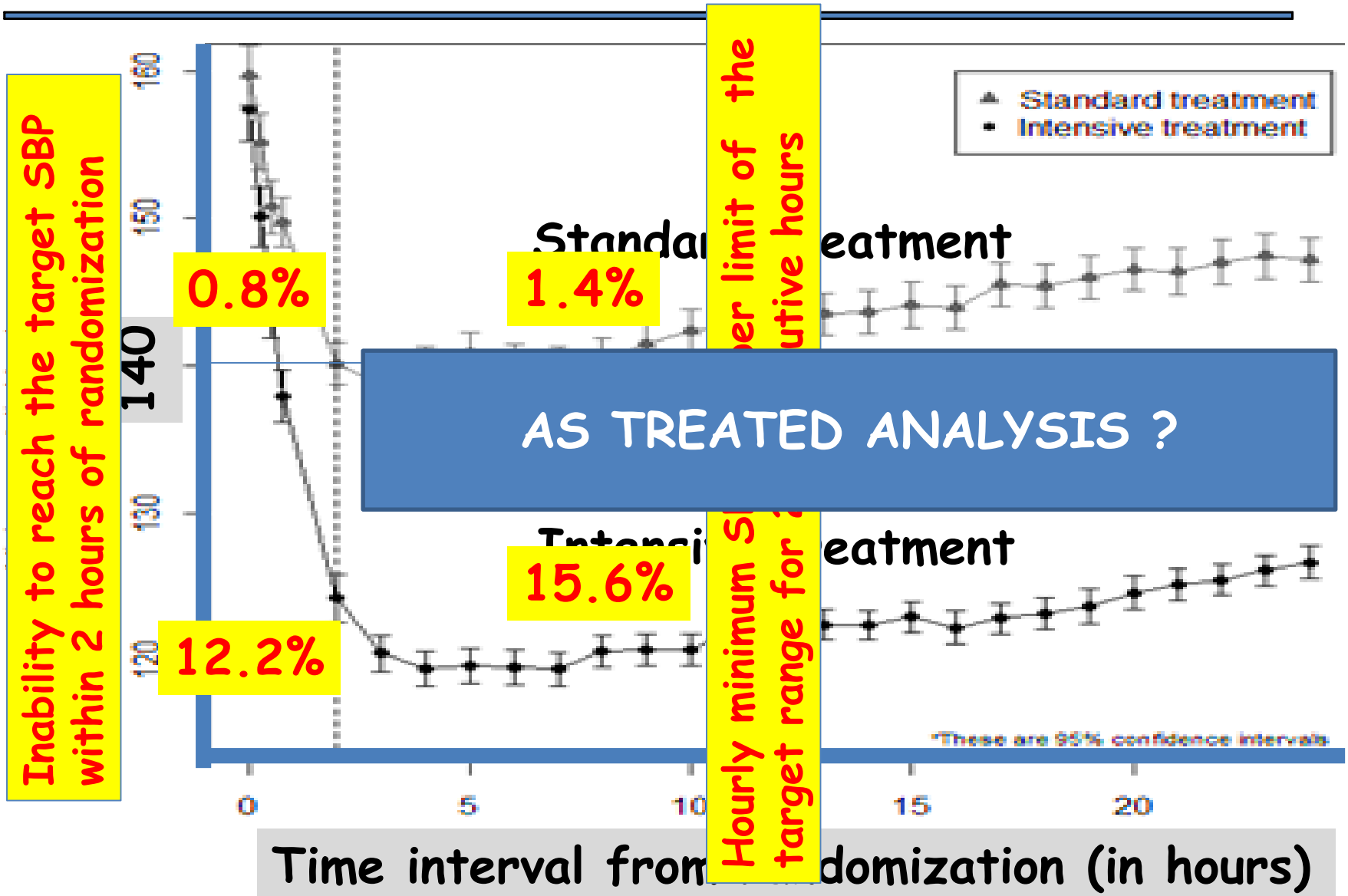

Categories of subjects according to intensive treatment systolic BP values achieved

