Sex differences in onset to hospital arrival time, prestroke disability, and clinical symptoms in patients with a large vessel occlusion: a MR CLEAN Registry substudy

Ali, M.; Meij, A. van der; Os, H.J.A. van; Zwet, E.W. van; Spaander, F.H.M.; Hofmeijer, J.; ... ; MR CLEAN Registry Investigators

Original research

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Mariam Ali ,[1] Anne van der Meij,[2] Hendrikus J A van Os,[2] Mahsoem Ali ,[3] Erik W Van Zwet,[4] Fianne H M Spaander,[5] Jeanette Hofmeijer,[6,7] Paul J Nederkoorn,[8] Ido R van den Wijngaard,[2,9] Charles B L M Majoie ,[10] Adriaan C G M van Es,[11] Wouter J Schonewille ,[12] Marianne A A van Walderveen,[13] Diederik W J Dippel ,[14] Marieke C Visser,[1] Nyika D Kruyt,[2] Marieke J H Wermer,[2] on behalf of the MR CLEAN Registry Investigators

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For numbered affiliations see end of article.

Correspondence to
Mariam Ali, Neurology, Amsterdam UMC Locatie VUmc, 1081 HV Amsterdam, Netherlands; m.ali2@amsterdamumc.nl

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ABSTRACT

Background Women have been reported to have worse outcomes after endovascular treatment (EVT), despite a similar treatment effect in non-clinical trial populations. We aimed to assess sex differences at hospital presentation with respect to workflow metrics, prestroke disability, and presenting clinical symptoms.

Methods We included consecutive patients from the Multicentre Randomised Controlled Trial of Endovascular Treatment for Acute Ischaemic Stroke in The Netherlands (MR CLEAN) Registry (2014–2018) who received EVT for anterior circulation large vessel occlusion (LVO). We assessed sex differences in workflow metrics, prestroke disability (modified Rankin Scale (mRS) score ≥1), and stroke severity and symptoms according to the National Institutes of Health Stroke Scale (NIHSS) score on hospital admission with logistic and linear regression analyses and calculated the adjusted OR (aOR).

Results We included 4872 patients (47.6% women). Compared with men, women were older (median age 76 vs 70 years) and less often achieved good functional outcome at 90 days (mRS ≤2: 35.2% vs 46.4%, aOR 0.70, 95% CI 0.60 to 0.82). Mean onset-to-door time was longer in women (2 hours 16 min vs 2 hours 7 min, adjusted delay 9 min, 95% CI 4 to 13). This delay contributed to longer onset-to-groin times (3 hours 26 min in women vs 3 hours 13 min in men, adjusted delay 13 min, 95% CI 9 to 17). Women more often had prestroke disability (mRS ≥1: 41.1% vs 29.1%, aOR 1.57, 95% CI 1.36 to 1.82). NIHSS on admission was essentially similar in men and women (mean 15±6 vs 15±6, NIHSS <10 vs ≥10, aOR 0.91, 95% CI 0.78 to 1.06). There were no clear sex differences in the occurrence of specific stroke symptoms.

Conclusion Women with LVO had longer onset-to-door times and more often prestroke disability than men. Raising awareness of these differences at hospital presentation and investigating underlying causes may help to improve outcome after EVT in women.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Several studies have reported worse outcomes after endovascular thrombectomy for anterior circulation large vessel occlusion in women compared with men, but the underlying cause of this possible difference remains unclear.

WHAT THIS STUDY ADDS

⇒ In this large real world population with observational data from the Multicentre Randomised Controlled Trial of Endovascular Treatment for Acute Ischaemic Stroke in The Netherlands (MR CLEAN) Registry, we confirmed the poor outcomes in women, and found that women more often had prestroke disability and longer onset-to-door-times compared with men. These sex differences may partly explain the poor outcomes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ More detailed studies of specific processes of prehospital workflow are necessary to understand the origin of the sex disparity in hospital arrival times. With further data it may become possible to create specific stroke awareness campaigns targeted towards women to reduce patient delay in seeking treatment.

