Supplementary Methods

Data analysis: multivariate model building procedures

Building of all multivariate models was guided by the following general rationale: (a) indicators of in-procedure blood pressure (BP)/BP excursions from the reference value are independent variables of interest. All other potential independent variables serve to improve the control of confounding; (b) the sample size is rather limited, so models can sustain a limited number of independent variables; (c) selection of adjustments needs to follow (i) the nature of the independent variables of interest—they might be affected by procedure duration (i.e., have a "time component"), as well as by the number of measurements taken. BP excursions are defined in respect to reference values; hence, may be influenced by them; (ii) (patho)physiological rationale—certain factors, e.g., stroke severity at presentation (National Institutes of Health Stroke Scale [NIHSS] score), affected vessel(s), existence of leptomeningeal collaterals, use of pharmacological fibrinolysis (recombinant tissue plasminogen activator [rtPA]), the level of achieved reperfusion (Thrombolysis in Cerebral Infarction [TICI] grade [TICI 2b-3=success; TICI 0-2a=failure]) may or are known to reflect on the control computed tomography findings (ischemic lesion volume [ILV], visible hemorrhages) and/or the 3-month functional outcome (modified Rankin Scale [mRS] score 0-2=favorable vs. 3-6=poor); hence, should be accounted for in the analysis of the respective outcomes; (iii) statistical significance—within the sample, some patient characteristics might be a source of confounding although without any obvious biological rationale and should be accounted for simply based on statistical significance; (d) consequently, all models need to include some adjustments by default, while others may be selected based on statistical significance; (e) some interactions need to be evaluated: is the potential effect of BP excursions from the reference value conditional on the reference value?; is it conditional on the level of reperfusion (TICI grade)?; is the potential effect of the reference or in-procedure BP conditional on the level of reperfusion?; (f) there is a risk of overfitting; hence, models should be selected based on biological and statistical plausibility.

The logic and algorithm of model selection is depicted in Figure A. For all outcomes, i.e., imaging (intermediate) (ILV, post-procedure hemorrhages) and the primary clinical endpoint (mRS score 0-2), the procedure started by fitting "full" models including a range of default and selected variables. The initial model contained only main effects and further models sequentially tested interactions of interest. In the next step, models were "reduced" to keep independent variables of interest and biologically and statistically plausible covariates required to demonstrate hypothesized independent associations or lack of such associations. Imaging outcomes were considered as independent variables in the analysis of the 3-month mRS, but were not included in the full models; they were introduced to "reduced" models. Hence, model selection in the analysis of the primary clinical endpoint included a further step of selecting the "final" models.

All full models included the following same "base" default independent variables: rate of excursions to >120% and to <80% of the reference BP, reference BP, weighted mean in-procedure BP, procedure duration (may also be a "proxy" of a more severe stroke/larger occlusion), number of in-procedure BP measurements, reperfusion success (TICI grade 2b-3 or 0-2a), existence of leptomeningeal collaterals ≥50% as on the unaffected side, on-admission NIHSS score and whether antihypertensive treatment was administered between admission and endovascular thrombectomy (EVT). Since data on the initial infarct volume were not available, we considered that on-admission NIHSS could be reasonably considered an independent that largely included (subsumed) the impact of the initial volume. We included also the use of antihypertensives between admission and EVT based on the following reasoning: decision to administer antihypertensives and subsequent (during EVT) decision to keep BP at lower levels/prevent excursions to higher values might have been guided by a larger (initial) infarct volume in order to prevent hemorrhagic transformation, and hence a spurious association between "better outcomes" (ILV, hemorrhages, 3-month functional outcome) and higher in-procedure BP, or "poorer outcomes" and lower in-procedure BP could be inferred. Therefore, on-admission NIHSS and use of antihypertensives between admission and EVT served as a kind of "proxy" to subsume the initial volume effects. A separate detailed analysis of on-admission BP, use of antihypertensives before EVT, use of sympathomimetics during EVT, weighted mean in-procedure BP and BP excursions was also performed (Supplementary Analysis of Blood Pressure).

In the analysis of the ILV, default adjustments additionally included the type of the affected vessel (middle cerebral artery segment 1 or segment 2, or involvement of internal carotid artery, i.e., tandem occlusion), while in the analysis of the presence of visible hemorrhages this was replaced with the use of rtPA as it seemed more plausible to account for a known risk factor for intracerebral hemorrhage. Only "base" default independent variables were included in the full models analyzing the 3-month functional outcome (probability of mRS 0-2 [vs. 3-6]).

In all full models, considered for inclusion through a stepwise selection procedure (P<0.200 to enter/stay) were: age, sex, comorbidities (hypertension, atrial fibrillation, any form of occlusive arterial disease, diabetes, heart or renal failure), stroke etiology by Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification (dichotomized as cardioembolic or unknown vs. large artery atherosclerosis), time elapsed since symptom onset till the first vessel image, type of the affected vessel (if not by default), use of rtPA (if not by default), use of sympathomimetics during EVT and pre-index stroke statin use. In the analysis of ILV and visible hemorrhages considered were also pre-index stroke use of antiplatelets and anticoagulants, while in the analysis of the 3-month functional outcome post-procedure use of statins was considered instead.

