

Supplemental material

Intra-arterial thrombolytics during endovascular thrombectomy for acute ischemic stroke in the MR CLEAN Registry

Sabine L. Collette, Reinoud P.H. Bokkers, Aryan Mazuri, Geert J. Lycklama à Nijeholt, Robert J. van Oostenbrugge, Natalie E. LeCouffe, Faysal Benali, Charles B.L.M. Majoie, Jan Cees de Groot, Gert Jan R. Luijckx, Maarten Uyttenboogaart; on behalf of the MR CLEAN Registry investigators.

Figure S1. Stratified analyses of the primary outcome

Table S1. Distribution of revascularization attempts and occlusion locations

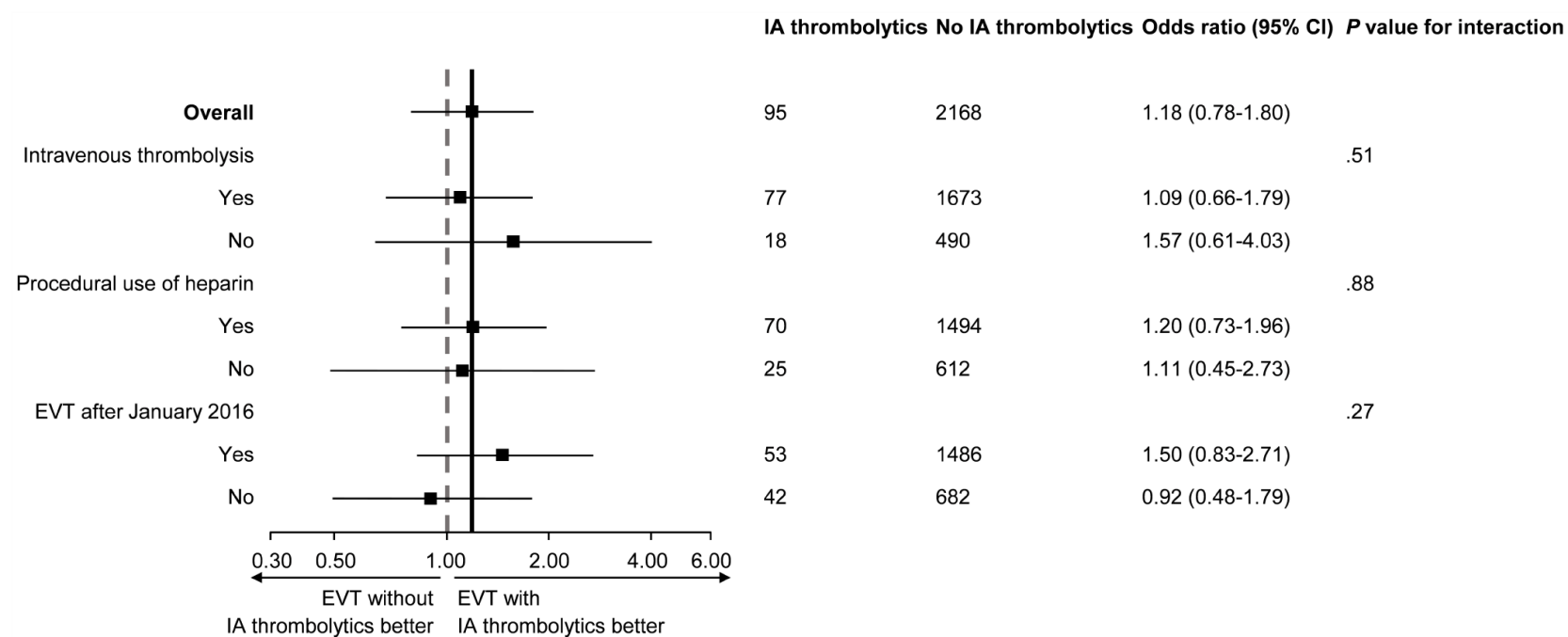
Table S2. Baseline characteristics

Table S3. Procedural variables

Table S4. Baseline characteristics

Table S5. Procedural variables

Supplemental Appendix. MR CLEAN Registry Investigators – group authors

Figure S1. Stratified analyses of the primary outcome

EVT, endovascular thrombectomy; IA, intra-arterial.

CI, confidence interval.

The forest plot shows the odds ratios for favorable functional outcome (defined as modified Rankin Scale score ≤ 2) at 90 days across the prespecified subgroups. The dashed vertical line indicates no effect. The solid vertical line indicates the overall effect.

