Baseline Blood Pressure Effect on the Benefit and Safety of Intra-Arterial Treatment in MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands)

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Background and Purpose—High blood pressure (BP) is associated with poor outcome and the occurrence of symptomatic intracranial hemorrhage in acute ischemic stroke. Whether BP influences the benefit or safety of intra-arterial treatment (IAT) is not known. We aimed to assess the relation of BP with functional outcome, occurrence of symptomatic intracranial hemorrhage and effect of IAT.

Methods—This is a post hoc analysis of the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands). BP was measured at baseline, before IAT or stroke unit admission. We estimated the association of baseline BP with the score on the modified Rankin Scale at 90 days and safety parameters with ordinal and logistic regression analysis. Effect of BP on the effect of IAT was tested with multiplicative interaction terms.

Results—Systolic BP (SBP) had the best correlation with functional outcome. This correlation was U-shaped; both low and high baseline SBP were associated with poor functional outcome. Higher SBP was associated with symptomatic intracranial hemorrhage (adjusted odds ratio, 1.25 for every 10 mm Hg higher SBP [95% confidence interval, 1.09–1.44]). Between SBP and IAT, there was no interaction for functional outcome, symptomatic intracranial hemorrhage, or other safety parameters; the absolute benefit of IAT was evident for the whole SBP range. The same was found for diastolic BP.

Conclusions—BP does not affect the benefit or safety of IAT in patients with acute ischemic stroke caused by proximal intracranial vessel occlusion. Our data provide no arguments to withhold or delay IAT based on BP.


Key Words: blood pressure ■ endovascular treatment ■ hypertension ■ ischemic stroke ■ thrombectomy

See related article, p 1717

Both low and high blood pressure (BP) are associated with poor functional outcome in acute ischemic stroke.1,2 The combination of reperfusion therapy and high BP may increase the risk of symptomatic intracranial hemorrhage (SICH).3–7 The American Heart Association/American Stroke Association (AHA/ASA) acute ischemic stroke guidelines recommend a BP threshold of 185/110 mmHg for intravenous thrombectomy.
thrombolysis (IVT) candidates. There is no consensus on how to proceed in patients with a BP above this IVT threshold: withhold IVT, delay IVT until BP spontaneously decreases or administer acute BP-lowering treatment.

Intra-arterial treatment (IAT) by means of stent thrombectomy for patients with acute ischemic stroke and a proximal arterial occlusion in the anterior circulation is highly effective. The average increase in likelihood of good functional outcome at 90 days after IAT is 19.5%. Three studies suggest that high BP is a risk factor for poor outcome and SICH in patients treated with IAT. It is currently unknown whether BP interacts with IAT effect.

The aim of this study was to assess the relation between BP before IAT with functional outcome and safety parameters and to assess whether BP affects the benefit and safety of IAT.

Methods
This is a post hoc analysis of data of the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands). The trial design and patient eligibility criteria have been reported previously. In short, MR CLEAN was a randomized clinical trial of IAT versus no IAT along with usual medical care in patients with a proximal intracranial arterial occlusion in the anterior circulation, who could be treated within 6 hours after symptom onset. Background medical management was delivered according to national standards and guidelines, and could include treatment with IVT within the first 4.5 hours after onset of symptoms.

Systolic BP (SBP) and diastolic BP (DBP) were measured at baseline, before emergency room admission and start of IAT (intervention arm) or stroke unit admission (control arm). Mean arterial pressure (MAP) was calculated using the following formula: MAP = (2xDBP+SBP)/3. Routine BP measurements were used. There were no detailed instructions for measurements, but all centers used automated BP measurement in the emergency room and stroke unit. BP >185/110 mm Hg was an exclusion criterion for entry into the study and this was registered prospectively. The MR CLEAN study protocol provided no recommendations on whether and how to treat BP exceeding 185/110 mm Hg in included patients, but treatment was allowed.