INTRODUCTION

Several observational studies have reported worse outcomes following endovascular treatment (EVT) for acute ischemic stroke due to large vessel occlusion (LVO) in women compared with men, despite a similar treatment effect according to most randomized controlled trials.[1–7] The underlying cause of this possible difference remains poorly understood. After stroke, in general, there are indications that a poorer outcome in women is related to worse prestroke disability.[8] Characteristics that are more common in women at the onset of stroke, such as

Table 1 Baseline characteristics of participants stratified by sex

	All patients (n=4872)	Women (n=2320)	Men (n=2552)	P value
Age (years) (median (IQR))	72 (62–81)	76 (65–83)	70 (61–78)	<0.001
Systolic blood pressure (mm Hg) (mean (SD))*	150 (26)	151 (26)	149 (25)	0.02
Diastolic blood pressure (mm Hg) (mean (SD))†	83 (16)	82 (17)	84 (15)	<0.001
Vascular risk factors (n/total No (%))				
Hypertension	2542/4779 (53.2)	1333/2278 (58.5)	1209/2501 (48.3)	<0.001
Hypercholesterolemia	1463/4673 (31.3)	690/2214 (31.2)	773/2459 (31.4)	0.84
Diabetes mellitus	820/4842 (16.9)	415/2304 (18.0)	405/2538 (16.0)	0.06
Current smoker	995/3645 (27.3)	411/1737 (23.7)	584/1908 (30.6)	<0.001
Atrial fibrillation	1162/4807 (24.2)	590/2290 (25.8)	572/2517 (22.7)	0.01
Vascular comorbidities (n/total No (%))				
Ischemic stroke	866/4833 (17.9)	431/2301 (18.7)	435/2532 (17.2)	0.16
Intracerebral hemorrhage	89/4511 (2.0)	47/2147 (2.1)	42/2364 (1.8)	0.60
Myocardial infarction	696/4781 (14.6)	251/2282 (11.0)	445/2499 (17.8)	<0.001
Peripheral arterial disease	439/4781 (9.2)	190/2278 (8.3)	249/2503 (9.9)	0.06
Medication use (n/total No (%))				
DOAC	233/4815 (4.8)	107/2296 (4.7)	126/2519 (5.0)	0.58
Coumarin	613/4831 (12.7)	320/2303 (13.9)	293/2528 (11.6)	0.02
Antiplatelets	1516/4810 (31.5)	686/2289 (30.0)	830/2521 (32.9)	0.03
Antihypertensive agent	2652/4775 (55.5)	1366/2279 (59.9)	1286/2496 (51.5)	<0.001
Statin	1726/4767 (36.2)	790/2275 (34.7)	936/2492 (37.6)	0.04
TOAST classification (n/total No (%))‡				
Large artery atherosclerosis	185/1393 (13.3)	61/646 (9.4)	124/747 (16.6)	<0.001
Cardioembolic	465/1393 (33.4)	245/646 (37.9)	220/747 (29.5)	<0.001
Small vessel occlusion	0	0	0	1.00
Other cause	120/1393 (8.6)	47/646 (7.3)	73/747 (9.8)	0.10
Undetermined cause	678/1393 (48.7)	312/646 (48.3)	366/747 (49.0)	0.79

*Number of missing values: 143 (2.9%), 74 (3.2%), and 69 (2.7%) in all patients, women, and men, respectively.
†Number of missing values: 167 (3.4%), 92 (4.0%), and 75 (2.9%) in all patients, women, and men, respectively.
‡Data were available for only 1393 participants from part I of the Multicentre Randomised Controlled Trial of Endovascular Treatment for Acute Ischaemic Stroke in The Netherlands (MR CLEAN) Registry.
DOAC, direct oral anticoagulants; NIHSS, National Institutes of Health Stroke Scale; TOAST, Trial of ORG 10172 in Acute Stroke Treatment.

advanced age and higher comorbidity burden, increase the likelihood of prestroke disability.[9] In addition, women are at risk for late arrival because they are more likely to live alone and less likely to call an ambulance for themselves.[10 11] Differences in clinical presentation of LVO could also contribute to these delays and may lead to underdiagnosis and undertreatment of women.[12] In a recent meta-analysis on sex differences in clinical presentation of ischemic stroke, we found that women more frequently presented with non-focal stroke symptoms, such as mental status changes, loss of consciousness, and headache, than men (pooled OR 1.20, 95% CI 1.04 to 1.38).[13] However, the possibility of misdiagnosis of LVO stroke seems to be low because neurological deficits are typically severe, but potential differences in clinical presentation of LVO stroke remain important because, for example, non-focal symptoms may lead to a delay in recognition.

