SUPPLEMENTARY MATERIAL

Timing and causes of death after endovascular thrombectomy in patients with acute ischemic stroke

Wouter M. Sluis, Wouter H. Hinsenveld, Robert-Jan B. Goldhoorn, Lianne H. Potters, Agnetha A.E. Bruggeman, Anouk van der Hoorn, Joseph C.J. Bot, Robert J. van Oostenbrugge, Hester F. Lingsma, Jeannette Hofmeijer, Wim H. van Zwam, Charles B.L.M. Majoie, H. Bart van der Worp

Table 1. The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 3, line 60	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Page 3, line 60 Page 3, line 61 n.a.
Introduction					

Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 5, line 93-97		
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5, line 97-100		
Methods					
Study Design	4	Present key elements of study design early in the paper	Page 6, line 103-106		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 6, line 103-112 and Page 6, line 120-155		

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 *(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	Page 6, line 107-112	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	Page 6, line 107-112 n.a. n.a.

Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Page 7, line 139-155 and Page 6, line 120 through Page 7, line 136	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	n.a.
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	Page 7, line 139-155 and Page 6, line 120 through Page 7, line 136		

Bias	9	Describe any efforts to address potential sources of bias	Page 7, line 130-132 Page 8, line 164-165		
Study size	10	Explain how the study size was arrived at	Page 9 line 169-173 and Figure 1 of the Supplement		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	n.a.		

Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (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	Page 8, line 158-166 Page 8, line 160-162 Page 8, line 164-165		
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	n.a.

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	n.a.
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	n.a.
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for nonparticipation at each stage. (c) Consider use of a flow diagram	Figure 1 of the Data Supplement	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Figure 1 of the Data Supplement

Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)	Page 12, Table 2 and Page 9 line 169-171 Data supplement Table 3		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure	Page 9, line 171-173 and Table 1		
		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, confounderadjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 19, line 234-241 and Table 4		
Other analyses	17	Report other analyses done— e.g., analyses of subgroups and interactions, and sensitivity analyses	Sensitivity analysis is found in the data supplement Table 2		
Discussion					
Key results	18	Summarise key results with reference to study objectives	Page 21, line 252-260		

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	Page 22, line 288-302	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Page 22, line 288-302
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	Page 24, line 304-309		
		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results	n.a.		
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable,	Separate declarations document		

		for the original study on which the present article is based			
Accessibility of protocol, raw data, and programming code		..	n.a.	RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	n.a.

