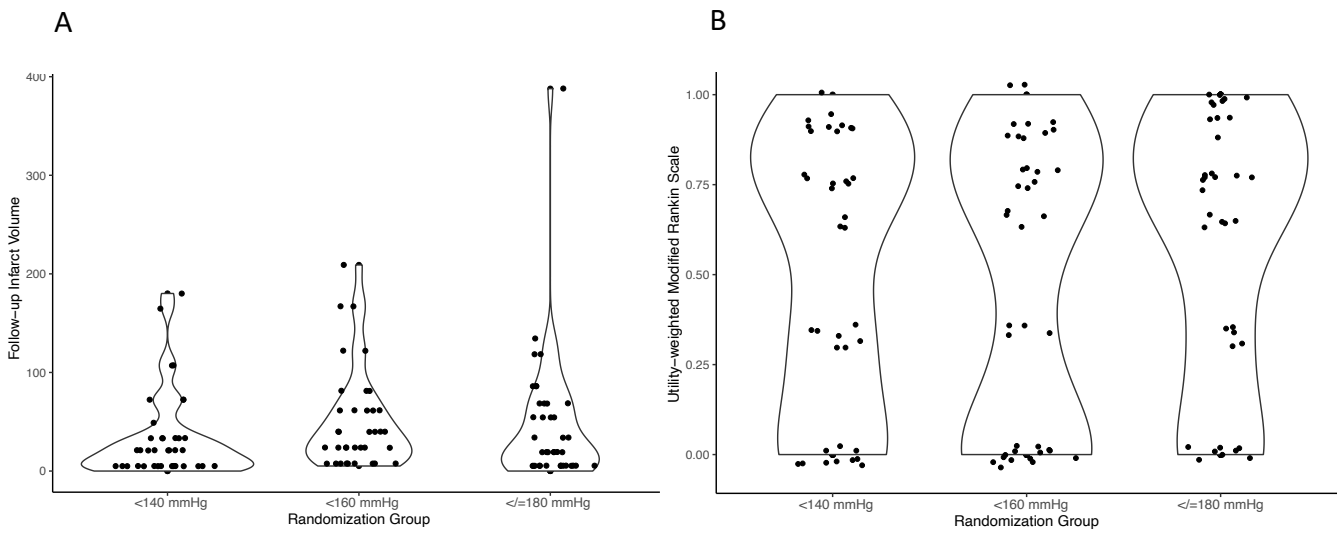
Supplemental Online Content

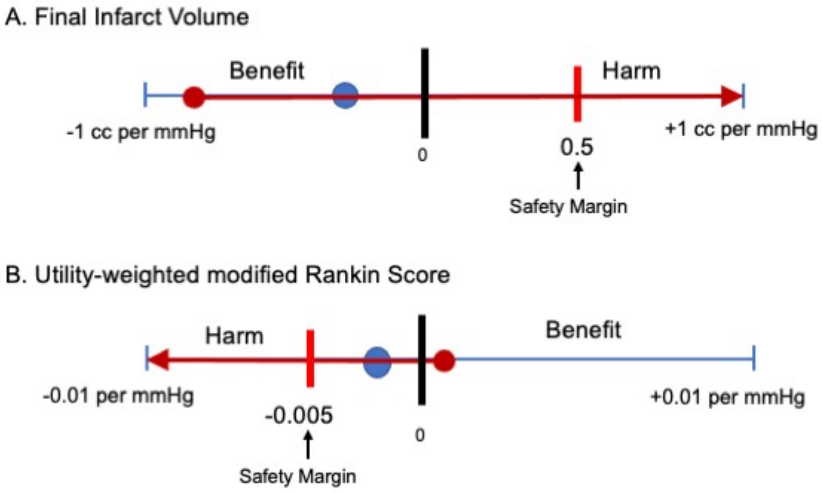
Mistry EA, Hart KW, Davis LT, et al. Blood pressure management after endovascular therapy for acute ischemic stroke: the BEST-II randomized clinical trial *JAMA*. doi:10.1001/jama.2023.14330