We aimed to assess sex differences at hospital presentation with respect to (1) workflow metrics, (2) prestroke disability, and (3) clinical symptoms of patients with anterior circulation LVO to improve our understanding of the difference in outcome after EVT between men and women in the real world setting.

METHODS

Study design and patient selection

We used data from consecutive patients with acute ischemic stroke due to anterior circulation LVO from the Multicentre Randomised Controlled Trial of Endovascular Treatment for Acute Ischaemic Stroke in The Netherlands (MR CLEAN) Registry, a prospective, observational cohort study for stroke intervention centers that perform EVT in The Netherlands.[14] All 18 centers performing EVT in The Netherlands participated in this registry. Enrollment started in March 2014, directly after the final randomization for the MR CLEAN trial, and ended in December 2018.[15] We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies.[16]

For the present study, we used data from all patients in the registry who fulfilled the following criteria: aged ≥18 years, treatment in a center that had participated in the MR CLEAN trial, start of EVT within 6.5 hours of symptom onset, and occlusion of the intracranial carotid artery, middle cerebral artery segment (M1/M2), or anterior cerebral artery segment (A1/A2), as confirmed on CT angiography. In addition, a non-contrast CT scan was performed on admission to rule out intracranial hemorrhage.

Table 2 Workflow metrics

Workflow times and treatment	Women (n=2320)	Men (n=2552)	Unadjusted OR/ difference (95% CI)	Adjusted OR/ difference (95% CI)
Onset-to-door time*§	2 hours 16 min (1 hour 27 min)	2 hours 7 min (1 hour 30 min)	10 min (5 to 15)	9 min (4 to 13)
Stratified by interhospital transfer				
Yes	3 hours 1 min (1 hour 9 min)	2 hours 53 min (1 hour 9 min)	7 min (2 to 13)	9 min (3 to 15)
No	1 hour 23 min (1 hour 17 min)	1 hour 15 min (1 hour 23 min)	9 min (2 to 15)	8 min (1 to 15)
Door-to-groin time†§	1 hour 4 min (43 min)	1 hour 3 min (41 min)	1 min (–2 to 3)	2 min (0 to 4)
Onset-to-groin time‡§	3 hours 26 min (1 hour 16 min)	3 hours 13 min (1 hour 13 min)	13 min (9 to 17)	13 min (9 to 17)
Interhospital transfer (n/total No (%))¶	1277/2319 (55.1)	1371/2550 (53.8)	1.05 (0.94 to 1.18)	1.07 (0.95 to 1.21)
IVT treatment (n/total No (%))**	1668/2305 (72.4)	1877/2541 (73.9)	0.93 (0.82 to 1.05)	1.05 (0.89 to 1.23)

Workflow variables are mean (SD), unless otherwise stated.
*Number of missing values: 89 (3.8%) and 96 (3.8%) in women and men, respectively.
†Number of missing values: 228 (9.8%) and 248 (9.7%) in women and men, respectively.
‡Number of missing values: 42 (1.8%) and 48 (1.9%) in women and men, respectively.
§Adjusted for age, National Institutes of Health Stroke Scale (NIHSS) at baseline, hypertension, prestroke modified Rankin Scale (mRS), interhospital transfer, treatment with IVT, use of general anesthesia, and admission outside office hours.
¶Adjusted for age, NIHSS at baseline, history of ischemic stroke, and prestroke mRS.
**Adjusted for age, hypertension, NIHSS at baseline, prestroke mRS, anticoagulants, history of ischemic or hemorrhagic stroke, admission outside office hours, and onset-to-door time.
EVT, endovascular treatment; IVT, intravenous thrombolysis.