Table S1. Distribution of revascularization attempts and occlusion locations

| Location | Primary attempt (n=26) | Adjuvant attempt (n=60) |
|---------------------------|-------------------------------|--------------------------------|
| Proximal occlusion | 18/26 (69.2) | 47/60 (78.3) |
| ICA | 0 (0) | 2/60 (3.3) |
| M1 | 7/26 (26.9) | 18/60 (30.0) |
| M2 | 11/26 (42.3) | 20/60 (33.3) |
| A1 | 0 (0) | 1/60 (1.7) |
| A2 | 0 (0) | 5/60 (8.3) |
| ACOM | 0 (0) | 1/60 (1.7) |
| Distal occlusion | 8/26 (30.8) | 13/60 (21.7) |
| M3 | 5/26 (19.2) | 8/60 (13.3) |
| M4 | 2/26 (7.7) | 1/60 (1.7) |
| A3 | 1/26 (3.8) | 3/60 (5.0) |
| PCOM and P1 | 0 (0) | 1/60 (1.7) |

A1, anterior cerebral artery, first segment; A2, anterior cerebral artery, second segment; A3, anterior cerebral artery, third segment; ACOM, anterior communicating artery; ICA, internal carotid artery; M1, middle cerebral artery, first segment; M2, middle cerebral artery, second segment; M3, middle cerebral artery, third segment; M4, middle cerebral artery, fourth segment; P1, posterior cerebral artery, first segment; PCOM, posterior communicating artery.

Table S2. Baseline characteristics

| Characteristics | Primary attempt (n=26) | Adjuvant attempt (n=65) | P value |
|--|---------------------------|----------------------------|---------|
| Age, median (IQR), years | 66 (53-77) | 67 (56-74) | .99 |
| Male, n (%) | 15/26 (58) | 32/65 (50) | .47 |
| Medical history, n (%) | | | |
| Atrial fibrillation | 7/26 (26.9) | 6/65 (9.2) | .05 |
| Diabetes mellitus | 2/26 (7.7) | 7/65 (10.8) | >.99 |
| Hypercholesterolemia | 5/26 (19.2) | 17/65 (26.2) | .49 |
| Hypertension | 11/26 (42.3) | 28/65 (43.1) | .95 |
| Myocardial infarction | 5/26 (19.2) | 6/65 (9.2) | .28 |
| Previous stroke | 4/26 (15.4) | 4/65 (6.2) | .22 |
| Current smoker, n (%) | 9/19 (47.4) | 16/48 (33.3) | .28 |
| Use of antiplatelet, n (%) | 9/26 (34.6) | 16/65 (24.6) | .33 |
| Use of anticoagulation, n (%) | 5/26 (19.2) | 2/65 (3.1) | .02 |
| Initial location occlusion on CTA, n (%) | | | |
| Left hemisphere | 19/26 (73.1) | 37/65 (56.9) | .15 |
| Intracranial ICA | 6/26 (23.1) | 24/65 (36.9) | .45 |
| M1 | 14/26 (53.8) | 29/65 (44.6) | |
| M2 | 6/26 (23.1) | 12/65 (18.5) | |
| A1 | 0/26 (0) | 0/65 (0) | |
| A2 | 0/26 (0) | 0/65 (0) | |
| Collateral status, n (%) | | | .64 |
| Absent collaterals | 1/25 (4.0) | 5/62 (8.1) | |
| <50% of occluded area | 10/25 (40.0) | 21/62 (33.9) | |
| 50-99% of occluded area | 10/25 (40.0) | 20/62 (32.3) | |
| 100% of occluded area | 4/25 (16.0) | 16/62 (25.8) | |
| NIHSS score, median (IQR) | 14 (7-17) | 17 (11-20) | .08 |
| Intravenous thrombolysis, n (%) | 20/26 (76.9) | 54/65 (83.1) | .56 |
| Pre-intervention SBP, mean (SD), mm Hg | 155 (26) | 150 (27) | .44 |

A1, anterior cerebral artery, first segment; A2, anterior cerebral artery, second segment; CTA, computed tomography angiography; ICA, internal carotid artery; M1, middle cerebral artery, first segment; M2, middle cerebral artery, second segment; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

IQR, interquartile range; n, number; SD, standard deviation.