All patients or their legal representatives provided written informed consent before randomization. A central medical ethics committee and the research board of each participating center approved the study protocol.

Outcome and Safety Measures
The primary analysis was interaction assessment between BP and IAT effect on the primary outcome of the trial, the modified Rankin Score (mRS) score at 90 days. Furthermore, interaction was assessed between BP and IAT on secondary clinical and radiological outcome measures. Secondary clinical outcome measures were functional independence (mRS 0–2) at 90 days, stroke severity at 5 to 7 days or discharge, if earlier, with the National Institutes of Health Stroke Score (NIHSS), and the Barthel Index. Radiological outcome measures included arterial recanalization measured with computed tomographic angiography or magnetic resonance angiogram at 24 hours, and infarct volume on noncontrast CT at 5 to 7 days. In patients with IAT, the modified thrombolysis in cerebral infarction (mTICI) score on digital subtraction angiography was used to assess reperfusion. The mTICI score is a 5-point scale, which ranges from 0 (no reperfusion) to 3 (complete antegrade reperfusion of the previously ischemic territory, with the absence of visualized occlusion in all distal branches).

Interaction between BP and IAT on safety parameters was also tested. Safety parameters included death, hemicraniectomy, SICH, and progression of ischemic stroke. SICH was defined as neurologic deterioration of 4 or more points on the NIHSS and neuroimaging confirming intracranial hemorrhage. We used the ECASS III (European Cooperative Acute Stroke Study) classification of intracranial hemorrhage. Progression of ischemic stroke was defined as neurologic deterioration with an increase of 2 or more points on the NIHSS, with follow-up brain CT or magnetic resonance imaging compatible with a diagnosis of ischemia and without other causes for neurologic deterioration.

Statistical Analysis
Patients were analyzed according to the “intention to treat” principle. All interaction and logistic regression analyses were adjusted for potential imbalances in prognostic variables at baseline; age, NIHSS, and collateral score. Adjusted odds ratios (ORs) are reported with 95% confidence intervals (CIs). All P values are 2-sided. Statistical analyses were performed with Stata/SE 14.1 (Stata Corp, College Station, TX). All analyses were done in the total MR CLEAN patient group.

Statistical Analysis of BP and Outcome
To assess whether the relation between BP and outcome was nonlinear, we used squared terms, restricted cubic spline, and fractional polynomials. We tested which model best fitted the data with the delta log likelihood ratio as the test statistic. The model that best fitted the relation of BP with functional outcome was used for further analysis. The log likelihood ratios were further used to assess which BP measurement (SBP, DBP, or MAP) had the strongest correlation with functional outcome. The nadir identified by the nonlinear models was used to divide the population in 2 subgroups. The effect of BP on outcome was estimated separately in these 2 subgroups with regression models. The effect of BP on functional outcome in these subgroups was determined using logistic regression.

Statistical Analysis of Baseline BP and Effect of IAT
The interaction between BP and IAT was tested with multivariable ordinal logistic regression analysis with an interaction term. We computed (common) ORs per 10 mm Hg SBP increase to assess the relation of SBP with the outcome on the mRS; full scale (ordinal regression analysis) and dichotomized (mRS 0–2 versus 3–6, logistic regression analysis). The absolute benefit of IAT for different BP values was computed using the estimated probability of good functional outcome (mRS 0–2) for the intervention and control arm.

Results
Patient Characteristics
For all 500 patients included in the trial, BP was measured and entered into the database. Mean baseline SBP (SD) was 145 mm Hg (±25), mean DBP was 82 mm Hg (±15), and mean MAP was 103 mm Hg (±16). Most SBP values were between 105 and 200 mm Hg (Figure I in the online-only Data Supplement). Four patients (1%) were included in the study, despite a BP of >185/110 mm Hg at randomization. In 29 additional patients, baseline BP was >185/110 mm Hg. In these 33 patients (7%), SBP alone exceeded the threshold value in 21 patients, DBP alone in 5 patients and both SBP and DBP in 7 patients. Of these 33 patients, 8 patients (24%) were acutely treated with antihypertensive therapy, 7 patients (21%) had a spontaneous reduction in BP to ≤185/110 mm Hg without treatment, and of the remaining 18 patients (55%), the BP course and possible BP-lowering treatment were not recorded.
Baseline BP and Outcome
The association between BP and functional outcome (ordinal mRS) was best fitted using fractional polynomial regression analysis. SBP had better correlation with functional outcome than MAP and DBP (P<0.01).