Although the recommended time window for EVT at the time of this study was 6 hours,[17] the time window was extended by 30 min compared with that in the MR CLEAN trial because the start of groin puncture was sometimes slightly delayed due to logistical reasons in clinical practice. EVT consisted of arterial catheterization followed by mechanical thrombectomy and thrombus aspiration, with or without delivery of a thrombolytic agent.

Clinical baseline characteristics were collected as previously described and included sex, age, blood pressure on admission, vascular risk factors, vascular comorbidity, medication use, and stroke etiology, classified according to the Trial of ORG 10172 in Acute Stroke Treatment criteria.[14 18]

Outcome measures

The main prehospital workflow related metric of interest was time from stroke onset to arrival at the emergency department of the intervention center (onset-to-door time) as a measure of prehospital delay. In addition, we assessed time from admission to the emergency department of the intervention center to groin puncture (door-to-groin time) as a measure for inhospital delay, time from stroke onset to groin puncture (onset-to-groin time), proportion of patients treated with intravenous thrombolytics (IVT), and proportion of patients with an interhospital transfer.

Admission and discharge functional status were based on the modified Rankin Scale (mRS). This is a 7 point scale ranging from 0 (no symptoms) to 6 (death).[19] Prestroke disability was defined as an mRS score of ≥1, and was evaluated and recorded at admission by the treating clinician.[15] Good neurological outcome at 90 days was defined as an mRS ≤2.[14]

Clinical symptoms and stroke severity were assessed according to the National Institutes of Health Stroke Scale (NIHSS) on admission. Stroke severity was dichotomized as NIHSS score <10 (mild to moderately severe stroke) and ≥10 (moderate to severe stroke).[20] The following symptoms were recorded from the NIHSS: change in level of consciousness, loss of consciousness/coma, gaze deviation, visual field deficit, facial weakness, motor deficit in the arm or leg, ataxia, numbness, aphasia, dysarthria, and neglect. Categories differentiating the left and right side in arm and leg motor function were merged.

Statistical analysis

We compared baseline characteristics between men and women using the t test or Mann–Whitney U test for continuous variables and the Pearson's χ^2 test for categorical variables. We used multivariable linear regression analysis to study the association between sex and workflow times and calculated adjusted β coefficients. For the remaining end points, we used multivariable binary logistic regression analyses and calculated the adjusted OR (aOR). All regression analyses were adjusted for relevant confounders based on previous literature and the expert opinion of two vascular neurologists.

For the regression analyses with prehospital and inhospital workflow times as outcomes, we adjusted for the following factors: age, NIHSS at baseline, hypertension (baseline systolic blood pressure >185 mm Hg and diastolic blood pressure >110 mm Hg), prestroke mRS, interhospital transfer, treatment with IVT, use of general anesthesia, and admission outside office hours. In addition, we analyzed onset-to-door time stratified by interhospital transfer, adjusting for all previous variables.

For the regression analysis with IVT treatment as an outcome, we adjusted for age, hypertension (baseline systolic blood pressure >185 mm Hg and diastolic blood pressure >110 mm Hg), NIHSS at baseline, prestroke mRS, anticoagulants, history of ischemic or hemorrhagic stroke, admission outside office hours, and onset-to-door time. The regression analysis for interhospital transfer was adjusted for age, NIHSS at baseline, history of ischemic stroke, and prestroke mRS.

The regression analysis for prestroke mRS score (dichotomized, with mRS score of ≥1 as prestroke disability) was adjusted for age, vascular risk factors, comorbidities, and medication use, as described in table 1. For mRS score at 90 days after stroke (dichotomized, with mRS score of 0–2 as good functional outcome), we adjusted for age, NIHSS at baseline, prestroke mRS, prior stroke, systolic blood pressure, peripheral artery disease, treatment with IVT, collateral score, and onset-to-groin time.

