Circulation: Cardiovascular Quality and Outcomes

ORIGINAL ARTICLE

Between-Center Variation in Outcome After Endovascular Treatment of Acute Stroke: Analysis of Two Nationwide Registries

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BACKGROUND: Insight in differences in patient outcomes between endovascular thrombectomy (EVT) centers can help to improve stroke care. We assessed between-center variation in functional outcome of patients with acute ischemic stroke who were treated with EVT. We analyzed to what extent this variation may be explained by modifiable center characteristics.

METHODS: We used nationwide registry data of patients with stroke treated with EVT in the Netherlands and in the Czech Republic. Primary outcome was modified Rankin Scale score at 90 days as an indicator of disability. We used multilevel ordinal logistic regression to quantify the between-center variation in outcomes and the impact of patient and center characteristics. Between-center variation was expressed as the relative difference in odds of a more favorable modified Rankin Scale score between a relatively better performing center (75th percentile) and a relatively worse performing center (25th percentile).

RESULTS: We included a total of 4518 patients treated in 33 centers. Adjusted for patient characteristics, the odds of a more favorable outcome in a center at the 75th percentile of the outcome distribution were 1.46 times higher (95% CI, 1.31–1.70) than the odds in a center at the 25th percentile. Adjustment for center characteristics, including the median time between stroke onset and reperfusion per center, decreased this relative difference in odds to 1.30 (95% CI, 1.18–1.50, P=0.01). This translates into an absolute difference in likelihood of good functional outcome of 8% after adjustment for patient characteristics and to 5% after further adjustment for modifiable center characteristics.

CONCLUSIONS: The considerable between-center variation in patient outcomes after EVT for acute ischemic stroke could be largely explained by center-specific characteristics, such as time to reperfusion. Improvement of these parameters may likely result in a decrease in center-specific differences, and an overall improvement in outcome of patients with acute ischemic stroke.

Key Words: hospitals ■ multicenter study ■ quality improvement ■ stroke ■ thrombectomy

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Endovascular thrombectomy (EVT) improves outcomes in patients with acute ischemic stroke due to a large vessel occlusion in the anterior circulation.[1] However, the implementation of EVT in clinical practice has been challenging because of changes required in local and regional workflows concerning acute ischemic stroke treatment.

Studies from the pre-EVT era have reported that outcomes of patients with acute ischemic stroke vary substantially between centers and that this variation can be

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WHAT IS KNOWN

- Variation in functional outcome of patients with acute ischemic stroke is only partially explained by patient characteristics, such as stroke severity and medical history, which are mostly unmodifiable.
- Modifiable characteristics of centers providing endovascular thrombectomy for acute ischemic stroke, for example number of endovascular thrombectomies performed or time to treatment, can differ between centers.

WHAT THE STUDY ADDS

- In this international cohort of acute ischemic stroke patients treated with endovascular thrombectomy, functional outcome of patients differed substantially between centers and could be largely explained by center characteristics, such as time to reperfusion.
- Decreasing between-center variation in outcome by improving center-specific parameters may likely result in an overall improvement in outcome of patients with acute ischemic stroke.

Nonstandard Abbreviations and Acronyms

EVT	endovascular thrombectomy
IQR	interquartile range
MR CLEAN	Multicenter Randomized Controlled Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands
mRS	modified Rankin Scale
NIHSS	National Institutes of Health Stroke Scale
SITS-TBY	Safe Implementation of Treatments in Stroke-Thrombectomy

partially explained by patient characteristics, but possibly also by specific center characteristics.[2–5] However, the exact impact of center characteristics, such as center type and stroke volume, on between-center differences in outcome has remained uncertain. Insight in the potential causes of variation in outcomes between centers could contribute to the improvement of stroke care.

Little is known about the between-center variation in outcomes in patients treated with EVT. Variation in outcomes after EVT between centers can be caused by differences in patient population (eg, differences in stroke severity), but also by structural differences (eg, numbers of EVTs performed), or differences in processes (eg, times to treatment). Center-specific structural and process factors are largely modifiable contrary to patient characteristics. Insight into modifiable factors that could explain between-center variation in outcomes may inform improvements of EVT work processes and thereby improve patient outcomes. In this study, we aim to assess the between-center differences in functional outcomes of patients with acute ischemic stroke treated with EVT and to analyze to what extent variation in outcomes can be explained by modifiable center characteristics.