We found a U-shaped relation between SBP and functional outcome with the nadir at 120 mm Hg; both low and high SBP were associated with poor functional outcome (Figure 1). The effect of SBP on functional outcome was comparable for IAT and control patients (Figure II A and II B in the online-only Data Supplement). There was a U-shaped relation of SBP with good functional outcome (mRS 0–2) and death at 90 days, with the nadir around 120 mm Hg (Figure III A and III B in the online-only Data Supplement). The associations of MAP and DBP with functional outcome were also concave, but for DBP, there was no evident relation of lower DBP with poor functional outcome (Figure IVA and IV B in the online-only Data Supplement).

On the basis of the nadir of the U-shape, 2 SBP subgroups were created (<120 and ≥120 mm Hg). In 69 patients (14%), SBP was lower than 120 mm Hg (Figure V in the online-only Data Supplement). Patients with SBP ≥120 mm Hg were on an average age of 6 years (P<0.001), smoked less often (14%; P=0.02), and more often had a history of hypertension (19%; P=0.01) or diabetes mellitus (9%; P=0.04) than patients having an SBP lower than 120 mm Hg (Table 1). Baseline characteristics of IAT and control patients were similar for the 2 SBP subgroups except for previous use of anticoagulant medication (IAT: 19% versus control: 0%) or diabetes mellitus (9%; P=0.01) or previous use of anticoagulant medication (IAT: 19% versus control: 0%).

In patients with SBP <120 mm Hg, lower SBP was associated with poor functional outcome (10 mm Hg lower SBP; adjusted common odds ratio [acOR]=0.63 [95% CI, 0.42–0.94]). In these patients, the likelihood of good functional outcome (mRS 0–2) decreased with 39% for each 10 mm Hg lower SBP. In patients with an SBP of ≥120 mm Hg, higher SBP was associated with poor functional outcome (acOR=0.83 [95% CI, 0.7–0.9] per 10 mm Hg SBP). In these patients, the likelihood of good functional outcome (mRS 0–2) decreased with 19% for each 10 mm Hg higher SBP. Death and other serious adverse events occurred more often in the SBP ≥120 mm Hg group. Higher SBP was associated with a higher probability of SICH (Figure IIIC in the online-only Data Supplement). For every 10 mm Hg higher SBP, the acOR for SICH was 1.25 (95% CI, 1.09–1.44), resulting in a 21% increased SICH likelihood.

Baseline BP and Effect of IAT
We found no interaction between SBP and the effect of IAT on functional outcome (P=0.90). The effect of SBP on outcome was the same in the control group (acOR=0.88 [95% CI, 0.80–1.00] per 10 mm Hg SBP increase) as in the intervention group (acOR=0.88 [95% CI, 0.79–0.98] per 10 mm Hg SBP increase). The association of SBP with good functional outcome (mRS 0–2) was similar in the control group (acOR=0.84 [95% CI, 0.73–0.98] per 10 mm Hg SBP increase) as in the intervention group (acOR=0.90 [95% CI, 0.77–1.04] per 10 mm Hg SBP increase). There was also no interaction between SBP and IAT for secondary clinical and radiological outcomes (Table 2). Figure 2 shows the association of high SBP with poor functional outcome for both treatment arms. The absolute effect of IAT is evident for every SBP quintile and there was no difference in the relative effect (P interaction=0.52). Furthermore, there was no association between SBP and reperfusion after intervention (P=0.56). In addition, SBP did not influence IAT effect on the occurrence of SICH (P=0.80) or any other safety parameter (Table 3). For DBP, there were comparable findings: no interaction between DBP and the effect of IAT on functional outcome (P=0.48), secondary outcomes or safety parameters (Tables I and II in the online-only Data Supplement).