The regression analysis for stroke severity (using NIHSS in two categories) was adjusted for the same variables as for the analysis of prestroke mRS score, as well as for the variable prestroke mRS. For the regression analysis on clinical symptoms, adjustments were made for age, comorbidities as described in table 1,

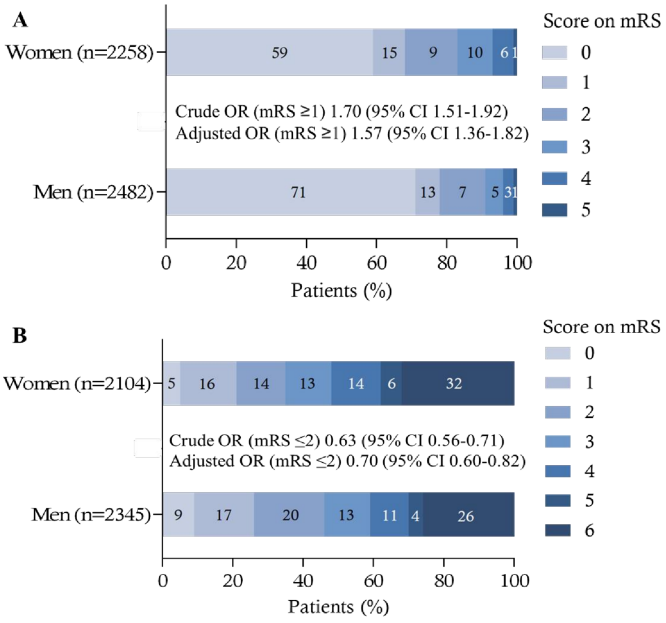

Figure 1 Distribution of modified Rankin Scale (mRS) scores before stroke (A) and 3 months after stroke (B).

and prestroke mRS. We constructed forest plots to display the effect estimates for NIHSS scores and per symptom.

For all analyses, complete case analysis was performed because we expected that data were missing not at random. A p value <0.05 was considered significant. SPSS V.25.0 (IBM Corp, Armonk, New York, USA) was used for the statistical analyses.

RESULTS

Of 5768 patients registered during the study period, 4872 were included in the current analysis: 2320 (47.6%) were women (online supplemental figure I). Compared with men, women were older at stroke onset (median age 76 vs 70 years) and were more likely to have a history of hypertension and atrial fibrillation, but were less likely to have a history of myocardial infarction or current smoking. Cardioembolic stroke was more common in women whereas large artery atherosclerosis stroke and stroke of other determined cause were less common. Other baseline characteristics are shown in table 1. Women less often achieved good functional outcome at 90 days compared with men (mRS ≤2: 35.2% vs 46.4%, aOR 0.70, 95% CI 0.60 to 0.82).

Workflow metrics

Mean onset-to-door time was longer for women compared with men (2 hours 16 min vs 2 hours 7 min, adjusted delay 9 min, 95% CI 4 to 13). This result was unchanged following stratification for interhospital transfer (table 2). Mean door-to-groin time was similar in men and women (1 hour 4 min vs 1 hour 3 min, adjusted delay 2 min, 95% CI 0 to 4). Onset-to-groin time (3 hours 26 min vs 3 hours 13 min, adjusted delay 13 min, 95% CI 9 to 17) was longer for women than men. We found no differences in the proportion of men and women treated with IVT or with interhospital transfer (table 2).

Prestroke disability

Women more often had prestroke disability compared with men (mRS ≥1: 41.1% vs 29.1%, aOR 1.57, 95% CI 1.36 to 1.82). The distribution of prestroke mRS scores is shown in figure 1.

Clinical symptoms and stroke severity

Figure 2 shows a forest plot for stroke severity and clinical symptoms. Men and women had comparable NIHSS scores at baseline (mean 15±6 vs 15±6, NIHSS <10 vs ≥10, aOR 0.91, 95% CI 0.78 to 1.06). There were no significant sex differences in the occurrence of specific clinical symptoms on admission except that women less frequently had visual field deficits compared with men (52.1% vs 55.3%, aOR 0.83, 95% CI 0.74 to 0.94).

DISCUSSION

We found that women with anterior circulation LVO, who were treated with EVT, had longer onset-to-door times. Also, women more often had prestroke disability and less often achieved good functional outcome than men. Onset-to-groin times were significantly longer, which seemed to be mainly caused by later arrival because inhospital workflow times were similar. Clinical symptoms on admission were similar except for a small difference in the occurrence of visual field deficits.