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

Figure 1. Flowchart of patient inclusion

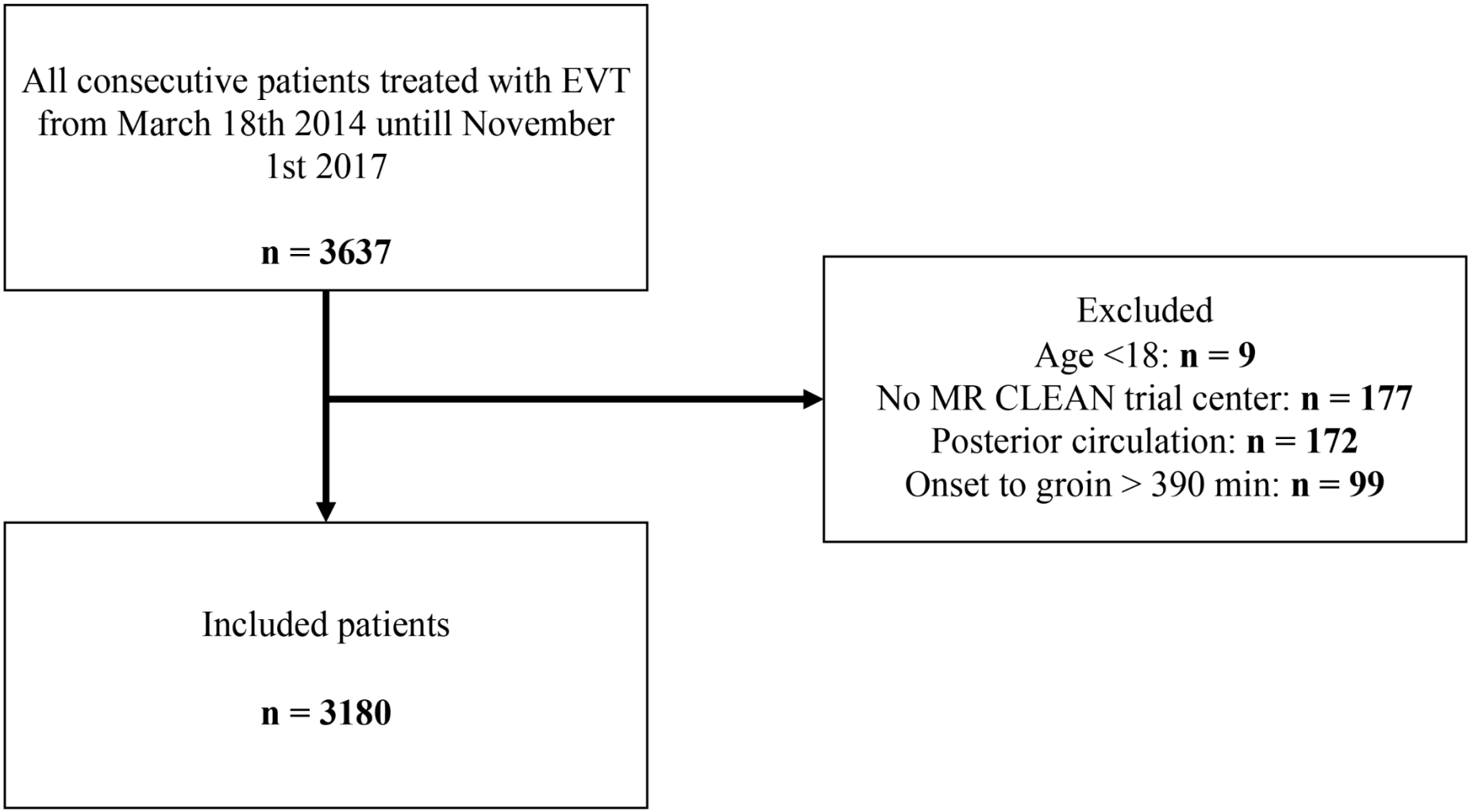
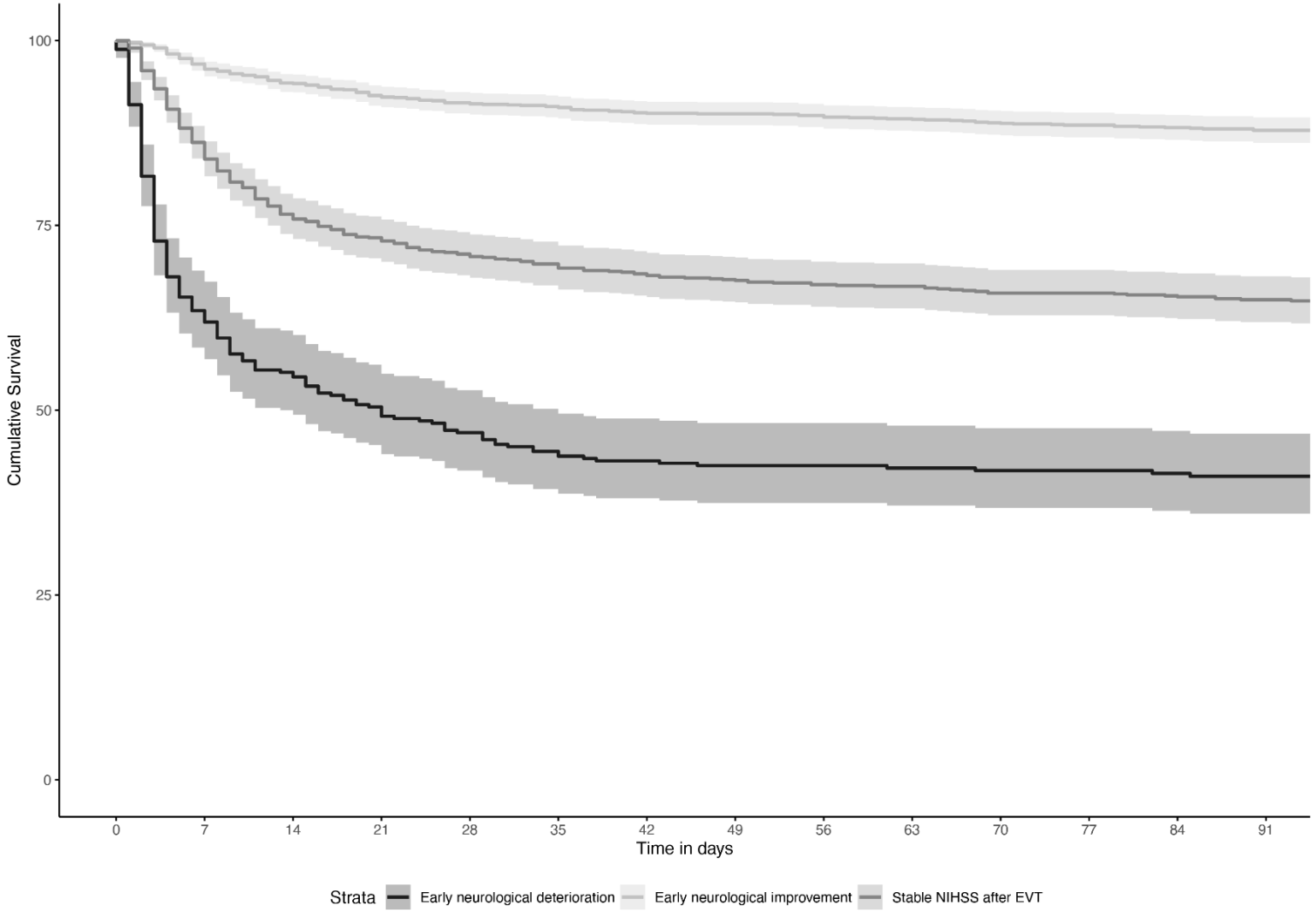