Table S3. Procedural variables

| Characteristics | Primary attempt (n=26) | Adjuvant attempt (n=65) | P value |
|--|-----------------------------------|------------------------------------|----------------|
| IA thrombolytics, <i>n</i> (%) | | | .62 |
| Urokinase | 17/26 (65.4) | 46/65 (70.8) | |
| Alteplase | 9/26 (34.6) | 19/65 (29.2) | |
| Dose IA thrombolytics, <i>median (IQR)</i> | | | |
| Urokinase, IU | 250,000 (125,000-375,000) | 250,000 (200,000-250,000) | .94 |
| Alteplase, mg | 20 (10-20) | 20 (16-20) | .75 |
| General anesthesia, <i>n</i> (%) | 9/25 (36.0) | 23/61 (37.7) | .88 |
| Time from stroke onset to groin puncture, <i>median (IQR)</i> , minutes | 193 (152-245) | 205 (158-254) | .56 |
| Time from groin puncture to recanalization or last contrast bolus, <i>median (IQR)</i> , minutes | 65 (45-75) | 80 (65-118) | .01 |

IA, intra-arterial.

IQR, interquartile range; n, number.

Table S4. Baseline characteristics

| Characteristics | Proximal occlusion (n=67) | Distal occlusion (n=21) | P value |
|--|--------------------------------------|------------------------------------|----------------|
| Age, median (IQR), years | 69 (56-77) | 65 (57-74) | .50 |
| Male, n (%) | 37/67 (56) | 9/21 (43) | .32 |
| Medical history, n (%) | | | |
| Atrial fibrillation | 8/67 (11.9) | 5/21 (23.8) | .29 |
| Diabetes mellitus | 6/67 (9.0) | 3/21 (14.3) | .44 |
| Hypercholesterolemia | 19/67 (28.4) | 3/21 (14.3) | .19 |
| Hypertension | 29/67 (43.3) | 11/21 (52.4) | .47 |
| Myocardial infarction | 10/67 (14.9) | 2/21 (9.5) | .72 |
| Previous stroke | 5/67 (7.5) | 3/21 (14.3) | .39 |
| Current smoker, n (%) | 20/50 (40.0) | 3/13 (23.1) | .34 |
| Use of antiplatelet, n (%) | 21/67 (31.3) | 4/21 (19.0) | .28 |
| Use of anticoagulation, n (%) | 7/67 (10.4) | 0/21 (0) | .19 |
| Initial location occlusion on CTA, n (%) | | | |
| Left hemisphere | 37/67 (55.2) | 16/21 (76.2) | .09 |
| Intracranial ICA | 22/67 (32.8) | 6/21 (28.6) | .57 |
| M1 | 33/67 (49.3) | 9/21 (42.9) | |
| M2 | 12/67 (17.9) | 6/21 (28.6) | |
| A1 | 0/67 (0) | 0/21 (0) | |
| A2 | 0/67 (0) | 0/21 (0) | |
| Collateral status, n (%) | | | .57 |
| Absent collaterals | 4/65 (6.2) | 2/19 (10.5) | |
| <50% of occluded area | 22/65 (33.8) | 6/19 (31.6) | |
| 50-99% of occluded area | 26/65 (40.0) | 5/19 (26.3) | |
| 100% of occluded area | 13/65 (20.0) | 6/19 (31.6) | |
| NIHSS score, median (IQR) | 16 (10-19) | 14 (6-19) | .32 |
| Intravenous thrombolysis, n (%) | 53/67 (79.1) | 18/21 (85.7) | .75 |
| Pre-intervention SBP, mean (SD), mm Hg | 149 (25) | 158 (29) | .17 |

A1, anterior cerebral artery, first segment; A2, anterior cerebral artery, second segment; CTA, computed tomography angiography; ICA, internal carotid artery; M1, middle cerebral artery, first segment; M2, middle cerebral artery, second segment; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

IQR, interquartile range; n, number; SD, standard deviation.

Table S5. Procedural variables

| Characteristics | Proximal occlusion (n=67) | Distal occlusion (n=21) | P value |
|--|--------------------------------------|------------------------------------|----------------|
| IA thrombolytics, <i>n</i> (%) | | | .48 |
| Urokinase | 47/67 (70.1) | 13/21 (61.9) | |
| Alteplase | 20/67 (29.9) | 8/21 (38.1) | |
| Dose IA thrombolytics, <i>median (IQR)</i> | | | |
| Urokinase, IU | 250,000 (200,000-375,000) | 200,000 (112,500-250,000) | .04 |
| Alteplase, mg | 20 (12-20) | 20 (15-20) | .77 |
| General anesthesia, <i>n</i> (%) | 23/63 (36.5) | 8/20 (40.0) | .78 |
| Time from stroke onset to groin puncture, <i>median (IQR)</i> , minutes | 195 (145-242) | 225 (193-283) | .04 |
| Time from groin puncture to recanalization or last contrast bolus, <i>median (IQR)</i> , minutes | 70 (55-108) | 78 (64-95) | .58 |

IA, intra-arterial.