Discussion
To our knowledge, this is the first study to assess the relation between BP and the effect of IAT. Our most important finding was that baseline BP does not change IAT effectiveness and does not interact with IAT on functional outcome and safety parameters.

We confirmed the strong association between SBP and functional outcome in ischemic stroke. This association was U-shaped; both low and high baseline SBP were associated with poor functional outcome. Furthermore, higher SBP was associated with an increased risk of SICH. Despite these associations, baseline BP did not change IAT effectiveness or safety.

Baseline BP and Outcome
We found a U-shaped relation of BP with functional outcome, with the nadir around 120 mm Hg. There were comparable shapes and inflection points for SBP relation with mortality and good functional outcome. Previous studies investigating BP relation with outcome, specifically in acute ischemic stroke, also showed that both low and high BP were associated with poor functional outcome.1,2
Table 1. Clinical Characteristics of Systolic Blood Pressure Subgroups With 120 mm Hg as Reference Point

<table>
<thead>
<tr>
<th></th>
<th>SBP&lt;120 mm Hg</th>
<th>SBP≥120 mm Hg</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (IQR)</td>
<td>60 (45–69)</td>
<td>66 (56–77)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>34 (49%)</td>
<td>258 (60%)</td>
<td>0.10</td>
</tr>
<tr>
<td>NIHSS, median (IQR)*</td>
<td>17 (13–21)</td>
<td>18 (14–22)</td>
<td>0.62</td>
</tr>
<tr>
<td>Clinical localization: left hemisphere, n (%)</td>
<td>41 (59%)</td>
<td>228 (53%)</td>
<td>0.31</td>
</tr>
<tr>
<td>SBP, mean, mm Hg (SD)</td>
<td>110±8</td>
<td>151±22</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Intravenous alteplase treatment, n (%)</td>
<td>60 (87%)</td>
<td>385 (89%)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

**Medical history**

<table>
<thead>
<tr>
<th>Medical history</th>
<th>SBP&lt;120 mm Hg</th>
<th>SBP≥120 mm Hg</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>14 (20%)</td>
<td>121 (28%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Ischemic stroke, n (%)</td>
<td>5 (7%)</td>
<td>49 (11%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>20 (29%)</td>
<td>207 (48%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>4 (6%)</td>
<td>64 (15%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>10 (14%)</td>
<td>65 (15%)</td>
<td>0.90</td>
</tr>
<tr>
<td>Peripheral artery disease, n (%)</td>
<td>3 (4%)</td>
<td>21 (5%)</td>
<td>0.85</td>
</tr>
<tr>
<td>Pre-stroke modified Rankin Scale score, n (%)</td>
<td>0.58</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

|                               |               |               |         |
| 0                             | 55 (80%)      | 349 (81%)     |         |
| 1                             | 7 (10%)       | 43 (10%)      |         |
| 2                             | 6 (9%)        | 19 (4%)       |         |
| >2                            | 1 (1%)        | 20 (5%)       |         |

**Medication and intoxications**

<table>
<thead>
<tr>
<th>Medication and intoxications</th>
<th>SBP&lt;120 mm Hg</th>
<th>SBP≥120 mm Hg</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smoking, n (%)</td>
<td>28 (41%)</td>
<td>115 (27%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Statin use, n (%)</td>
<td>22 (32%)</td>
<td>121 (28%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Antiplatelet use, n (%)</td>
<td>16 (23%)</td>
<td>128 (30%)</td>
<td>0.27</td>
</tr>
<tr>
<td>Anticoagulant use, n (%)</td>
<td>6 (9%)</td>
<td>33 (8%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Antihypertensive medication use, n (%)</td>
<td>28 (41%)</td>
<td>214 (50%)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