Figure 2. Cumulative survival from day 1 to day 90 stratified by stroke severity after treatment



Abbreviations: NIHSS = national institute of health stroke scale, EVT = endovascular treatment

Table 2. Sensitivity analysis without imputed data

Predictors*	**Odds Ratio (95% CI)**
Age	1.06 (1.04-1.08)
Functional dependency†	1.87 (1.06-3.30)
Glucose at baseline	1.14 (1.05-1.23)
CRP at baseline	1.01 (1.00-1.02)
Absent collaterals	3.33 (1.40-7.90)
Collateral filling <50% of occluded area	2.37 (1.25-4.52)
History of diabetes	2.43 (1.38-4.28)
Previous use of APT	1.66 (1.01-2.75)
NIHSS at 24-48 hours	1.21 (1.17-1.25)

* all numbers are odds ratio's with corresponding 95% confidence interval

† modified Rankin scale (mRS) of 3 or higher at baseline

Abbreviations: CRP = c-reactive protein, APT = anti platelet therapy, NIHSS = national institute of health stroke scale

Table 3. Predictor values with a missing percentage of 5% or higher

Predictors*	**Missing values** n (%)
CRP	642 (20.2)
INR	597 (18.8)
In-hospital stroke	451 (14.2)
Glucose	367 (11.5)
NIHSS after 24-48 hours	327 (10.3)
Duration of procedure	283 (8.9)
Onset to end of procedure	204 (6.4)
Collateral score	202 (6.4)
General anesthesia	194 (6.1)
Occlusion site	187 (5.9)

Abbreviations: CRP = c-reactive protein, INR = international normalized ratio, NIHSS = national institute of health stroke scale

Supplemental table 4. Difference in determined causes of death between part 1 and part 2 of the registry

Cause*	**All patients**	**Part 1**	**Part 2**
		April 2014 - June 2016	June 2016 – November 2017
	n = 821	**n= 378**	**n= 443**
Pneumonia	215 (26.2)	87 (23.0)	128 (28.9)
Intracranial hemorrhage†	142 (17.3)	65 (17.2)	77 (17.4)
Withdrawal of life sustaining treatment	110 (13.4)	53 (14.0)	57 (12.9)
Space-occupying infarction	101 (12.3)	55 (14.6)	46 (10.4)
Stroke progression	56 (6.8)	25 (6.6)	31 (7.0)
Cardiac death	45 (5.5)	23 (6.1)	22 (5.0)
Recurrent ischemic stroke	29 (3.5)	14 (3.7)	15 (3.4)

Withholding artificial food	18 (2.2)	11 (2.9)	7 (1.6)
Infection, other	16 (1.9)	4 (1.1)	12 (2.7)
Cancer	15 (1.8)	6 (1.6)	9 (2.0)
Neurological deterioration e.c.i. ‡	15 (1.8)	6 (1.6)	9 (2.0)
Sudden death	14 (1.7)	5 (1.3)	9 (2.0)
Extracranial hemorrhage	11 (1.3)	6 (1.6)	5 (1.1)
Respiratory insufficiency, other	11 (1.3)	3 (0.8)	8 (1.8)
Urinary tract infection	10 (1.2)	9 (2.4)	1 (0.2)
Renal failure	4 (0.5)	1 (0.3)	3 (0.7)
Pulmonary embolism	3 (0.4)	1 (0.3)	2 (0.5)
Multi-organ failure	2 (0.2)	2 (0.5)	0 (0.0)
Endocarditis	1 (0.1)	0 (0.0)	1 (0.3)

