Supplementary Online Content

Murthy SB, Cho S-M, Gupta A, et al. A pooled analysis of diffusion-weighted imaging lesions in patients with acute intracerebral hemorrhage. *JAMA Neurol*. Published online July 20, 2020. doi:10.1001/jamaneurol.2020.2349

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

eAppendix. STROBE Statement—Checklist of Items That Should Be Included in Reports of Observational Studies

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3,4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6
Objectives	3	State specific objectives, including any prespecified hypotheses	5,6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow–up, and data collection	6,7, Supplemental File
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow–up *Case–control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross–sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case–control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-9
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	11, Figure 1

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10,11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9,10
		(*b*) Describe any methods used to examine subgroups and interactions	9,10
		(*c*) Explain how missing data were addressed	9,10
		(*d*) *Cohort study*—If applicable, explain how loss to follow–up was addressed *Case–control study*—If applicable, explain how matching of cases and controls was addressed *Cross–sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	10
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow–up, and analysed	11, Figure 1
		(b) Give reasons for non–participation at each stage	11, Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11–13
		(b) Indicate number of participants with missing data for each variable of interest	11–13
		(c) *Cohort study*—Summarise follow–up time (eg, average and total amount)	11
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	11-12
		Case–control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross–sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder–adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12,13
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13
Discussion			
Key results	18	Summarise key results with reference to study objectives	13, 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16,17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	16,17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

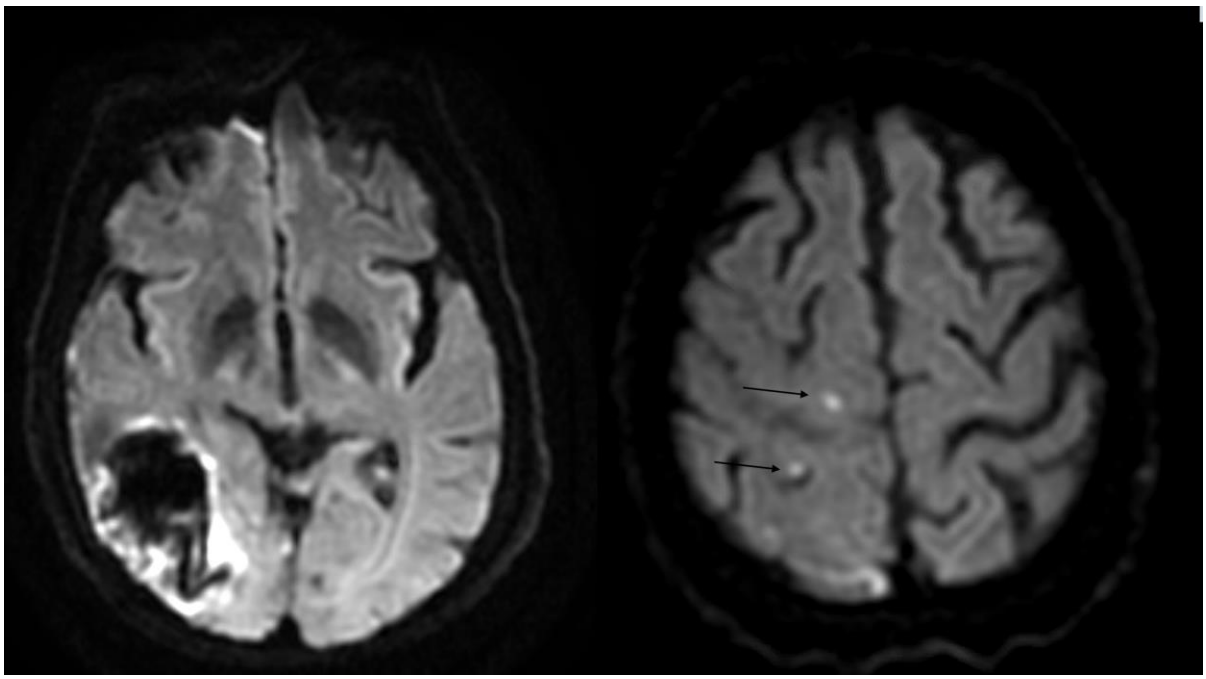
*Give information separately for cases and controls in case–control studies and, if applicable, for exposed and unexposed groups in cohort and cross–sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe–statement.org.