IQR, interquartile range; n, number.

Supplemental Appendix. MR CLEAN Registry Investigators – group authors**Executive committee**

Diederik W.J. Dippel¹; Aad van der Lugt²; Charles B.L.M. Majoie³; Yvo B.W.E.M. Roos⁴; Robert J. van Oostenbrugge⁵; Wim H. van Zwam⁶; Jelis Boiten¹⁴; Jan Albert Vos⁸

Study coordinators

Ivo G.H. Jansen³; Maxim J.H.L. Mulder^{1,2}; Robert-Jan B. Goldhoorn^{5,6}; Kars C.J. Compagne²; Manon Kappelhof³; Josje Brouwer⁴; Sanne J. den Hartog^{1,2,40}; Wouter H. Hinsenveld^{5,6}

Local principal investigators

Diederik W.J. Dippel¹; Bob Roozenbeek¹; Aad van der Lugt²; Adriaan C.G.M. van Es²; Charles B.L.M. Majoie³; Yvo B.W.E.M. Roos⁴; Bart J. Emmer³; Jonathan M. Coutinho⁴; Wouter J. Schonewille⁷; Jan Albert Vos⁸; Marieke J.H. Wermer⁹; Marianne A.A. van Walderveen¹⁰; Julie Staals⁵; Robert J. van Oostenbrugge⁵; Wim H. van Zwam⁶; Jeannette Hofmeijer¹¹; Jasper M. Martens¹²; Geert J. Lycklama à Nijeholt¹³; Jelis Boiten¹⁴; Sebastiaan F. de Bruijn¹⁵; Lukas C. van Dijk¹⁶; H. Bart van der Worp¹⁷; Rob H. Lo¹⁸; Ewoud J. van Dijk¹⁹; Hieronymus D. Boogaarts²⁰; J. de Vries²²; Paul L.M. de Kort²¹; Julia van Tuijl²¹; Jo P. Peluso²⁶; Puck Fransen²²; Jan S.P. van den Berg²²; Boudewijn A.A.M. van Hasselt²³; Leo A.M. Aerden²⁴; René J. Dallinga²⁵; Maarten Uyttenboogaart²⁸; Omid Eschgi²⁹; Reinoud P.H. Bokkers²⁹; Tobien H.C.M.L. Schreuder³⁰; Roel J.J. Heijboer³¹; Koos Keizer³²; Lonneke S.F. Yo³³; Heleen M. den Hertog²²; Tomas Bulut³⁵; Paul J.A.M. Brouwers³⁴

Imaging assessment committee

Charles B.L.M. Majoie³ (chair); Wim H. van Zwam⁶; Aad van der Lugt²; Geert J. Lycklama à Nijeholt¹³; Marianne A.A. van Walderveen¹⁰; Marieke E.S. Sprengers³; Sjoerd F.M.

Jenniskens²⁷;René van den Berg³;Albert J. Yoo³⁸;Ludo F.M. Beenen³;Alida A. Postma⁶;Stefan D. Roosendaal³;Bas F.W. van der Kallen¹³;Ido R. van den Wijngaard¹³;Adriaan C.G.M. van Es²;Bart J. Emmer³;Jasper M. Martens¹²; Lonneke S.F. Yo³³;Jan Albert Vos⁸; Joost Bot³⁶, Pieter-Jan van Doormaal²; Anton Meijer²⁷;Elyas Ghariq¹³; Reinoud P.H. Bokkers²⁹;Marc P. van Proosdij³⁷;G. Menno Krietemeijer³³;Jo P. Peluso²⁶;Hieronymus D. Boogaarts²⁰;Rob Lo¹⁸;Dick Gerrits³⁵;Wouter Dinkelaar²Auke P.A. Appelman²⁹;Bas Hammer¹⁶;Sjoert Pegge²⁷;Anouk van der Hoorn²⁹;Saman Vinke²⁰.