METHODS

Study Population

We used data from 2 nationwide registries, one from the Netherlands (MR CLEAN [Multicenter Randomized Controlled Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands] registry), and the other from the Czech Republic (SITS-TBY [Safe Implementation of Treatments in Stroke-Thrombectomy] registry). Data from the MR CLEAN registry cannot be made available for purposes of reproducing the results or replicating the procedure, as no patient approval has been obtained for sharing coded data. Syntax and output files of statistical analyses will be made available upon reasonable request.

The MR CLEAN registry is a multicenter, prospective observational cohort study, which started directly after the last inclusion in the MR CLEAN trial,[6] and comprises all consecutive acute ischemic stroke patients undergoing EVT in the Netherlands. Enrollment started with 16 centers that also participated in the MR CLEAN trial. Three centers started performing EVT later and added patients to the MR CLEAN registry. The MR CLEAN registry has previously been described in more detail.[7] For the present study, we used data from patients who received EVT between March 2014 and November 2017.

SITS is an international collaboration founded by the Karolinska Institute and was set up as an instrument to enhance safe implementation of intravenous thrombolysis in acute ischemic stroke in clinical practice. The SITS-TBY registry contains prospectively collected data from acute ischemic stroke patients who were treated with EVT. This global registry consists of a standard data entry protocol and can be used by individual stroke centers to document thrombectomy data and to compare outcomes with other centers and countries. For the present study, we used SITS-TBY Registry data from patients treated between January 2014 and December 2017 in 15 centers in the Czech Republic.[8]

From both registries, we selected stroke patients aged 18 years or older with intracranial large vessel occlusion in the anterior circulation, who were treated with EVT within 6.5 hours after onset of symptoms or last seen well. Patients were excluded for the present study when information on one or more of these inclusion criteria was missing.

A central medical ethics committee evaluated the study protocol of the MR CLEAN registry and granted permission to perform the study as a registry, as the study required no additional interventions or procedures beyond those performed as usual care. Ethics approval was obtained from the local institutional review board for the analysis of the Czech data from the SITS-TBY registry. Study results are reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement.[9]

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Data Collection

We collected baseline patient data on age, sex, previous ischemic stroke, diabetes, atrial fibrillation, hypertension, hypercholesterolemia, smoking status, prestroke modified Rankin Scale (mRS) score, baseline National Institutes of Health Stroke Scale (NIHSS) score, occlusion side, and occlusion segment on computed tomography angiography. The mRS is a 7 point disability scale ranging from 0 (no symptoms) to 6 (death). The NIHSS, ranging from 0 to 42, is a scale that quantifies stroke symptoms. A higher score indicates more and worse neurological deficits.

Data on workflow were intravenous alteplase treatment, transfer status (first presentation at a primary stroke center or at an intervention center), times from stroke onset to door of the first hospital, groin puncture, and reperfusion, time from door of the first hospital to groin puncture, and time from groin puncture to reperfusion. Onset of stroke was defined as the time of symptom onset or the time of last seen well. The definition of time of reperfusion or end of procedure slightly differed between the 2 registries. In the MR CLEAN registry, this was defined as the time of successful reperfusion, last contrast bolus, or end of procedure, while in the SITS-TBY registry, this was defined as the time of closure of the puncture site. The time of arrival at the door of the first hospital was collected for each patient. This means that for nontransferred patients, this time point refers to the arrival at the intervention center, and for transferred patients, this time point refers to the arrival at the primary stroke center.

Additional center characteristics were collected, including center type (university hospital, nonuniversity teaching hospital, or nonuniversity nonteaching hospital) and availability of endovascular treatment for intracranial aneurysms. In addition, for each center, we calculated the mean number of patients treated with EVT per 3 months using all registered patients in the study period without applying any of our inclusion criteria. Furthermore, we calculated the percentage of patients with an onset-to-groin puncture time of >390 minutes for each center, using only data of patients with the occlusion in the anterior circulation, as an indicator of guideline adherence.

The primary outcome was mRS score at 90 days, which we analyzed both ordinal as dichotomized. Other outcome data were NIHSS scores at 24 to 48 hours.