Our study specifically focused on contributors to poor outcomes in the prehospital phase in the real world setting. This is different from most previous studies, making direct comparisons for several outcomes difficult. Furthermore, substantial variability in the design, inclusion criteria, and adjustment for

Presenting symptoms, n (%)	Men (*n*=2552)	Women (*n*=2320)	aOR (95% CI)	OR (95% CI)	aOR (95% CI)
NIHSS score, mean (±SD)/median (IQR)†	15 (6)/16 (11-20)	15 (6)/15 (11-19)		1.01 (0.88-1.16)*	0.91 (0.78-1.06)*
Change in level of consciousness	454/2552 (17.8)	477/2320 (20.6)		1.20 (1.04-1.39)	1.14 (0.97-1.32)
Loss of consciousness/coma	24/2552 (0.9)	32/2320 (1.4)		1.53 (0.90-2.60)	1.58 (0.87-2.88)
Gaze deviation	1642/2552 (64.3)	1547/2320 (66.7)		1.11 (0.99-1.25)	0.99 (0.87-1.12)
Visual field deficit	1410/2552 (55.3)	1209/2320 (52.1)		0.88 (0.79-0.99)	0.83 (0.74-0.94)
Facial weakness	2203/2552 (86.3)	1955/2320 (84.3)		0.85 (0.72-1.00)	0.84 (0.71-1.00)
Motor deficit, arm	2326/2552 (91.1)	2132/2320 (91.9)		0.97 (0.81-1.17)	0.93 (0.77-1.13)
Motor deficit, leg	2151/2552 (84.2)	2014/2320 (86.8)		1.09 (0.94-1.27)	1.06 (0.91-1.24)
Ataxia	196/2552 (7.7)	176/2320 (7.6)		0.99 (0.80-1.22)	0.99 (0.79-1.24)
Numbness	1228/2552 (48.1)	1073/2320 (46.3)		0.93 (0.83-1.04)	0.90 (0.80-1.02)
Aphasia	1492/2552 (58.5)	1302/2320 (56.1)		0.91 (0.81-1.02)	0.90 (0.80-1.02)
Dysarthria	1716/2552 (67.2)	1572/2320 (67.8)		1.02 (0.91-1.15)	0.97 (0.86-1.11)
Neglect	1283/2552 (50.3)	1153/2320 (49.7)		0.98 (0.87-1.09)	0.93 (0.83-1.05)

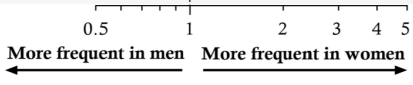

Figure 2 Clinical symptoms and stroke severity recorded from the NIHSS score on admission. *Dichotomized at <10 and ≥10.[20] †Number of missing values: 33 (1.4%) and 36 (1.4%) in men and women, respectively. aOR, adjusted OR; NIHSS, National Institutes of Stroke Scale.

confounders hampers comparisons across studies. Although data for the role of sex in outcome after EVT are scarce and conflicting, multiple articles have been published recently pointing out these disparities. However, these studies had a smaller sample size and, most importantly, did not correct their analyses for potential confounders, decreasing the reliability of their results. Also, in contrast with most EVT studies highlighting sex specific aspects of inhospital management, our study specifically focused on sex differences in the prehospital phase and recommends to assess why women have later hospital arrival.

We found four studies that reported similar time metrics in terms of onset-to-door times, door-to-groin times, and onset-to-groin times between men and women with LVO.[4 7 21 22] However, these studies either had a small sample size or their analysis was not adjusted for potential confounders that might affect prehosptial and in-hospital workflow times.

Similar to the findings in previous studies on stroke in general, we showed that women more often have prestroke disability.[9 23 24] In our population, women were older than men, more often had hypertension, and had a higher prevalence of atrial fibrillation. These characteristics have been associated with a worse prestroke functional status and higher stroke severity,[25] although in our study men and women had similar NIHSS on admission.