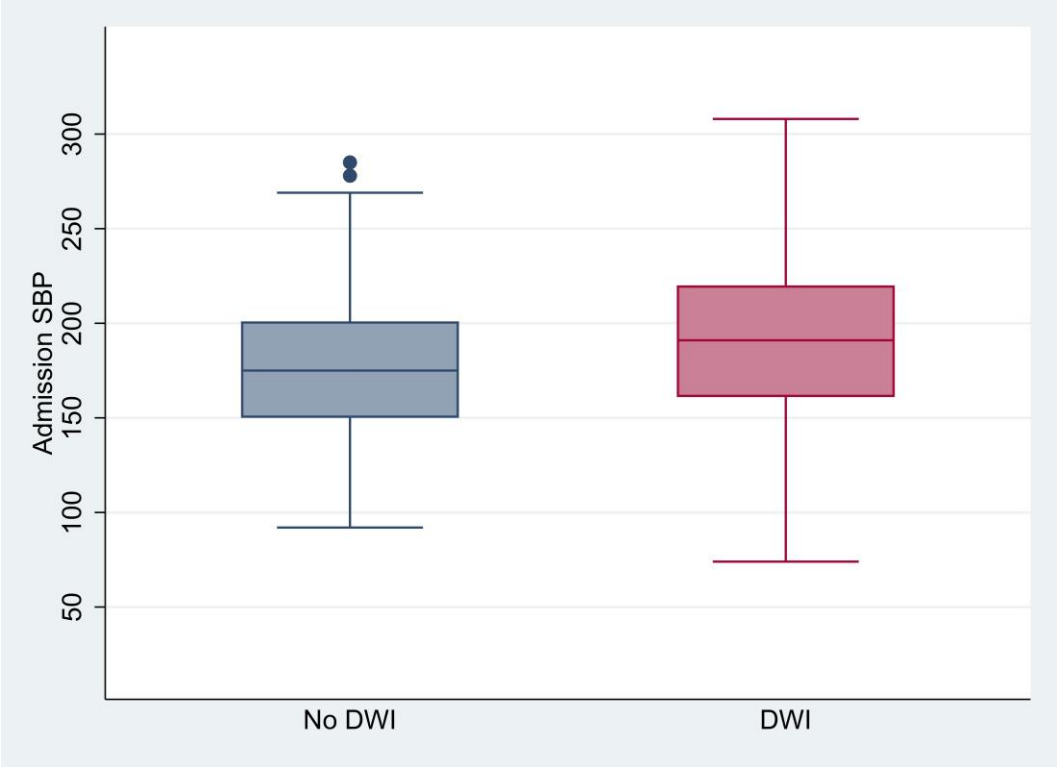
eMethods. Cohorts.

MISTIE III was a randomized, controlled, open-label, blinded endpoint trial that found image guided, minimally invasive surgery followed by gentle thrombolytic irrigation of the catheterized intracerebral hemorrhage clot to decrease mortality, but was neutral on the primary endpoint of improved functional outcome in patients with moderate to large ICH, compared to standard medical management.[1] ATACH-2 was a randomized, multicenter, open-label trial to determine the relative efficacy of intensive versus standard antihypertensive treatment initiated within 4.5 hours after symptom onset and continued for the next 24 hours in patients with spontaneous supratentorial ICH.[2] The trial found no difference in the primary endpoint of death or major disability at 90 days. i-DEF was a multicenter, randomized, placebo-controlled, double-blind phase 2 trial that evaluated random allocation of deferoxamine mesylate infusion versus saline (placebo) infusions in patients with ICH, and found no difference in the primary outcome of modified Rankin Scale score (mRS) of 0–2.[3] The ERICH study is a multicenter, prospective, case-control study of primary ICH in non-Hispanic white, non-Hispanic black, and Hispanic participants.[4]