**Imaging**

<table>
<thead>
<tr>
<th>Imaging</th>
<th>SBP&lt;120 mm Hg</th>
<th>SBP≥120 mm Hg</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASPECTS on NCCT, median (IQR)†</td>
<td>9 (8–10)</td>
<td>9 (8–10)</td>
<td>0.92</td>
</tr>
<tr>
<td>Level of occlusion on noninvasive vessel imaging, n (%)‡</td>
<td>0.84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICA</td>
<td>1 (1%)</td>
<td>3 (1%)</td>
<td></td>
</tr>
<tr>
<td>ICA-T</td>
<td>20 (29%)</td>
<td>114 (27%)</td>
<td></td>
</tr>
<tr>
<td>M1</td>
<td>44 (64%)</td>
<td>275 (64%)</td>
<td></td>
</tr>
<tr>
<td>M2</td>
<td>4 (6%)</td>
<td>35 (8%)</td>
<td></td>
</tr>
<tr>
<td>A1</td>
<td>0</td>
<td>3 (1%)</td>
<td></td>
</tr>
</tbody>
</table>

**Collateral score on CTA, median (IQR)§**

|                               |               |               |         |
| 2                             | 2 (2–3)       | 2 (1–3)       | 0.27    |

**Workflow**

<table>
<thead>
<tr>
<th>Workflow</th>
<th>SBP&lt;120 mm Hg</th>
<th>SBP≥120 mm Hg</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset to SEH (min, median (IQR)</td>
<td>72 (45–175)</td>
<td>101 (49–200)</td>
<td>0.12</td>
</tr>
<tr>
<td>Onset to intravenous alteplase (min, median (IQR)</td>
<td>79 (64–108)</td>
<td>86 (66–112)</td>
<td>0.35</td>
</tr>
<tr>
<td>Onset to randomization (min,median (IQR)</td>
<td>179 (146–237)</td>
<td>202 (152–265)</td>
<td>0.09</td>
</tr>
<tr>
<td>Onset to IAT (min, median (IQR)</td>
<td>245 (230–290)</td>
<td>265 (210–315)</td>
<td>0.85</td>
</tr>
<tr>
<td>Onset to reperfusion (min, median (IQR)</td>
<td>316 (291–351)</td>
<td>342 (264–397)</td>
<td>0.93</td>
</tr>
<tr>
<td>Duration of procedure (min, median (IQR)</td>
<td>69 (48–101)</td>
<td>71 (51–95)</td>
<td>0.88</td>
</tr>
</tbody>
</table>

IAT indicates intra-arterial treatment; ICA-T, internal carotid artery tandem; CTA, computed tomographic angiography; IQR, interquartile range; NCCT, noncontrast CT; and SBP, systolic blood pressure.

*Scores on the National Institutes of Health Stroke Scale (NIHSS). The NIHSS is a 15-item scale. Values for 30 of the 7500 items were missing (0.4%).
†The Alberta Stroke Program Early Computed Tomography Score (ASPECTS). Noncontrast computed tomography was not performed in 1 patient, and three patients had strokes in the territory of the anterior cerebral artery.
‡Vessel imaging was not performed in 1 patient.
§Missing in 6 patients because of CTA not performed or of insufficient quality.
Of the 3 previous studies on BP and outcome after IAT, one did not investigate the relation of BP with functional outcome, the second study found that higher SBP was associated with poor functional outcome after IAT, and the third study found SBP not to be a predictor of outcome after multivariable analysis. The second and the third study did not test for nonlinearity. All studies were not designed to assess interaction of BP with treatment effect because there was no control group without IAT.

Our data provide no insight in the treatment of certain BP levels in the acute phase; an increased BP may be an effective response in patients with intracranial large vessel occlusion, and we cannot predict what will happen when we artificially lower BP. Randomized trials of BP lowering in these patients are clearly warranted, as it concerns a strong prognostic factor and the clinical context is different from previous, neutral trials of BP lowering.