In contrast with previous studies on ischemic stroke in general, we did not find sex differences in the use of IVT.[26–28] Less frequent use of IVT in women compared with men was first documented in a previous meta-analysis of 18 studies published between 2000 and 2008 (pooled OR 0.70, 95% CI 0.55 to 0.88).[11] The odds of treatment were still lower for women in an updated systematic review and meta-analysis of 17 studies published between 2008 and 2018, but more recent data suggest that the magnitude of this sex difference decreased (pooled OR 0.87, 95% CI 0.82 to 0.93).[29] In the MR CLEAN Registry, only patients with LVO were included in whom the neurological deficits are typically severe. This most likely explains why we found no sex differences in treatment with IVT. Moreover, in our study, sex differences were not observed among interhospital transfers. Similar results with respect to interhospital transfers were reported by three previous studies assessing sex differences in outcome after EVT.[4 23 30] However, these studies did not adjust for confounders that might affect interhospital transfer (eg, age and NIHSS score at baseline).

The major strength of the study was our large, well described population of almost 5000 patients recruited from a nationwide prospective registry. This registry included consecutive patients from all intervention centers in The Netherlands and, therefore, our results likely reflect daily clinical practice. Moreover, the distribution of men and women included in our study was equal.

Our study had some limitations. First, only data for patients who received EVT are recorded in the MR CLEAN Registry. Therefore, we had no information on patients who did not receive EVT due to, for example, late arrival or because they did not have a suspicion of stroke. Because women with ischemic stroke have a higher prevalence of non-focal stroke symptoms compared with men, we cannot exclude the fact that female ischemic stroke patients with LVO were missed more.[13] Therefore, we cannot estimate the size of this patient population and their impact on our results. In particular, this selection could possibly explain why we did not observe significant sex differences regarding clinical symptoms. Another limitation of our study was that we had no information on prehospital delay to distinguish between delays in calling emergency medical services and the use of transportation modes (as measures of patient delay) and delay because of inhospital workflow in the primary stroke center and interhospital transfer (as measures of system delay). This information might have provided more insight into the various elements of prehospital workflow. Furthermore, information about living status was lacking (eg, living alone vs living with family or carers). Because older patients may be more likely to live alone and present later after a stroke compared with younger patients, selection bias towards the exclusion of older women who more frequently live alone has possibly occurred.[9 11] Future investigation of living status could provide additional insights about sex differences in onset-to-door times. Lastly, even though we adjusted our analyses for known confounding factors, we cannot exclude the presence of residual confounding.

Our study indicates that onset-to-door times are prolonged in women with anterior circulation LVO. More detailed studies of specific processes of prehospital workflow are necessary to understand the origin of the sex disparity in hospital arrival times. Stroke education/awareness campaigns targeted at women have focused only on stroke prevention through monitoring of vascular risk factors and disparities in stroke symptoms. Importantly, the American Heart Association's Go Red for Women campaign on stroke symptoms did not specifically focus on the need for fast activation of emergency medical services after onset of stroke symptoms. As a result of poorer health education, women may be less aware of the emergency nature of the disease. Based on our results, we suggest that campaigns should focus on both the recognition of stroke symptoms and activation of emergency medical services to reduce delays in seeking .

CONCLUSION

Our study indicates important sex differences in onset-to-door times and prestroke disability in patients with anterior circulation LVO, but no substantial differences between men and women in terms of clinical symptoms. These sex differences may contribute to differences in outcome after EVT. Additional research of underlying causes of sex differences in arrival times is needed to establish equitable access to treatment and improve outcome in women with LVO.

Author affiliations
[1]Neurology, Amsterdam UMC, Location VUmc, Amsterdam, The Netherlands
[2]Neurology, Leiden University Medical Center, Leiden, The Netherlands
[3]Surgery, Amsterdam UMC, Location VUmc, Amsterdam, Netherlands
[4]Medical Statistics, Leiden University Medical Center, Leiden, The Netherlands
[5]Neurology, Zaans Medical Center, Zaandam, The Netherlands
[6]Neurology, Rijnstate Hospital, Arnhem, The Netherlands
[7]University of Twente Faculty of Science and Technology, Enschede, The Netherlands
[8]Neurology, Amsterdam UMC, Location AMC, Amsterdam, The Netherlands
[9]Neurology, HMC Westeinde, The Hague, The Netherlands
[10]Radiology and Nuclear Medicine, Amsterdam UMC, Location AMC, Amsterdam, The Netherlands
[11]Radiology and Nuclear Medicine, Leiden University Medical Center, Leiden, The Netherlands
[12]Neurology, Sint Antonius Hospital, Nieuwegein, The Netherlands
[13]Radiology, Leiden University Medical Center, Leiden, The Netherlands
[14]Neurology, Erasmus MC University Medical Center, Rotterdam, The Netherlands