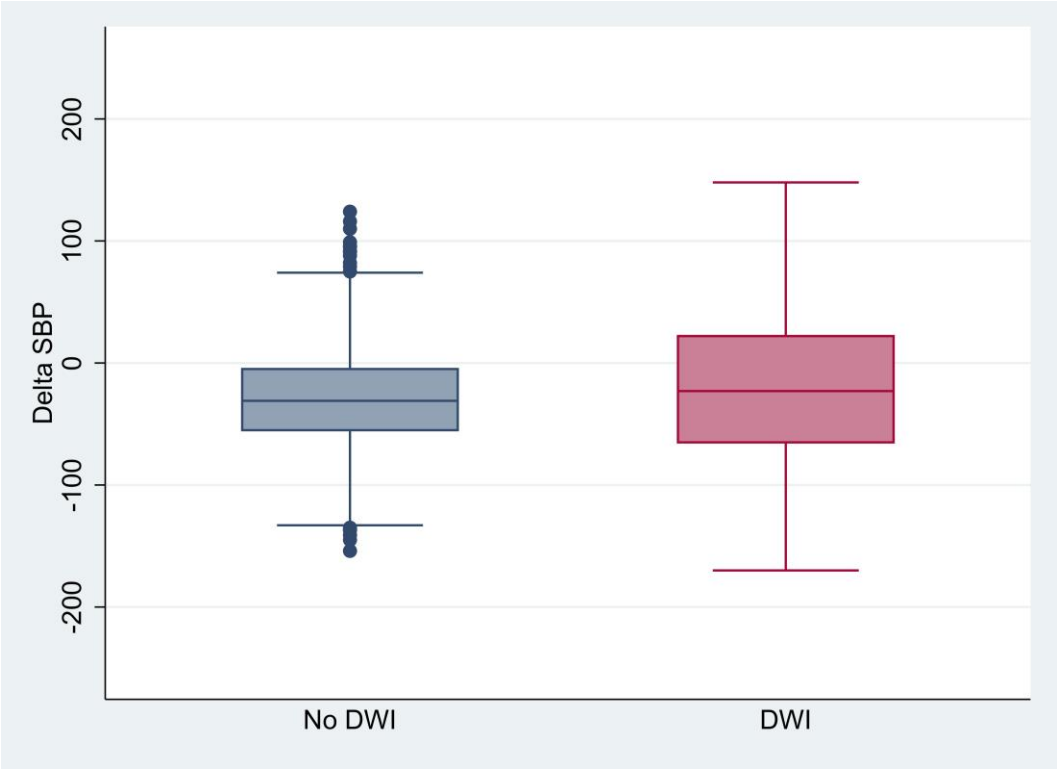
eFigure 1. Magnetic Resonance Imaging Scan of the Brain Showing a DWI Lesion After Acute Intracerebral Hemorrhage



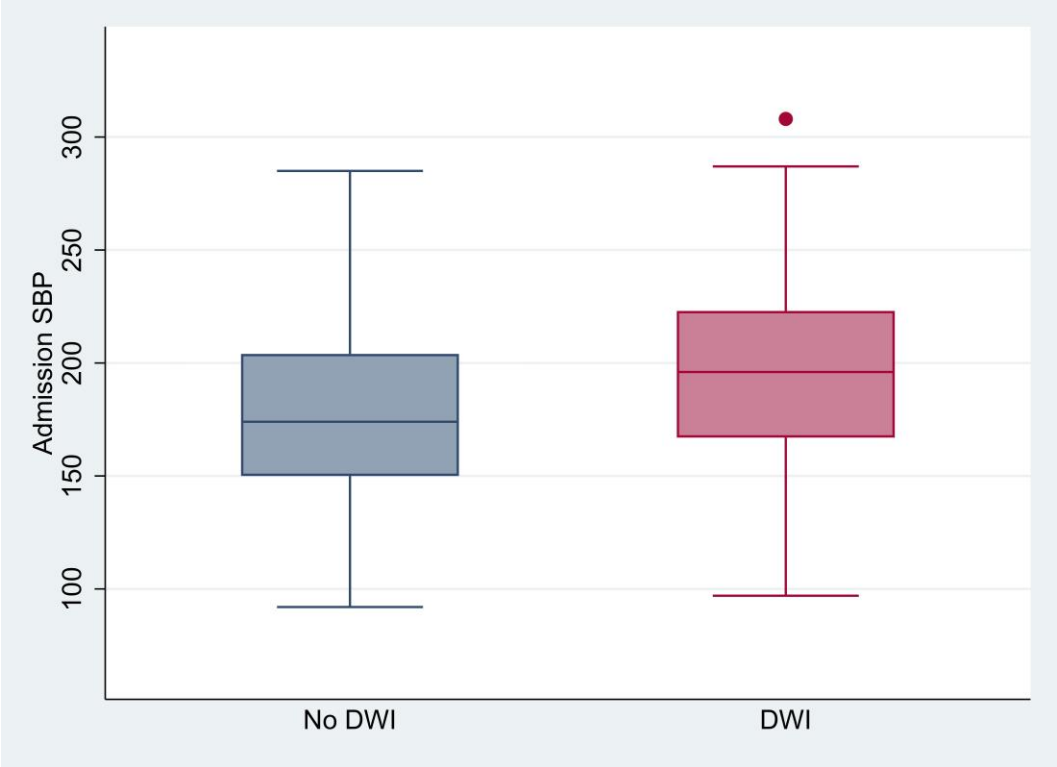
eFigure 2. Box Plots Showing Distribution of Baseline SBP Among Patients With and Without DWI Lesions