Our study showed that higher SBP increased the risk of SICH. There were no SICHS in the <120 mm Hg group. These data are in line with the studies of randomized IVT trials that found high BP to be associated with SICH. We found no interaction of baseline BP with IAT on SICH or other safety parameters, so IAT may be considered safe, independently of BP.

**Baseline BP and Effect of IAT**

Our analysis emphasizes that the effect of IAT is evident for the whole BP range despite the strong relation of BP with functional outcome. In addition, BP did not influence IAT effect on the occurrence of SICH or any other safety parameter. Most SBP values were within a 105 to 200 mm Hg range. Our data provide no argument that within this range, the effect of IAT diminishes or IAT may even be harmful.

The BP threshold for IVT candidates was established during the pilot study preceding the NINDS trial. Therefore, it was used in the NINDS trial. Since then, AHA/ASA acute ischemic stroke guidelines recommend this BP threshold for IVT candidates. There is overwhelming evidence of the association of high BP with poor outcome in acute ischemic stroke. This is true for acute ischemic stroke patients treated with and without IVT. In only one of these studies, IST3 (International Stroke Trial), the interaction between BP and IVT on outcome was analyzed. The association between BP and functional outcome or occurrence of SICH was not affected by IVT in this study. Further analyses in large IVT trials could shed more light on this subject and specifically on the appropriateness of this BP threshold.

The first guideline update on IAT does not state whether a certain BP threshold should be used in IAT candidates. Our data provide no evidence for a BP threshold in IAT candidates, at least within the range of 105 to 200 mm Hg. As this is the first
study to investigate the relation of BP with IAT effect, we aim to
do a similar analysis in the pooled individual patient data of the
HERMES collaboration. This data set contains patient data of 7
trials with now more than 1700 patients in total.11–17

Limitations
There were only 69 patients with an SBP of <120 mmHg, which has led to limited precision of our association estimates,
especially at the lower end of the SBP range. However, it is
clinically acceptable to assume that in acute ischemic stroke
with low SBP (<80 mmHg), functional outcome will be poor. Auto regulation at this low level may be disturbed, and
required perfusion pressure will probably not be reached.39

Four patients in MR CLEAN had a BP exceeding 185/110
mmHg at randomization. Consequently, they should be con-
sidered protocol violations. These patients were included in
the main paper and in this study, according to the intention
to treat principle. In total, 33 of the 500 patients (7%) had a
baseline BP of >185/110 mm Hg. As few patients (5%) in MR
CLEAN had an SBP <105 mm Hg or >200 mm Hg, uncer-
tainty on IAT effect remains outside this SBP range.

Unfortunately, details about the course of BP during or after
intervention are not available in our patients. Also, we had no
data on the time interval between BP measurement and groin
puncture. Nevertheless, even with one inherently inaccurate
measurement, we found a strong association with outcome.
Multiple measurements will probably result in precise esti-
mates and provide more precise estimates. Further studies
should provide more insight in: the interplay between BP rise
and fall during intervention; the relation between BP, collater-
als and ischemic core; and the risk of hemorrhage.

Conclusions
In patients with acute ischemic stroke due to proximal intra-
cranial vessel occlusion, baseline BP does not affect the ben-
efit or safety of IAT, although BP is an independent prognostic
factor of poor outcome in these patients. Our data provide no
to arguments to withhold or delay IAT because of high BP.

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Appendix

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References


Baseline Blood Pressure Effect on the Benefit and Safety of Intra-Arterial Treatment in MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands)


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/content/48/7/e187.full.pdf

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Correction to: Baseline Blood Pressure Effect on the Benefit and Safety of Intra-Arterial Treatment in MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands)

In the article by Mulder et al, “Baseline Blood Pressure Effect on the Benefit and Safety of Intra-Arterial Treatment in MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands),” which published online ahead of print on April 21, 2017, and appeared in the July 2017 issue of the journal (Stroke. 2017;48:1869–1876. DOI: 10.1161/STROKEAHA.116.016225), corrections are needed.