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Collaborators MR CLEAN Registry Investigators – group authors 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[5,44]; Wim H. van Zwam[6,44]; 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[5,6,44]; Kars C.J. Compagne[2]; Manon Kappelhof[3]; Josje Brouwer[4]; Sanne J. den Hartog[1,2,40]; Wouter H. Hinsenveld[5,6]; Lotte van den Heuvel[1,40]. Local principal investigators Diederik W.J. Dippel[1]; Bob Roozenbeek[1];

Aad van der Lugt[2]; Pieter Jan van Doormaal[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]; Adriaan C.G.M. van Es[10]; Julie Staals[5,44]; Robert J. van Oostenbrugge[5,44]; Wim H. van Zwam[6,44]; 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]; Issam Boukrab[26]; Jo P. Peluso[26]; Puck Fransen[22]; Jan S.P. van den Berg[22]; Heleen M. den Hertog[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]; Rob A.R. Gons[32]; Lonneke S.F. Yo[33]; Emiel J.C. Sturm[35,47]; Tomas Bulut[35]; Paul J.A.M. Brouwers[34]; Anouk D. Rozeman[42]; Otto Elgersma[41]; Michel J.M. Remmers[43]; Thijs E.A.M. de Jong[46]. Imaging assessment committee Charles B.L.M. Majoie[3](chair); Wim H. van Zwam[6,44]; 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[6,45]; Stefan D. Roosendaal[3]; Bas F.W. van der Kallen[13]; Ido R. van den Wijngaard[13]; Adriaan C.G.M. van Es[10]; 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[41]; Auke P.A. Appelman[29]; Bas Hammer[16]; Sjoert Pegge[27]; Anouk van der Hoorn[29]; Saman Vinke[20]; Sandra Cornelissen[2]; Christiaan van der Leij[6]; Rutger Brans[6]; Jeanette Bakker[41]; Maarten Uyttenboogaart[28]; Miou Koopman[3]; Lucas Smagge[2]; Olvert A. Berkhemer[1,3,6]; Jeroen Markenstein[3]; Eef Hendriks[3]; Patrick Brouwer[10]; Dick Gerrits[35]. 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[5,44]; Wim H. van Zwam[6,44]; 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[5,44](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[1]; Laurine van der Steen[3]. Clinical/imaging data aquisition 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]; Nikki Boodt[1,2,40]; Anne F.A.V Pirson[5]; Agnetha A.E. Bruggeman[3]; Nadinda A.M. van der Ende[1,2]; Rabia Deniz[3]; Susanne G.H. Olthuis[5,44]; Floor Pinckaers[6,44]. 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)[44] and MHeNs School for Mental Health and Neuroscience, Maastricht, the Netherlands[45]; 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, (currently Deventer Hospital[47]); 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; Department of Neurology[42], Radiology[41], Albert Schweitzer Hospital, Dordrecht;Department of Neurology[43], Radiology[46], Amphia Hospital, Breda.

Contributors MarA and MJHW: conception and design of the study, and drafting of the manuscript. MarA, AvdM, HJAvO, and MahA: data and statistical analysis. EWvZ: supervision of statistical analysis. AvdM, JH, WJS, MAAvW, IRvdW, and ACGMvE: acquisition of clinical data. CBLMM and DWJD: members of the trial executive committee and critical review and revision. FHMS, PJN, MCV, and NDK: critical review and revision for valuable intellectual content. MarA is guarantor of the data.

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ORCID iDs
Mariam Ali http://orcid.org/0000-0003-3409-7835
Mahsoem Ali http://orcid.org/0000-0002-0511-6323
Charles B L M Majoie http://orcid.org/0000-0002-7600-9568
Wouter J Schonewille http://orcid.org/0000-0002-4070-9730
Diederik W J Dippel http://orcid.org/0000-0002-9234-3515

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