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

eFigure 1. Scatter plot showing distribution of raw final infarct volume(A) and utility-weighted modified Rankin score (B) by the randomization group



eFigure 2. Multiple Primary Outcome Results



The slope of association between post-endovascular treatment systolic blood pressure target and final infarct volume is shown in A. The point estimate of treatment effect is shown (Blue dot) with one-sided 95% confidence interval. Because the confidence interval is not all to the right of the safety margin, the results do not support a finding of futility. The slope of association between post-endovascular treatment systolic blood pressure target and utility-weighted modified Rankin score is shown in B. The point estimate of treatment effect is shown (Blue dot) with one-sided 95% confidence interval. Because the confidence interval is not all to the left of the safety margin, the results do not support a finding of futility.

eTable 1. Baseline Characteristics by Site				
	Site 1 (N=46)	Site 2 (N=6)	Site 3 (N=68)	Total (N=120)
Age in years	69.0 [62.0, 84.0]	71.0 [69.5, 73.3]	72.0 [62.8, 77.0]	71.0 [62.8, 77.0]
Female	30 (65.2%)	3 (50.0%)	36 (52.9%)	69 (57.5%)
Male	16 (34.8%)	3 (50.0%)	31 (45.6%)	50 (41.7%)
Race				
Multi-racial	2 (4.3%)	0 (0%)	1 (1.5%)	3 (2.5%)
Black or African American	3 (6.5%)	0 (0%)	6 (8.8%)	9 (7.5%)
Native Hawaiian or Other Pacific Islander	1 (2.2%)	0 (0%)	0 (0%)	1 (0.8%)
White or Caucasian	38 (82.6%)	6 (100%)	61 (89.7%)	105 (87.5%)
Other	2 (4.3%)	0 (0%)	0 (0%)	2 (1.7%)
Ethnicity				
Hispanic or Latino	1 (2.2%)	0 (0%)	1 (1.5%)	2 (1.7%)
Not Hispanic or Latino	45 (97.8%)	6 (100%)	63 (92.6%)	114 (95.0%)
Unknown	0 (0%)	0 (0%)	4 (5.9%)	4 (3.3%)
Hypertension (%)	34 (73.9%)	5 (83.3%)	53 (77.9%)	92 (76.7%)
Diabetes (%)	16 (34.8%)	2 (33.3%)	22 (32.4%)	40 (33.3%)
Hyperlipidemia (%)	33 (71.7%)	4 (66.7%)	58 (85.3%)	95 (79.2%)
Atrial fibrillation (%)	23 (50.0%)	4 (66.7%)	26 (38.2%)	53 (44.2%)
Time from last known well to the presentation (minute; Median [Q1, Q3])	212 [119, 417]	287 [198, 354]	231 [130, 446]	225 [126, 443]
Pre-stroke modified Rankin score (Median [Q1, Q3])	0 [0, 2.00]	0 [0, 0]	0 [0, 1.00]	0 [0, 1.00]
Baseline antiplatelet use (%)	16 (34.8%)	0 (0%)	30 (44.1%)	46 (38.3%)
Baseline anticoagulant use (%)	9 (19.6%)	2 (33.3%)	11 (16.2%)	22 (18.3%)
Intravenous thrombolysis administered (%)	17 (37.0%)	3 (50.0%)	34 (50.0%)	54 (45.0%)
Baseline glucose (Median [Q1, Q3])	120 [108, 148]	124 [101, 163]	120 [107, 150]	120 [107, 149]
Baseline platelet count (Median [Q1, Q3])	218 [187, 263]	212 [177, 342]	226 [181, 269]	225 [184, 269]
Baseline NIHSS (Median [Q1, Q3])	16.0 [12.0, 22.0]	10.0 [7.50, 14.8]	16.0 [11.0, 23.0]	16.0 [11.0, 22.0]
Baseline ASPECT score (Median [Q1, Q3])	9.00 [7.25, 9.00]	8.00 [8.00, 9.50]	7.00 [6.00, 8.00]	8.00 [7.00, 9.00]
Location of the vessel occlusion				
ICA	7 (15.2%)	0 (0%)	14 (20.6%)	21 (17.5%)
M1	28 (60.9%)	6 (100%)	45 (66.2%)	79 (65.8%)
M2	14 (30.4%)	1 (16.7%)	14 (20.6%)	29 (24.2%)
Modified Tan score on baseline CTA				
0	0 (0%)	0 (0%)	3 (4.4%)	3 (2.5%)