Acute abdomen	1 (0.1)	1 (0.3)	0 (0.0)
Euthanasia	1 (0.1)	1 (0.3)	0 (0.0)
Status epilepticus	1 (0.1)	1 (0.3)	0 (0.0)

* all numbers are n (%) unless stated otherwise, † any type of symptomatic (NIHSS increase ≥4) intracranial hemorrhage (Heidelberg Bleeding Classification I, II or III), ‡ patients who died after new focal deficits or coma without an apparent cause in whom no imaging was performed

Abbreviations: e.c.i. = e causa ignota, COPD = chronic obstructive pulmonary disease

Table 5. MR CLEAN Registry Investigators

Executive committee

Diederik W.J. Dippel[1];Aad van der Lugt[2];Charles B.L.M. Majoie[3];Yvo B.W.E.M. Roos[4];Robert J. van Oostenbrugge[5,41];Wim H. van Zwam[6,41];Jelis Boiten[14];Jan Albert Vos[8]

Study coordinators

Ivo G.H. Jansen[3];Maxim J.H.L. Mulder[1,2];Robert- Jan B. Goldhoorn[5,6,41];Kars C.J. Compagne[2];Manon Kappelhof[3];Josje Brouwer[4];Sanne J. den Hartog[1,2,40];Wouter H. Hinsenveld [5,6];

Local principal investigators

Diederik W.J. Dippel[1];Bob Roozenbeek[1];Aad van der Lugt[2];Adriaan C.G.M. van Es[2];Charles B.L.M. Majoie[3];Yvo B.W.E.M. Roos[4];Bart J. Emmer[3];Jonathan M. Coutinho[4];Wouter J. Schonewille[7];Jan Albert Vos[8]; Marieke J.H. Wermer[9];Marianne A.A. van Walderveen[10];Julie Staals[5,41];Robert J. van Oostenbrugge[5,41],Wim H. van Zwam[6,41];Jeannette Hofmeijer[11];Jasper M. Martens[12];Geert J. Lycklama à Nijeholt[13];Jelis Boiten[14];Sebastiaan F. de Bruijn[15];Lukas C. van Dijk[16];H. Bart van der Worp[17];Rob H. Lo[18];Ewoud J. van Dijk[19];Hieronymus D. Boogaarts[20];J. de Vries[22];Paul L.M. de Kort[21]; Julia van Tuijl[21] ; Jo P. Peluso[26];Puck Fransen[22];Jan S.P. van den Berg[22];Boudewijn A.A.M. van Hasselt[23];Leo A.M.

Aerden[24];René J. Dallinga[25];Maarten Uyttenboogaart[28];Omid Eschgi[29];Reinoud P.H. Bokkers[29];Tobien H.C.M.L. Schreuder[30];Roel J.J. Heijboer[31];Koos Keizer[32];Lonneke S.F. Yo[33];Heleen M. den Hertog[22];Tomas Bulut[35]; Paul J.A.M. Brouwers[34].

Imaging assessment committee

Charles B.L.M. Majoie[3](chair);Wim H. van Zwam[6,41];Aad van der Lugt[2];Geert J. Lycklama à Nijeholt[13];Marianne A.A. van Walderveen[10];Marieke E.S. Sprengers[3];Sjoerd F.M. Jenniskens[27];René van den Berg[3];Albert J. Yoo[38];Ludo F.M. Beenen[3];Alida A. Postma[6,42], Stefan D. Roosendaal[3];Bas F.W. van der Kallen[13];Ido R. van den Wijngaard[13];Adriaan C.G.M. van Es[2];Bart J. Emmer[3];Jasper M. Martens[12]; Lonneke S.F. Yo[33];Jan Albert Vos[8]; Joost Bot[36], Pieter-Jan van Doormaal[2]; Anton Meijer[27];Elyas Ghariq[13]; Reinoud P.H. Bokkers[29];Marc P. van Proosdij[37];G. Menno Krietemeijer[33];Jo P. Peluso[26];Hieronymus D. Boogaarts[20];Rob Lo[18];Wouter Dinkelaar[2]Auke P.A. Appelman[29];Bas Hammer[16];Sjoert Pegge[27];Anouk van der Hoorn[29];Saman Vinke[20].