Systolic BP goals (<140 mm Hg) achieved within 2 hrs post randomization	Systolic BP goals (<140 mm Hg) maintained 2-20 hrs post randomization	Category
Yes	Yes	Reduced and maintained
Yes	No †	Reduced but not maintained
No	No/yes	Not reduced

†Hourly minimum SBP > 140 mm Hg for 2 consecutive hours

Categories of subjects according to intensive treatment systolic BP values achieved

Intensive treatment	Standard treatment	Category
342 (68.4%)	15 (3.0%)	Reduced and maintained
97 (19.4%)	277 (55.6%)	Reduced but not maintained
61 (12.2%)	206 (41.4%)	Not reduced

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342 (68.4%)	15 (3.0%)	Reduced and maintained
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Primary outcome: Death or disability (modified Rankin scale 4-6) at 90 days post-randomization

Outcome	Not reduced	Reduced and maintained	Reduced but not maintained
Death or disability - number/total number observed (%)	129/261 (49.4)	181/352 (51.4)	213/367 (58.0)
Relative Risk (95% CI)	Reference	1.04 (0.83, 1.30) P=0.7	1.17 (0.94, 1.46) P=0.14

Secondary outcome: Death within 90 days post-randomization

Outcome	Not reduced	Reduced and maintained	Reduced but not maintained
Death- number/total number observed (%)	14/267 (5.2)	15/357 (4.2)	38/374 (10.2)
Relative Risk (95% CI)	Reference	0.80 (0.38, 1.66) P=0.55	1.93 (1.05, 3.57) P=0.03

Secondary outcome: Neurological deterioration within 24 hours post-randomization

Outcome	Not reduced	Reduced and maintained	Reduced but not maintained
Neurological deterioration- number/total number observed (%)	15/267 (5.6)	37/357 (10.4)	43/374 (11.5)
Relative Risk (95% CI)	Reference	1.84 (1.01, 3.36) P=0.04	2.05 (1.13, 3.68) P=0.01

Secondary outcome: Serious adverse events within 90 days post-randomization

Outcome	Not reduced	Reduced and maintained	Reduced but not maintained
Serious adverse events -number/total number observed (%)	47/267 (17.6)	80/357 (22.7)	101/374 (27.0)
Relative Risk (95% CI)	Reference	1.27 (0.88, 1.82) P=0.18	1.53 (1.08, 2.1) P=0.01

Conclusions

- We lack statistically significant evidence of reduction in death or disability among subjects who achieved intensive SBP reduction goals within 2 hours regardless of whether SBP values were maintained in intensive SBP reduction goals for 21-22 hours post randomization.

- Subjects who achieved intensive SBP reduction goals within 2 hours but were not maintained in intensive SBP reduction goals for 21-22 hours post randomization appeared to have higher rates of death, neurological deterioration, and serious adverse events.

Thank you

Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH)-2 trial investigators' meeting, Honolulu, Hawaii, April 26th, 2016