Writing committee

Diederik W.J. Dippel¹(chair);Aad van der Lugt²;Charles B.L.M. Majoie³;Yvo B.W.E.M. Roos⁴;Robert J. van Oostenbrugge⁵;Wim H. van Zwam⁶;Geert J. Lycklama à Nijeholt¹³;Jelis Boiten¹⁴;Jan Albert Vos⁸;Wouter J. Schonewille⁷;Jeannette Hofmeijer¹¹;Jasper M. Martens¹²;H. Bart van der Worp¹⁷;Rob H. Lo¹⁸

Adverse event committee

Robert J. van Oostenbrugge⁵(chair);Jeannette Hofmeijer¹¹;H. Zwenneke Flach²³

Trial methodologist

Hester F. Lingsma⁴⁰

Research nurses / local trial coordinators

Naziha el Ghannouti¹;Martin Sterrenberg¹;Wilma Pellikaan⁷;Rita Sprengers⁴;Marjan Elfrink¹¹;Michelle Simons¹¹;Marjolein Vossers¹²;Joke de Meris¹⁴;Tamara Vermeulen¹⁴;Annet Geerlings¹⁹;Gina van Vemde²²;Tiny Simons³⁰;Gert Messchendorp²⁸;Nynke Nicolaij²⁸;Hester Bongenaar³²;Karin Bodde²⁴;Sandra Kleijn³⁴;Jasmijn Lodico³⁴; Hanneke Droste³⁴;Maureen

Wollaert⁵; Sabrina Verheesen⁵; D. Jeurissen⁵; Erna Bos⁹; Yvonne Drabbe¹⁵; Michelle Sandiman¹⁵; Nicoline Aaldering¹¹; Berber Zweedijk¹⁷; Jocova Vervoort²¹; Eva Ponjee²²; Sharon Romviel¹⁹; Karin Kanselaar¹⁹; Denn Barning¹⁰.

PhD / Medical students:

Esmee Venema⁴⁰; Vicky Chalos^{1,40}; Ralph R. Geuskens³; Tim van Straaten¹⁹; Saliha Ergezen¹; Roger R.M. Harmsma¹; Daan Muijres¹; Anouk de Jong¹; Olvert A. Berkhemer^{1,3,6}; Anna M.M. Boers^{3,39}; J. Huguet³; P.F.C. Groot³; Marieke A. Mens³; Katinka R. van Kranendonk³; Kilian M. Treurniet³; Manon L. Tolhuisen^{3,39}; Heitor Alves³; Annick J. Weterings³; Eleonora L.F. Kirkels³; Eva J.H.F. Voogd¹¹; Lieve M. Schupp³; Sabine L. Collette^{28,29}; Adrien E.D. Groot⁴; Natalie E. LeCouffe⁴; Praneeta R. Konduri³⁹; Haryadi Prasetya³⁹; Nerea Arrarte-Terreros³⁹; Lucas A. Ramos³⁹.

List of affiliations

Department of Neurology¹, Radiology², Public Health⁴⁰, Erasmus MC University Medical Center;

Department of Radiology and Nuclear Medicine³, Neurology⁴, Biomedical Engineering & Physics³⁹, Amsterdam UMC, University of Amsterdam, Amsterdam;

Department of Neurology⁵, Radiology⁶, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM);

Department of Neurology⁷, Radiology⁸, Sint Antonius Hospital, Nieuwegein;

Department of Neurology⁹, Radiology¹⁰, Leiden University Medical Center;

Department of Neurology¹¹, Radiology¹², Rijnstate Hospital, Arnhem;

Department of Radiology¹³, Neurology¹⁴, Haaglanden MC, the Hague;

Department of Neurology¹⁵, Radiology¹⁶, HAGA Hospital, the Hague;

Department of Neurology¹⁷, Radiology¹⁸, University Medical Center Utrecht;

Department of Neurology¹⁹, Neurosurgery²⁰, Radiology²⁷, Radboud University Medical Center, Nijmegen;

Department of Neurology²¹, Radiology²⁶, Elisabeth-TweeSteden ziekenhuis, Tilburg;

Department of Neurology²², Radiology²³, Isala Klinieken, Zwolle;

Department of Neurology²⁴, Radiology²⁵, Reinier de Graaf Gasthuis, Delft;

Department of Neurology²⁸, Radiology²⁹, University Medical Center Groningen;

Department of Neurology³⁰, Radiology³¹, Atrium Medical Center, Heerlen;

Department of Neurology³², Radiology³³, Catharina Hospital, Eindhoven;

Department of Neurology³⁴, Radiology³⁵, Medisch Spectrum Twente, Enschede;

Department of Radiology³⁶, Amsterdam UMC, Vrije Universiteit van Amsterdam, Amsterdam;

Department of Radiology³⁷, Noordwest Ziekenhuisgroep, Alkmaar;

Department of Radiology³⁸, Texas Stroke Institute, Texas, United States of America.