Writing committee

Diederik W.J. Dippel[1](chair);Aad van der Lugt[2];Charles B.L.M. Majoie[3];Yvo B.W.E.M. Roos[4];Robert J. van Oostenbrugge[5,41];Wim H. van Zwam[6,41];Geert J. Lycklama à Nijeholt[13];Jelis Boiten[14];Jan Albert Vos[8];Wouter J. Schonewille[7];Jeannette Hofmeijer[11];Jasper M. Martens[12];H. Bart van der Worp[17];Rob H. Lo[18]

Adverse event committee

Robert J. van Oostenbrugge[5,41](chair);Jeannette Hofmeijer[11];H. Zwenneke Flach[23]

Trial methodologist

Hester F. Lingsma[40]

Research nurses / local trial coordinators

Naziha el Ghannouti[1];Martin Sterrenberg[1];Wilma Pellikaan[7];Rita Sprengers[4];Marjan Elfrink[11];Michelle Simons[11];Marjolein Vossers[12];Joke de Meris[14];Tamara Vermeulen[14];Annet Geerlings[19];Gina van Vemde[22];Tiny Simons[30];Gert Messchendorp[28];Nynke Nicolaij[28];Hester Bongenaar[32];Karin Bodde[24];Sandra Kleijn[34];Jasmijn Lodico[34]; Hanneke Droste[34];Maureen Wollaert[5];Sabrina Verheesen[5];D. Jeurrissen[5];Erna Bos[9];Yvonne Drabbe[15];Michelle Sandiman[15];Nicoline Aaldering[11];Berber Zweedijk[17];Jocova Vervoort[21];Eva Ponjee[22];Sharon Romviel[19];Karin Kanselaar[19];Denn Barning[10].

PhD / Medical students:

Esmee Venema[40]; Vicky Chalos[1,40]; Ralph R. Geuskens[3]; Tim van Straaten[19];Saliha Ergezen[1]; Roger R.M. Harmsma[1]; Daan Muijres[1]; Anouk de Jong[1];Olvert A. Berkhemer[1,3,6];Anna M.M. Boers[3,39]; J. Huguet[3];P.F.C. Groot[3];Marieke A. Mens[3];Katinka R. van Kranendonk[3];Kilian M. Treurniet[3];Manon L. Tolhuisen[3,39];Heitor Alves[3];Annick J. Weterings[3],Eleonora L.F. Kirkels[3],Eva J.H.F. Voogd[11];Lieve M. Schupp[3];Sabine L. Collette[28,29];Adrien E.D. Groot[4];Natalie E. LeCouffe[4];Praneeta R. Konduri[39];Haryadi Prasetya[39];Nerea Arrarte-Terreros[39];Lucas A. Ramos[39].

List of affiliations

Department of Neurology[1], Radiology[2], Public Health[40], Erasmus MC University Medical Center;

Department of Radiology and Nuclear Medicine[3], Neurology[4], Biomedical Engineering & Physics[39],

Amsterdam UMC, location University of Amsterdam;

Department of Neurology[5], Radiology & Nuclear Medicine[6], Maastricht University Medical Center+; School for Cardiovascular Diseases Maastricht (CARIM)[41]; and MHeNs School for Mental Health and Neuroscience, Maastricht, the Netherlands[42];

Department of Neurology[7], Radiology[8], Sint Antonius Hospital, Nieuwegein;

Department of Neurology[9], Radiology[10], Leiden University Medical Center;

Department of Neurology[11], Radiology[12], Rijnstate Hospital, Arnhem;

Department of Radiology[13], Neurology[14], Haaglanden MC, the Hague;

Department of Neurology[15], Radiology[16], HAGA Hospital, the Hague;

Department of Neurology[17], Radiology[18], University Medical Center Utrecht;

Department of Neurology[19], Neurosurgery[20], Radiology[27], Radboud University Medical Center, Nijmegen;

Department of Neurology[21], Radiology[26], Elisabeth-TweeSteden ziekenhuis, Tilburg;

Department of Neurology[22], Radiology[23], Isala Klinieken, Zwolle;

Department of Neurology[24], Radiology[25], Reinier de Graaf Gasthuis, Delft;

Department of Neurology[28], Radiology[29], University Medical Center Groningen;

Department of Neurology[30], Radiology[31], Atrium Medical Center, Heerlen;

Department of Neurology[32], Radiology[33], Catharina Hospital, Eindhoven;

Department of Neurology[34], Radiology[35], Medisch Spectrum Twente, Enschede;

Department of Radiology[36], Amsterdam UMC, Vrije Universiteit van Amsterdam, Amsterdam;

Department of Radiology[37], Noordwest Ziekenhuisgroep, Alkmaar;

Department of Radiology[38], Texas Stroke Institute, Texas, United States of America.