Statistical Analysis

Because of the nested structure of the data, we used multilevel mixed-effects ordinal logistic regression with a random intercept for center to quantify the between-center variation in mRS scores at 90 days. To analyze the impact of patient characteristics and modifiable center characteristics on between-center variation in functional outcomes, the analysis was performed in a stepwise manner. We started with a model with adjustment for 12 patient characteristics: age, sex, previous ischemic stroke, diabetes, atrial fibrillation, hypercholesterolemia, hypertension, smoking, occlusion side, occlusion segment, baseline NIHSS score, and prestroke mRS score. Percentage of intravenous alteplase treatment and percentage of transferred patients were included as center characteristics (in the next model) and not as patient-level variables. Subsequently, center characteristics were added in 3 sets as fixed effects to the model. The first set of center characteristics concerned factors that are slightly modifiable: mean number of treated patients per 3 months, type of center, availability of endovascular treatment for intracranial aneurysms, percentage of patients treated with onset-to-groin puncture time >390 minutes, percentage of transferred patients, and percentage of patients receiving intravenous alteplase treatment. Then a second set of center characteristics, all concerning the times to treatment mentioned above, was added as fixed effect to the model. These characteristics are modifiable to a larger extent than those in the first set. Finally, the country variable was added as center characteristic to the model.

To help interpreting the estimated between-center differences in outcomes, we used the random intercept variance (tau2) to calculate the relative difference in odds of a more favorable outcome (ordinal mRS score) at 90 days between a center located at the 25th percentile of the outcome distribution (relatively worse performing center) and a center at the 75th percentile of the outcome distribution (relatively better performing center).[10] This relative difference in odds was calculated with the formula: exp (2×0.67×tau). The value 2×0.67 is the Z value corresponding to the width of the 50% CI in a normal (Gaussian) distribution. The differences in between-center variation between the 4 steps of the analysis were each compared against the previous step with a likelihood ratio test.

The effect of each center characteristic on the between-center variation in outcomes, independently of the other center characteristics, was estimated by comparing a model with patient characteristics and all center characteristics against the same model with one specific center characteristic taken out with a likelihood ratio test. Common odds ratios were estimated for each center characteristic using a model including patient characteristics and all center characteristics.

Furthermore, we estimated the impact of the between-center variation in outcome for an average patient. For this estimation, we dichotomized mRS scores in 0–2 (good functional outcome) and 3–6 (poor functional outcome). An average patient was constructed by using the mean values for each patient characteristic, the mean values of the center characteristics availability of endovascular treatment for intracranial aneurysms and type of center, and the median values of the remaining center characteristics. For this average patient, the expected outcome at 90 days was calculated based on the model with adjustment for patient characteristics and again with adjustment for patient characteristics and all center characteristics.

To make unbiased estimates of regression effects, we substituted missing data using multiple imputation with 10 iterations, assuming missingness at random.[11,12] The center variables percentage of transferred patients, percentage of patients treated with intravenous alteplase, median time from onset to door intervention center, median time from first door to groin puncture, and median time from groin puncture to reperfusion were computed from imputed variables. All reported baseline data are not imputed. We used Stata/SE statistical package version 15.1 (StataCorp, College Station, TX) for all analyses.

RESULTS

Baseline Characteristics

A total of 4518 patients, from 19 centers in the Netherlands and 14 centers in the Czech Republic,

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were included (Figure 1). One center that reported 5 patients with incomplete data was excluded from the analysis.

The median age of the patients was 72 years (interquartile range [IQR] 62–80) and 2306 (51%) were male (Table 1). The prestroke mRS score was 0 or 1 in 3633 (82%) patients. The median NIHSS score at baseline was 16 (IQR, 11–19). The median time from onset to reperfusion was 243 minutes (IQR 195–306). The number of included patients receiving EVT per center in the study period ranged from 23 to 397 in the MR CLEAN registry, and from 1 to 195 in the Czech SITS-TBY registry. Median number of included patients per center for both registries together was 109 (IQR 58–192). The percentage of transferred patients per center ranged from 0 to 77% (median 62, IQR 45–68) in the MR CLEAN registry, and from 0% to 42% (median 16, IQR 4–33) in the Czech SITS-TBY registry (Table 2).

At 90 days, 1561 (42%) of 3696 patients had a good functional outcome (mRS score 0–2). The median NIHSS score at 24 to 48 hours was 9 (IQR, 3–16). Data on the mRS score at 90 days were missing in 822 (18%) patients and data on the NIHSS score at 24 to 48 hours in 753 (17%) patients. Information on both outcome parameters was missing in 210 (4.6%) patients.