1. On page 1870, in the last sentence of the 6th paragraph, the citation to reference 24 was deleted.
2. On page 1873, in the next to last paragraph, citation to reference 36 was changed to 34.

This correction has been made to the issue and to the current online version of the article, which is available at http://stroke.ahajournals.org/content/48/7/1869.
Supplementary Figure I. Distribution of systolic blood pressure in total MR CLEAN population. 95% of baseline blood pressures were within 105-200 mm Hg range (grey vertical lines).
Supplemental Figure II. Relationship of systolic blood pressure (SBP) with functional outcome (modified Rankin Scale (mRS) at 90 days); in the control group (A) and the intra-arterial treatment group (B).
Supplemental Figure III. Relationship of systolic blood pressure with good functional outcome, defined as modified Rankin Scale (mRS) of 0-2 at 90 days (A), mortality at 90 days (B), and occurrence of symptomatic intracranial hemorrhage (SICH; C).
**Supplemental Figure IV.** Relationship of diastolic blood pressure (DBP; A) and mean arterial blood pressure (MAP; B) with functional outcome (modified Rankin Scale (mRS) at 90 days).
Supplemental Figure V. Treatment allocation and systolic blood pressure (SBP) in the MR CLEAN trial.
**Supplemental Table I.** Interaction between diastolic blood pressure and intra-arterial treatment on primary and secondary outcomes. Intra-arterial treatment interaction effects were computed with ordinal logistic regression using the total systolic blood pressure range (adjusted for age, NIHSS and collateral score).

<table>
<thead>
<tr>
<th></th>
<th>Treatment interaction p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRS at 90 days – median (IQR)</td>
<td>0.48</td>
</tr>
<tr>
<td>mRS 0-2 at 90 days – n. (%)</td>
<td>0.91</td>
</tr>
<tr>
<td>NIHSS at 5-7 days or discharge - median (IQR)*</td>
<td>0.48</td>
</tr>
<tr>
<td>Barthel Index 19-20 at 90 days – n./total n. (%)</td>
<td>0.84</td>
</tr>
<tr>
<td>No intracranial occlusion on follow-up CTA – n./ total n. (%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Final infarct volume on follow-up NCCT total n. – median (IQR)†</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Abbreviations: mRS = modified Rankin Scale; NIHSS = National Institutes of Health Stroke Scale; mTICI = modified Thrombolysis in Cerebral Infarction; CTA = Computed Tomography Angiography; NCCT = Non Contrast Computed Tomography

* Scored in survivors only (56 died), 18 missing
† Final infarct volume on NCCT after 5 days (range 3-9 days)
**Supplemental Table II.** Interaction between diastolic blood pressure and intra-arterial treatment on safety parameters. Intra-arterial treatment interaction effects were computed with ordinal logistic regression using the total systolic blood pressure range (adjusted for age, NIHSS and collateral score).

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Treatment interaction (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death within 90 days - n (%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Hemicraniectomy – n (%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Symptomatic ICH - n (%)</td>
<td>0.92</td>
</tr>
<tr>
<td>Parenchymal hematoma type 1</td>
<td>-†</td>
</tr>
<tr>
<td>Parenchymal hematoma type 2</td>
<td>0.47</td>
</tr>
<tr>
<td>Hemorrhagic infarction type 1</td>
<td>-†</td>
</tr>
<tr>
<td>Hemorrhagic infarction type 2</td>
<td>0.60</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>†</td>
</tr>
<tr>
<td>Progression of Ischemic stroke - n (%)</td>
<td>0.84</td>
</tr>
</tbody>
</table>

Abbreviation: ICH = Intra Cerebral Hemorrhage, NA = not applicable
*Only first events of one type are listed. Patients experiencing multiple events of one type have been counted once.
†Too few events for interaction analysis
Appendix

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