1	10 (21.7%)	1 (16.7%)	23 (33.8%)	34 (28.3%)
2	23 (50.0%)	1 (16.7%)	28 (41.2%)	52 (43.3%)
3	7 (15.2%)	3 (50.0%)	9 (13.2%)	19 (15.8%)
Final recanalization grade				
mTICI2b	12 (26.1%)	1 (16.7%)	37 (54.4%)	50 (41.7%)
mTICI 2c	5 (10.9%)	1 (16.7%)	12 (17.6%)	18 (15.0%)
mTICI 3	29 (63.0%)	4 (66.7%)	19 (27.9%)	52 (43.3%)
Type of anesthesia used				
General	2 (4.3%)	2 (33.3%)	19 (27.9%)	23 (19.2%)
Conscious Sedation	33 (71.7%)	0 (0%)	48 (70.6%)	81 (67.5%)
Last systolic BP prior to groin puncture (Mean with SD)	148 (23.1)	140 (30.3)	150 (23.4)	149 (23.5)
Last diastolic BP prior to groin puncture (Mean with SD)	83.2 (15.0)	77.5 (13.6)	88.9 (19.3)	86.1 (17.7)

eTable 2. Details of post-endovascular treatment blood pressure management				
	SBP <140 mmHg (n=40)	SBP <160 mmHg (n=40)	SBP ≤180 mmHg (n=40)	Overall Cohort (n=120)
Hourly post-EVT SBP (10th and 90th %tile)	[103,139]	[108,153]	[103,157]	[104,150]
Hourly Avg post-EVT SBP (mean ±SD; mmHg)	122 (15)	130 (18)	129 (20)	127 (18)
Avg post-EVT DBP (mean ±SD; mmHg)	66 (12)	74 (15)	75 (16)	72 (15)
Any antihypertensive agent used post-EVT (%)	29 (72.5%)	22 (55%)	10 (25%)	61 (50.8%)
Proportion of time spent below target	85%	92%	99%	92%
Type of anti-hypertensive(s) used				
Nicardipine[a] (%)	25/29 (86.2%)	17/22 (77.3%)	7/10 (70%)	49/61 (80.3%)
Labetalol (%)	3/29 (10.3%)	2/22 (9.1%)	1/10 (10%)	6/61 (9.8%)
Hydralazine (%)	0/29 (0%)	1/22 (4.5%)	1/10 (10%)	2/61 (3.3%)
Metoprolol (%)	1/29 (3.4%)	1/22 (4.5%)	1/10 (10%)	3/61(4.9%)
Carvedilol (%)	0/29(0%)	1/22 (4.5%)	0/10(0%)	1/61 (1.6%)
[a]Recommended as first line agent per trial protocol				

eTable 3. BP target modification information							
BP target modified	**Lower target of < 140mmHg (N=40)**		**Intermediate target of < 160mmHg (N=40)**		**High target of <=180mmHg (control) (N=40)**		**Total (N=120)**
Yes	1 (2.5%)		1 (2.5%)		1 (2.5%)		3 (2.5%)
	Reason	New target	Reason	New target	Reason	New target	
	Reocclusion of the ICA	120-180 mmHg	Vessel injury and extravasation of contrast was noted on subsequent CT scan	<120 mmHg	Large infarct and procedural considerations	<140 mmHg	

eTable 4. Details of missing outcome data	
Final Infarct Volume	
Randomization group	Reason for missing outcome
<140	Transitioned to comfort care before 36 +/-12 hours
<140	Uninterpretable imaging study
<160	Uninterpretable imaging study
<160	Imaging study unavailable
<160	Transitioned to comfort care before 36 +/-12 hours
<160	Imaging study unavailable
</=180	Uninterpretable imaging study
Utility-weighted modified Rankin score	
<140	Patient could not be reached despite multiple attempts
<140	Patient could not be reached despite multiple attempts
<140	Patient could not be reached despite multiple attempts
<160	Patient could not be reached despite multiple attempts
</=180	Patient could not be reached despite multiple attempts
</=180	Patient could not be reached despite multiple attempts
</=180	Patient could not be reached despite multiple attempts

