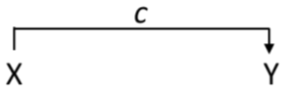
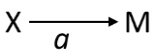
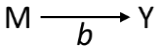
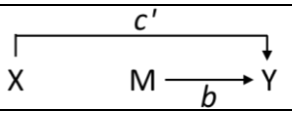
Supplementary Online Content

Boers AMM, Jansen IGH, Brown S, et al. Mediation of the relationship between endovascular therapy and functional outcome by follow-up infarct volume in patients with acute ischemic stroke. *JAMA Neurol*. Published online January 7, 2019. doi:10.1001/jamaneurol.2018.3661

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

eTable 1. Four-step approach for testing mediation

Step	Analysis	Visual representation
Step 1	Regression analysis with X predicting Y to test for path c, $Y = B_0 + B_1X + e$	
Step 2	Regression analysis with X predicting M to test for path a, $M = B_0 + B_1X + e$	
Step 3	Regression analysis with M predicting Y to test the significance of path b, $Y = B_0 + B_1M + e$	
Step 4	Multiple regression analysis with X and M predicting Y, $Y = B_0 + B_1X + B_2M + e$	

eTable 2. Associations of predictors with 90-day modified Rankin Scale score in multivariable modeling

Predictor	Odds Ratio	Lower 95% confidence limit	Upper 95% confidence limit	p-value
Follow-up infarct volume (per 10 ml)	0.92	0.90	0.94	<.001
Endovascular therapy	2.21	1.52	3.21	<.001
Age (per 10 years)	0.62	0.57	0.67	<.001
NIHSS at baseline (per 5 points)	0.82	0.74	0.90	0.001
Hemorrhage: HI-1	0.96	0.73	1.27	0.79
Hemorrhage: HI-2	0.73	0.54	0.99	0.043
Hemorrhage: PH-1	0.92	0.63	1.33	0.64
Hemorrhage: PH-2	0.82	0.54	1.25	0.36
Hemorrhage: remote PH	1.41	0.65	3.03	0.38
Hemorrhage: Intraventricular	0.29	0.13	0.64	0.002
Hemorrhage: Subarachnoid	0.73	0.34	1.56	0.42
Hemorrhage: Subdural	0.17	0.01	3.28	0.24
Symptom side left (vs right)	0.91	0.75	1.11	0.36
ASPECTS Caudate involvement	1.09	0.85	1.40	0.49
ASPECTS Lentiform involvement	0.81	0.60	1.11	0.20
ASPECTS Internal Capsule involvement	0.45	0.35	0.58	<.001
ASPECTS Insula involvement	0.78	0.60	1.01	0.057
ASPECTS M1 involvement	0.93	0.72	1.20	0.57
ASPECTS M2 involvement	0.82	0.64	1.06	0.13
ASPECTS M3 involvement	0.98	0.74	1.29	0.88
ASPECTS M4 involvement	0.82	0.63	1.08	0.15
ASPECTS M5 involvement	0.77	0.60	0.99	0.042
ASPECTS M6 involvement	0.77	0.58	1.02	0.066

Abbreviations: NIHSS, National Institutes of Health Stroke Scale score; HI, Hemorrhagic infarct; PH, parenchymal hematoma; ASPECTS, Alberta Stroke Program Early CT score

eTable 3. Mediating effect of FIV on the association between treatment and ordinal 90-day mRS in subgroup of patients with imaging obtained after 48 hours after onset only

	Unadjusted				Adjusted			
Pathway	**Effect measure**	**Value**	**95% CI**	**p-value**	**Effect measure**	**Value**	**95% CI**	**p-value**
a	β	-0.27	-0.46 – -0.09	0.004	β	-0.13	-0.23 – -0.04	0.007
b	cOR	0.43	0.38 – 0.49	<0.001	acOR	0.47	0.37 – 0.58	<0.001
c	cOR	1.75	1.33 – 2.29	<0.001	acOR	1.81	1.36 – 2.39	<0.001
c'	cOR	1.54	1.17 – 2.02	0.002	acOR	1.74	1.31 – 2.31	<0.001

FIV transformed by ln(FIV+1). Path *a* represents the regression coefficient of the association between treatment (control or endovascular therapy) and FIV; *b* between FIV and 90-day mRS; *c* between treatment and 90-day mRS; and *c'* between treatment and 90-day mRS, controlling for FIV. Multivariable regression analysis included FIV, location, Hemorrhage type, age, and National Institutes of Health and Stroke Scale score.

Abbreviations: FIV, follow-up infarct volume; mRS, modified Rankin Scale; (a)cOR, (adjusted) common odds ratio; CI, confidence interval