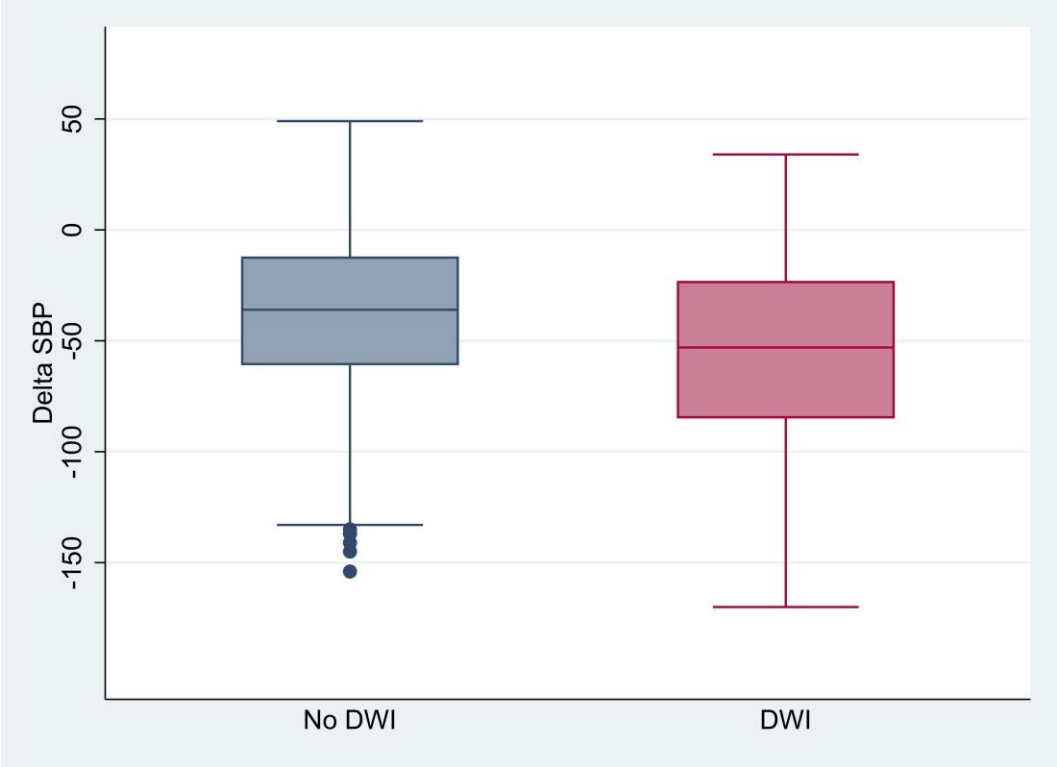
eFigure 3. Box Plots Showing Distribution of Change in SBP During 24 Hours Among Patients With and Without DWI Lesions



eFigure 4. Box Plots Showing Distribution of Baseline SBP Among Patients With and Without DWI Lesions in the ERICH Cohort Only