Secondary outcome: Hematoma expansion within 24 hours post-randomization

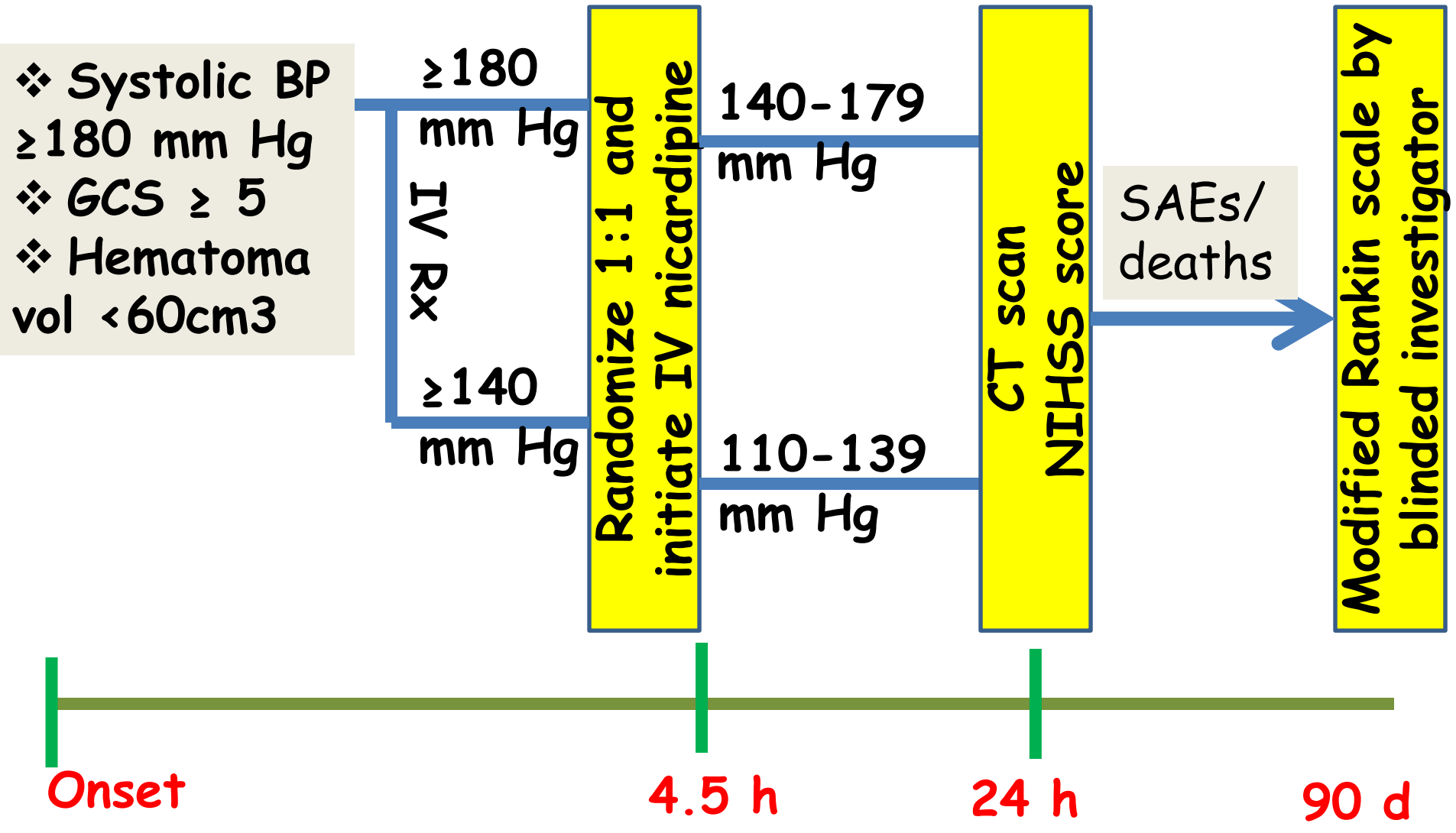
Outcome	Not reduced	Reduced and maintained	Reduced not maintained
Hematoma expansion- number/total number observed (%)	50/226 (22.1)	63/326 (19.3)	76/323 (23.5)
Relative Risk (95% CI)	Reference	0.87 (0.60, 1.27) P=0.4	1.06 (0.74, 1.5) P=0.7

Tertiary outcome: ED 5D utility index at 90 days post-randomization

Outcome	Not reduced	Reduced and maintained	Reduced not maintained
EQ5D utility index- Median	0.8 (0.4-0.8)	0.7 (0.4-0.8)	0.7 (0.4-0.8)
Relative Risk (95% CI)	Reference	-0.008 (-0.05, -0.04) P=0.75	-0.063 (-0.11, -0.01) P=0.011

Trial design: ATACH-2

re. Qureshi AI, Palesch YY. Neurocrit Care. 2011;15(3):559-76.



Secondary outcome: Cardiac adverse events within 7 days post-randomization

Outcome	Not reduced	Reduced and maintained	Reduced not maintained
Cardiac adverse events within 7 days -number/total number observed (%)	17/267 (6.4)	42/357 (11.2)	42/374 (11.2)
Relative Risk (95% CI)	Reference	1.76 (0.99, 3.10) P=0.05	1.76 (1.00, 3.09) P=0.04