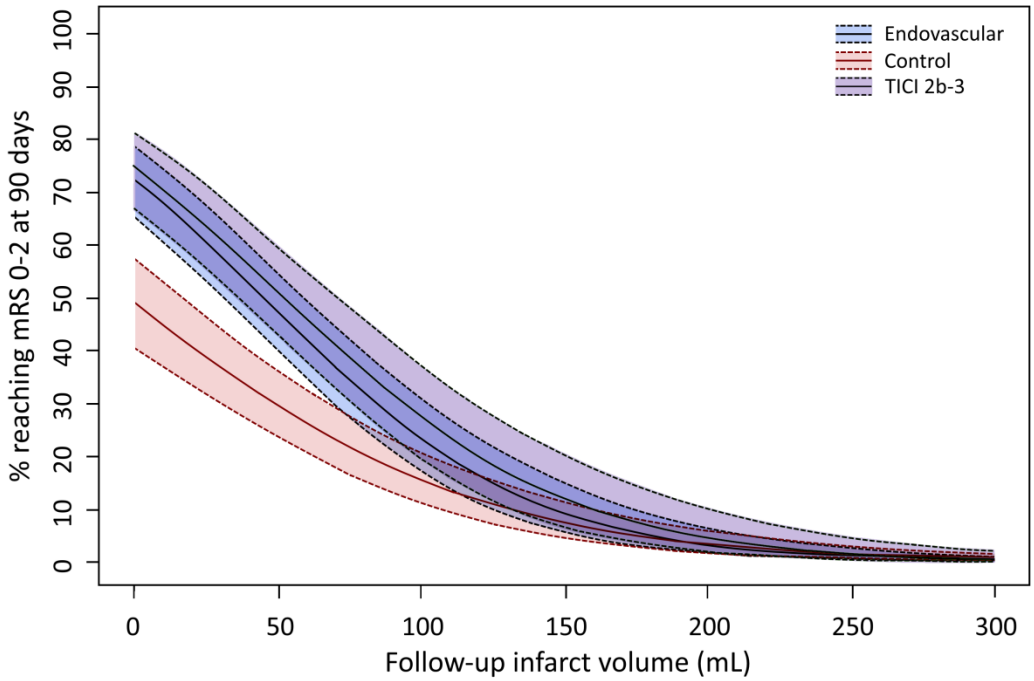
eTable 4. Mediating effect of FIV on the association between treatment and ordinal 90-day mRS in subgroup of patients with MRI modality only

	Unadjusted				Adjusted			
Pathway	**Effect measure**	**Value**	**95% CI**	**p-value**	**Effect measure**	**Value**	**95% CI**	**p-value**
a	β	-0.17	-0.48 – 0.15	0.30	β	-0.05	-0.21 – 0.10	0.52
b	cOR	0.40	0.33 – 0.49	<0.001	acOR	0.45	0.31 – 0.64	<0.001
c	cOR	1.70	1.11 – 2.60	0.015	acOR	2.07	1.29 – 3.31	0.003
c'	cOR	1.61	1.04 – 2.48	0.032	acOR	2.08	1.30 – 3.34	0.003

FIV transformed by ln(FIV+1). Path *a* represents the regression coefficient of the association between treatment (control or endovascular therapy) and FIV; *b* between FIV and 90-day mRS; *c* between treatment and 90-day mRS; and *c'* between treatment and 90-day mRS, controlling for FIV. Multivariable regression analysis included FIV, location, Hemorrhage type, age, and National Institutes of Health and Stroke Scale score.

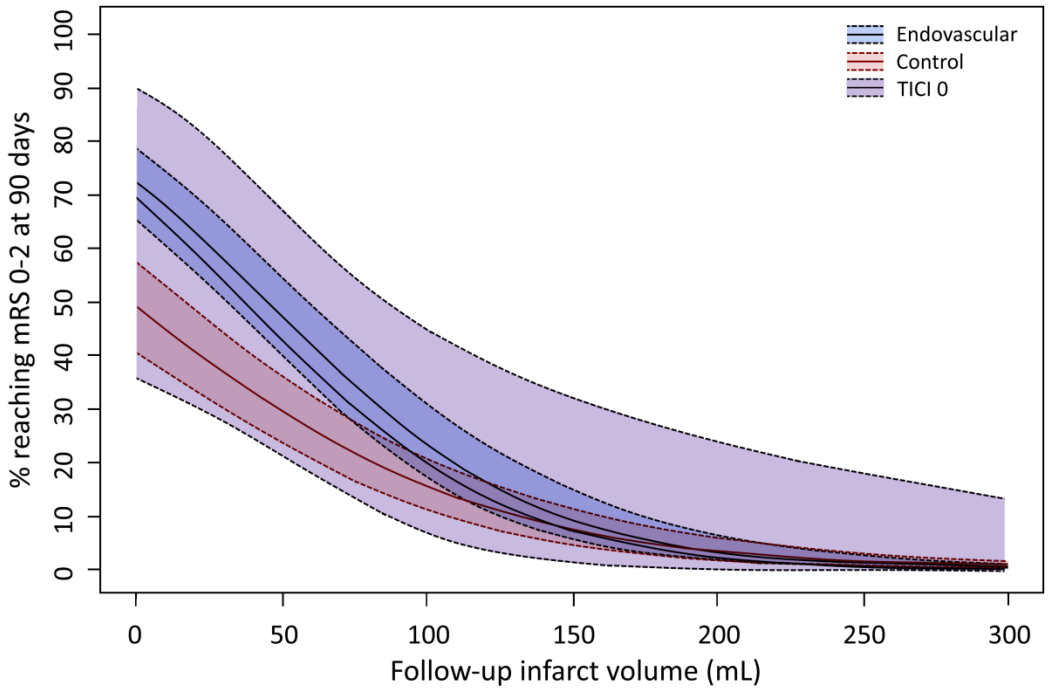
Abbreviations: FIV, follow-up infarct volume; mRS, modified Rankin Scale; (a)cOR, (adjusted) common odds ratio; CI, confidence interval

eFigure 1. Relation between adjusted FIV and estimated probability of functional independence between EVT, control, and reperfusion patients



Relation between adjusted FIV and estimated probability of functional independence (point estimates ± 95% CI), shown for patients allocated to EVT and control and who achieved substantial reperfusion (TICI 2b-3)

eFigure 2. Relation between adjusted FIV and estimated probability of functional independence between EVT, control, and nonreperfusion patients



Relation between adjusted FIV and estimated probability of functional independence (point estimates ± 95% CI), shown for patients allocated to EVT and control and who did not achieve reperfusion (TICI 0)