eFigure 5. Box Plots Showing Distribution of Change in SBP Over 24 hours Among Patients With and Without DWI Lesions in the ERICH Cohort Only



eTable 1. Characteristics of ICH Patients With and Without MRI in the Pooled Cohort			
Characteristic	**MRI Done (N=1788)**	**MRI Not Done (N=2994)**	**P value**
Age, mean SD, y	61.2 (13.3)	61.9 (13.5)	0.29
Male	1044 (58.3)	1827 (61.0)	0.07
Race White Black Other	 751 (42.0) 493 (27.6) 544 (30.4)	 1073 (35.8) 771 (25.8) 1150 (38.4)	**0.04**
Diabetes mellitus	459 (25.7)	792 (26.9)	0.55
Hypertension	1457 (81.5)	2576 (86.0)	**<0.001**
Coronary artery disease	216 (12.1)	410 (13.7)	0.11
Prior ischemic stroke / transient ischemic attack	261 (14.5)	554 (18.5)	**<0.001**
Atrial fibrillation	120 (6.7)	297 (9.9)	**<0.001**
Peripheral vascular disease	34 (1.9)	71 (2.3)	0.85
ICH location Lobar Deep Brainstem/ Cerebellum	 622 (34.8) 1005 (56.2) 161 (9.0)	 677 (22.6) 2043 (68.2) 274 (9.2)	**<0.001**
ICH volume baseline (mean, SD)	18.2 (9.2)	24.3 (10.3)	**<0.001**
IVH volume baseline (mean SD)	1.5 (6.2)	1.6 (9.1)	0.90
GCS baseline, med IQR	15 (12-15)	14 (9-15)	**<0.001**
Mortality at 3 months	139 (7.7)	523 (17.5)	**<0.001**
mRS 4-6 at 3 months	585 (32.8)	1380 (46.1)	**<0.001**
Abbreviations: GCS, Glasgow coma scale; ICH, intracerebral hemorrhage; IQR, interquartile range; IVH, intraventricular hemorrhage; MRI, magnetic resonance imaging; SD, standard deviation.			

eTable 2. Mixed Effects Logistic Regression of Factors Associated With DWIHLs, Stratified by Hematoma Location

Characteristic	Lobar ICH		Deep ICH	
	OR (95% CI)	***P* value**	**OR (95% CI)**	***P* value**
Age	0.98 (0.97-1.01)	0.28	0.97 (0.96-0.99)	**0.016**
Male sex	1.52 (0.97-2.37)	0.07	1.06 (0.75-1.49)	0.72
Race				
White	Reference		Reference	
Black	2.05 (1.17-3.59)	**0.012**	1.55 (1.04-2.53)	**0.03**
Hispanic	1.07 (0.58-1.95)	0.84	0.87 (0.52-1.45)	0.59
Other	0.41 (0.01-16.6)	0.64	0.62 (0.19-2.00)	0.43
Prior anticoagulant therapy	0.98 (0.45-2.13)	0.97	0.38 (0.12-1.19)	0.09
Hematoma volume, baseline (per 10 mL)	1.15 (1.02-1.29)	**0.024**	1.17 (1.03-1.33)	**0.017**
Presence of IVH	0.45 (0.25-0.81)	**0.008**	1.39 (0.95-2.03)	0.08
Baseline SBP (per 10 mm Hg)	1.12 (1.03-1.18)	**0.003**	1.12 (1.06-1.20)	**<0.001**
Delta SBP	1.01 (0.94-1.10)	0.28	1.01 (0.97-1.10)	0.92
Cerebral microbleeds	1.71 (1.05-2.79)	**0.032**	1.86 (1.26-2.74)	**0.002**
Leukoaraiosis, moderate to severe	1.71 (1.01-2.89)	**0.047**	1.28 (0.93-1.96)	0.09

Covariates selected based on a significance of p<0.1 in the univariable analysis.
Abbreviations: CI, confidence interval; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; OR, odds ratio; SBP, systolic blood pressure

eTable 3. Multivariable Analysis of Factors Associated With DWIHLs, Stratified by Study Design (Randomized Trial vs Epidemiological Study)