eTable 5. Details of hemorrhage grade by randomization group			
	SBP <140 mmHg (n=14)	SBP <160 mmHg (n=12)	SBP ≤180 mmHg (n=12)
Hemorrhagic Infarct 1 (%)	1 (7.1%)	2 (16.7%)	4 (33.3%)
Hemorrhagic Infarct 2 (%)	9 (64.3%)	5 (41.7%)	4 (33.3%)
Parenchymal Hematoma 1 (%)	3 (21.4%)	1 (8.3%)	2 (16.7%)
Parenchymal Hematoma 2 (%)	1 (7.1%)	4 (33.3%)	2 (16.7%)

eTable 6. Details of serious adverse events (SAE)	
Randomization group	SAE Description MeDRA Term
</=180	Femoral artery Pseudoaneurysm
<160	Sepsis and cardiac failure
<160	Aspiration Pneumonia
<160	Aspiration Pneumonia
<140	Carotid artery re-occlusion
<140	Subarachnoid hemorrhage
<140	Gastrointestinal hemorrhage associated with gastric ulcer
<140	New contralateral large vessel occlusion stroke

eTable 7. Subgroup analyses				
	Coefficient	95% CI Lower Bound	95% CI Upper Bound	P-value
Final infarct volume outcome				
Age	1.1986	-11.215	13.612	0.8503
Age (nonlinear)	-14.417	-30.784	1.95112	0.0874
ASPECT score	-24.233	-80.812	32.3467	0.4032
Modified Tan score	-69.511	-223.79	84.7724	0.3835
eTICI 2c	-102.45	-375.97	171.075	0.4646
eTICI 3	-25.826	-238.56	186.907	0.8125
Randomization	-1.545	-7.2083	4.11837	0.5941
Age * Randomization	-0.0073	-0.0863	0.0718	0.8576
Age (non-linear) * Randomization	0.0923	-0.0136	0.19831	0.0907
ASPECT score * Randomization	0.1303	-0.2182	0.4789	0.4653
Modified Tan score * Randomization	0.2591	-0.6777	1.19595	0.5911
eTICI 2c * Randomization	0.4301	-1.2642	2.12435	0.6199
eTICI 3 * Randomization	0.0462	-1.2578	1.35027	0.9448
Uw-mRS outcome				
Age	-0.0904	-0.18495	0.00423	0.0645
Age (nonlinear)	0.1102	-0.01481	0.23511	0.0877
ASPECT Score	0.0447	-0.38453	0.47396	0.8387
Modified Tan Score on Baseline CTA	0.2087	-0.8699	1.28737	0.706
Final Recanalization Grade: 2c	-0.93	-2.98567	1.12562	0.3776
Final Recanalization Grade: 3	-0.6941	-2.30185	0.91366	0.4004
Randomization	-0.0331	-0.07504	0.00891	0.1259
Age*Randomization	0.0006	-0.00005	0.00116	0.0742
Age (non-linear) * Randomization	-0.0007	-0.00155	0.00007	0.0756
ASPECT Score*Randomization	-0.0001	-0.00275	0.00256	0.9454
Modified Tan Score on Baseline CTA*Randomization	-0.0006	-0.00713	0.00602	0.8687
Final Recanalization Grade: 2c*Randomization	0.0065	-0.0062	0.01925	0.3175
Final Recanalization Grade: 3*Randomization	0.005	-0.00491	0.01494	0.3251

eTable 8. Predicted Probabilities of Success for Future Trials Comparing <140 vs </=180 mmHg and <160 vs </=180 Arms

Total N	PPOS	
	<140 vs <=180mmHg	<160 vs <=180mmHg
400	16%	9%
800	21%	12%
1500	25%	14%
2000	27%	16%
2400	28%	17%

Statistical Models

The primary statistical models and hypotheses are:

- FIV = intercept + beta1*baseline ASPECT score + beta2*study arm

H0: The coefficient of study group is less than or equal to 0.5.
H1: The coefficient of study group is greater than 0.5.

- uw_mRS = intercept + beta1*pre-stroke mRS + beta2*study arm

H0: the coefficient of study arm is greater than or equal to -0.005.
H1: the coefficient of study arm is less than -0.005.