Between-Center Variation in Outcome

Regarding the between-center comparisons, the odds of a more favorable mRS score at 90 days were 1.46 times higher (95% CI, 1.31–1.70) in a center at the higher end (75th percentile) of the outcome distribution than in a center at the lower end (25th percentile), after adjustment for patient characteristics (Table 3). After addition of the first and second set of center characteristics to the model, which included logistics parameters, this relative difference in odds decreased to 1.30 (95% CI, 1.18–1.50; P=0.01; Figure 2). When we also adjusted for country, this relative difference in odds between centers at the 25th and 75th percentile of the outcome distribution was 1.26 (95% CI, 1.15–1.47; P=0.10). To adjust for time-dependent changes in patient management not captured in our primary analysis, we added a time factor (year of intervention) to the primary multivariable analysis. Results were similar, and can be found in Table S1.

Of the center characteristics, only the median time from groin puncture to reperfusion had a statistically significant effect on the between-center variation in outcome, independently of the other center characteristics (Table 4). For every 10 minutes increase of the median time from groin puncture to reperfusion of an intervention center, the odds on a more favorable score on the mRS decreased with 12% (odds ratio, 0.88 [95% CI, 0.80–0.98]).

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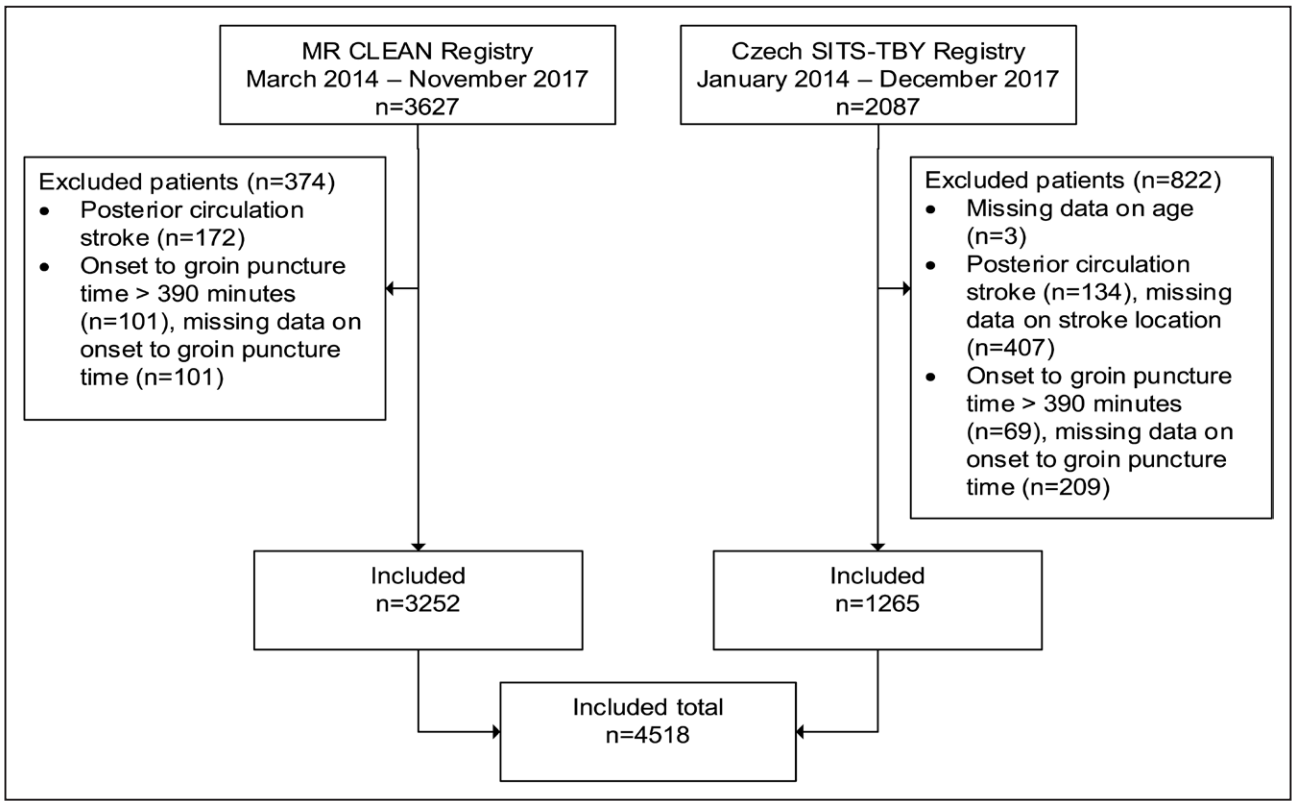