Analysis of the 3-month functional outcome indicated a statistically significant interaction between the rate of BP excursions to >120% of the reference and TICI grade achieved (Figure A), suggesting no association between excursions and the outcome in patients with TICI grade 0-2a and a strong association of a higher rate with higher odds of mRS 0-2 in patients with TICI grade 2b-3 (Supplementary Table 5). Conversely, it indicated no association between TICI 2b-3 and mRS 0-2 in patients with no BP excursions to >120% of the reference, and increasingly stronger association with higher odds of mRS 0-2 with the increasing rate of excursions (Supplementary Table 5, Model final C, D). However, since there were only 40 patients with TICI 0-2a, only 10 of whom achieved mRS 0-2, there is some uncertainty about this interaction. Therefore, two types of "final" models were generated (Figure A): not accounting and accounting for this interaction. We consider that models without the interaction generally better describe the data due to the mentioned uncertainty and: (a) lack of indication that systolic blood pressure (SBP)/mean arterial pressure (MAP) excursions in the subset of patients with TICI 0-2a were harmful—similar proportions of those with mRS 0-2 (4/10, 40% for SBP, 20% for MAP) and those with mRS 3-6 (20/30, 33.3% for SBP, 20% for MAP) had zero BP excursion rates to >120% of the reference; (b) higher reference SBP/MAP was consistently associated with higher odds of mRS 0-2, both in patients with TICI 0-2a and with TICI 2b-3 (Supplementary Table 5); (c) at the start of EVT, TICI outcome is unknown. Present data indicate a potential benefit of higher rates of SBP/MAP excursions to >120% and, at worst, no benefit (but no harm); (d) differences in formal statistical indicators of model fits (Bayesian information criterion [BIC]) between the final models without and with the interaction term were minor (Supplementary Table 5, Models final A and B vs. C and D). Finally, each of these models was fitted without and with an account for ILV (Figure A). Namely, higher ILV was consistently associated with lower odds of mRS 0-2 in the "reduced" and "final" models (Supplementary Table 5), but introduction of ILV had another consequence: strength of association between mRS 0-2 and several independent variables (BP excursion rates to >120%, existence of good collaterals, TICI grade, pre-index stroke statin use) was considerably reduced or the association was no more apparent (Supplementary Table 5). This phenomenon is typical for "mediator" variables and a possibility of mediated (via ILV) associations between BP excursion rates, existence of collaterals and TICI grade and 3-month mRS 0-2 appeared plausible: all these variables were also independently associated with

ILV (Supplementary Table 3). Mediation analysis was performed specifically to test the hypothesis of an indirect association between in-procedure BP excursions to >120% of the reference and the 3-month functional outcome *via* ILV (BP excursions → ILV → 3-month mRS) with adjustments included in the "reduced" model analyzing ILV and "final" (without interactions) model analyzing mRS 0-2.

	Intermediate (computed tomography [CT]) outcomes		Primary clinical endpoint
Types of models	**Ischemic lesion volume (ILV)**	**Post-procedure visible hemorrhages**	**mRS at 3 months 0-2 (vs. 3-6)**
FULL **Initial:** default and selected independents, main effects, no interactions **Sequentially testing interactions:** a) rate of BP excursions*reference BP; b) rate of excursions*TICI grade; c) reference BP*TICI, in-procedure mean BP*TICI	• **Default:** rate of BP excursions to >120% of the reference, rate of excursions to <80%, reference BP, in-procedure mean BP, EVT duration, number of BP measurements taken, on-admission NIHSS score, TICI grade, affected vessel, collaterals ≥50% as unaffected side, use of antihypertensives before EVT • **Selected:** sex	• **Default:** rate of BP excursions to >120% of the reference, rate of excursions to <80%, reference BP, in-procedure mean BP, EVT duration, number of BP measurements taken, on-admission NIHSS score, TICI grade, use of antihypertensives before EVT • **Selected:** stroke etiology, history of coronary artery disease	• **Default:** rate of BP excursions to >120% of the reference, rate of excursions to <80%, reference BP, in-procedure mean BP, EVT duration, number of BP measurements taken, on-admission NIHSS score, TICI grade, collaterals ≥50% as unaffected side, use of antihypertensives before EVT • **Selected:** stroke etiology, pre-/post-stroke statin use, age
REDUCED Keep: a) excursion rates (primary interest); b) biologically & statistically plausible other effects (default or selected, interactions)	**Kept effects:** rate of BP excursions to >120%, rate of BP excursions to <80%, reference BP, rate to >120%*reference BP interaction, NIHSS score, TICI grade, collaterals, sex	**Kept effects:** rate of BP excursions to >120%, rate of BP excursions to <80%, reference BP, in-procedure mean BP, NIHSS score, TICI grade, stroke etiology, history of coronary artery disease	**A. Without interaction and CT outcomes** **Kept effects:** rate of BP excursions to >120% rate of BP excursions to <80%, reference BP, in-procedure mean BP, NIHSS score, TICI grade, collaterals, stroke etiology, pre-/post-stroke statin use, age **B. Without interaction, with CT outcomes** As A+ILV and hemorrhages **C. With interaction, without CT outcomes** As A+rate to >120%*TICI interaction **D. With interaction and CT outcomes** As C+ILV and hemorrhages
FINAL Further model reduction by final exclusion of the initial default effects and apparently irrelevant CT findings			**A. Without interaction and CT outcomes** **Kept effects:** rate of BP excursions to >120% rate of BP excursions to <80%, reference BP, NIHSS score, TICI grade, collaterals, stroke etiology, pre-/post-stroke statin use, age **B. Without interaction and CT outcomes** As A+ILV **C. With interaction, Without CT outcomes** As A+rate to >120%*TICI interaction **D. With interaction and CT outcomes** As C+ILV

Figure A. Schematic representation of the model selection strategy. All models were fitted separately for systolic blood pressure and mean arterial pressure. mRS, modified Rankin Scale; BP, blood pressure; TICI, Thrombolysis in Cerebral Infarction; EVT, endovascular thrombectomy; NIHSS, National Institutes of Health Stroke Scale; rtPA, recombinant tissue plasminogen activator.

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