Characteristic	ATACH-2, MISTIE 3, and I-DEF		ERICH Only	
	OR (95% CI)	***P* value**	**OR (95% CI)**	***P* value**
Age	0.99 (0.97-1.01)	0.43	0.97 (0.96-0.99)	**0.004**
Male sex	1.25 (0.77-2.02)	0.35	1.32 (0.95-1.82)	0.10
Race				
White	Reference		Reference	
Black	2.73 (1.42-5.24)	**0.002**	1.62 (1.10-2.39)	**0.016**
Other	1.08 (0.65-1.81)	0.75	0.88 (0.57-1.35)	0.56
Prior anticoagulant therapy	0.64 (0.21-1.93)	0.43	0.68 (0.35-1.35)	0.27
Hematoma volume, baseline (per 10 mL)	1.17 (1.03-1.33)	**0.015**	1.08 (0.98-1.20)	0.10
Presence of IVH	1.16 (0.70-1.93)	0.55	1.10 (0.78-1.53)	0.59
Baseline SBP (per 10 mm Hg)	1.14 (1.06-1.22)	**<0.001**	1.15 (1.06-1.28)	**0.001**
Delta SBP[1]	----		1.00 (0.99-1.01)	0.37
Cerebral microbleeds	1.76 (1.18-2.84)	**0.02**	1.93 (1.38-2.72)	**<0.001**
Leukoaraiosis, moderate to severe	1.45 (0.85-2.45)	0.17	1.55 (1.08-2.23)	**0.018**
Treatment arm assignment	1.19 (0.72-1.96)	0.49	Not Applicable	

Covariates selected based on a significance of p<0.1 in the univariable analysis

Abbreviations: CI, confidence interval; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; OR, odds ratio; SBP, systolic blood pressure

[1] indicates significant interaction between admission SBP and delta SBP (p=0.01) for the analysis of the 3 trials. No such interaction was noted in the analysis of the ERICH cohort (p=0.65)

eTable 4. Multivariable Logistic Regression of Factors Associated With DWI Lesions Excluding Patients From the i-DEF Trial		
Characteristic	**OR (95% CI)**	***P* value**
Age	0.98 (0.97-0.99)	**0.004**
Male sex	1.33 (1.01-1.75)	**0.04**
Race		
White	Reference	
Black	1.64 (1.17-2.30)	**0.004**
Hispanic	0.89 (-0.62-1.29)	0.54
Other	0.64 (0.22-1.88)	0.42
Prior anticoagulant therapy	0.63 (0.35-1.13)	0.12
Hematoma volume, baseline (per 10 mL)	1.12 (1.02-1.22)	**0.008**
Presence of IVH	1.07 (0.79-1.43)	0.66
Hematoma location		
Lobar	Reference	
Deep	0.81 (0.58-1.11)	0.19
Brainstem or cerebellar	1.10 (0.65-1.82)	0.73
Baseline SBP (per 10 mm Hg)	1.13 (1.07-1.18)	**<0.001**
Delta SBP[1]	----	---
Presence of cerebral microbleeds	1.85 (1.39-2.46)	**<0.001**
Leukoaraiosis, moderate to severe	1.59 (1.17-2.17)	**0.003**
Covariates selected based on a significance of p<0.1 in the univariable analysis Abbreviations: CI, confidence interval; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; OR, odds ratio; SBP, systolic blood pressure [1] indicates significant interaction between admission SBP and delta SBP (p=0.03)		

References

1. Hanley DF, Thompson RE, Rosenblum M, et al. Efficacy and safety of minimally invasive surgery with thrombolysis in intracerebral haemorrhage evacuation (MISTIE III): a randomised, controlled, open-label, blinded endpoint phase 3 trial. *Lancet.* 2019;393(10175):1021-1032.
2. Qureshi AI, Palesch YY, Barsan WG, et al. Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage. *N Engl J Med.* 2016;375(11):1033-1043.
3. Selim M, Foster LD, Moy CS, et al. Deferoxamine mesylate in patients with intracerebral haemorrhage (i-DEF): a multicentre, randomised, placebo-controlled, double-blind phase 2 trial. *Lancet Neurol.* 2019;18(5):428-438.
4. Woo D, Rosand J, Kidwell C, et al. The Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH) study protocol. *Stroke.* 2013;44(10):e120-125.