Figure 1. Inclusion flowchart study population.
MR CLEAN indicates Multicenter Randomized Controlled Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; and SITS-TBY, Safe Implementation of Treatments in Stroke-Thrombectomy.

Table 1. Baseline Patient Characteristics

	MR CLEAN registry (n=3253)	Czech SITS-TBY registry (n=1265)
Age, y, median (IQR)	72 (61–81)	72 (63–79)
Male sex, n (%)	1694 (52)	612 (48)
Medical history, n (%)		
Previous ischemic stroke	545 (17)	154 (12)
Diabetes	519 (16)	325 (26)
Atrial fibrillation	769 (24)	416 (35)
Hypercholesterolemia	956 (31)	423 (34)
Hypertension	1671 (52)	940 (75)
Smoking	693 (28)	173 (14)
Prestroke mRS score, n (%)		
0	2148 (68)	953 (76)
1	422 (13)	110 (9)
2	237 (7)	119 (10)
>2	374 (12)	60 (5)
NIHSS score at baseline, median (IQR)	16 (11–20)	15 (11–18)
Occlusion side on CTA, left hemisphere, n (%)	1720 (53)	513 (53)
Occlusion segment on CTA, n (%)		
ICA-T+ICA	790 (26)	100 (11)
M1	1756 (58)	632 (66)
M2	441 (15)	219 (23)
Other*	24 (0.8)	0
Intravenous alteplase treatment, n (%)	2478 (76)	1000 (79)
Transfer from primary stroke center, n (%)	1755 (54)	187 (15)
Time intervals, min, median (IQR)		
Onset-to-groin puncture	192 (150–250)	170 (135–220)
Onset to reperfusion	250 (198–311)	230 (190–290)
Groin puncture to reperfusion	50 (30–75)	55 (35–77)
Onset to door intervention center (nontransferred patients)	59 (39–105)	70 (55–97)
Onset to door primary stroke center (transferred patients)	53 (36–90)	60 (45–90)
Door intervention center to groin puncture (nontransferred patients)	90 (69–117)	83 (64–117)
Door primary stroke center to groin puncture (transferred patients)	145 (121–176)	148 (109–190)

Missing data: previous ischemic stroke 0.9%, diabetes 0.8%, atrial fibrillation 2%, hypercholesterolemia 4%, hypertension 2%, smoking 18%, prestroke mRS score 2%, baseline NIHSS 9%, occlusion side 7%, occlusion segment 12%, intravenous alteplase treatment 0.2%, transfer from primary stroke center 3%, time from groin puncture to reperfusion 7%, time from onset to door intervention center (nontransferred patients) 6%, time from onset to door primary stroke center (transferred patients) 29%, time from door intervention center to groin puncture (nontransferred patients) 11%, and time from door primary stroke center to groin puncture (transferred patients) 32%. CTA indicates computed tomography angiography; ICA, internal carotid artery; ICA-T, terminal internal carotid artery; IQR, interquartile range; M1, middle cerebral artery segment 1; M2, middle cerebral artery segment 2; MR CLEAN, Multicenter Randomized Controlled Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SITS-TBY, Safe Implementation of Treatments in Stroke-Thrombectomy.

*Occlusion in segment 1 or 2 of the anterior cerebral artery, or in segment 3 of the middle cerebral artery.

Table 2. Baseline Center Characteristics

	MR CLEAN registry (19 centers)	Czech SITS-TBY registry (14 centers)
Slightly modifiable center characteristics (set 1)		
Mean number of treated patients per 3 mo, median (IQR)*	16 (12–22)	11 (7–16)
Type of center, n (%)		
University hospital	7 (37)	8 (57)
Nonuniversity teaching hospital	5 (26)	3 (21)
Nonuniversity nonteaching hospital	7 (37)	3 (21)
Availability of endovascular treatment for intracranial aneurysms, n (%)	10 (53)	14 (100)
Percentage of treated patients with onset-to-groin puncture time >390 min, median (IQR)*	2.0 (1.7–3.3)	5.3 (1.6–8.2)
Percentage of transferred patients, median (IQR)	62 (45–68)	16 (4.2–32)
Percentage of patients receiving intravenous alteplase treatment, median (IQR)	77 (73–80)	83 (76–84)
Largely modifiable center characteristics (set 2)		
Median time from onset to door intervention center, median (IQR)	142 (118–151)	70 (64–72)
Median time from first door to groin puncture, median (IQR)	114 (105–130)	95 (82–103)
Median time from groin puncture to reperfusion, median (IQR)	48 (45–55)	50 (45–60)

IQR indicates interquartile range; MR CLEAN, Multicenter Randomized Controlled Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; and SITS-TBY, Safe Implementation of Treatments in Stroke-Thrombectomy.

*We included all registered patients without applying any of our inclusion criteria to construct this variable, MR CLEAN registry: 3627 patients, Czech SITS-TBY registry: 2087 patients.

The estimated frequency of good functional outcome (mRS score 0–2) at 90 days after EVT for an average patient with acute ischemic stroke for each center was 36% in a center at the lower end (25th percentile) and 44% in a center at the higher end (75th percentile) of the outcome distribution (Figure 3). This decreased to 38% and 43%, respectively, after adjustment for modifiable center characteristics.

DISCUSSION

Our study shows that functional outcomes of acute ischemic stroke patients treated with EVT vary substantially between centers. The impact of center characteristics on between-center variation in outcomes was large. Adjustment for center characteristics decreased the relative difference in odds of a more favorable outcome between centers at the 25th and 75th percentile of the outcome distribution from 1.46 to 1.26 and decreased the absolute difference in estimated frequency for an average patient to achieve a good functional outcome from 8% to 5%. Even a small difference in outcome after EVT can have a major impact for an individual

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Table 3. Effect of Combined Center Characteristics on Between-Center Variation in Outcome After EVT for Acute Ischemic Stroke

Variables included in the multilevel ordinal logistic regression model	Relative difference in odds of a more favorable outcome between a relatively better performing center (75th percentile) and a relatively worse performing center (25th percentile) (95% CI)
Patient characteristics*	1.46 (1.31–1.70)
Patient characteristics + set 1 center characteristics:	1.41 (1.27–1.64); *P*=0.73
Mean number of treated patients per 3 mo	
Type of center	
Availability of endovascular treatment for intracranial aneurysms	
Percentage of patients treated with onset-to-groin puncture time >390 min	
Percentage of transferred patients	
Percentage of patients receiving intravenous alteplase treatment	
Patient characteristics + set 1 + set 2 center characteristics:	1.30 (1.18–1.50); *P*=0.01
Median time from onset to door intervention center	
Median time from first door to groin puncture	
Median time from groin puncture to reperfusion	
Patient characteristics + set 1 and 2 center characteristics + country	1.26 (1.15–1.47); *P*=0.10

Outcomes in the multilevel ordered logistic regression analysis were measured with the mRS at 90 d. Likelihood ratio tests were performed to compare the relative difference in odds of each step of the analysis with the previous step (*P* value provided). Center characteristics were added in 2 separate sets to the model based on relative modifiability. EVT indicates endovascular thrombectomy; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.

*Patient characteristics were age, sex, previous ischemic stroke, diabetes, atrial fibrillation, hypercholesterolemia, hypertension, smoking, occlusion side, occlusion segment, baseline NIHSS score, and prestroke mRS score.

patient and also for society considering the incidence of stroke worldwide.

Other studies have shown that between-center variation in mortality and functional recovery rates after ischemic stroke can be explained to some extent by patient characteristics.[2–5] However, the variation in outcome between regions and between centers remained largely unexplained. Furthermore, in these previous studies, the effect of center characteristics on between-center differences in outcome after stroke could not be established with certainty.[2,3,5] Our study provides information on the association between center characteristics and functional outcome at a more detailed level in a unique set of acute stroke patients treated with EVT. In accordance with previous studies, the size and direction of the effect of center type and center size remained unclear.[2,3,5] Possibly, other, not included patient characteristics, such as the Alberta Stroke Program Early Computed Tomography score or collateral score, may have differed between large and small EVT centers or between centers types. Also, the number of EVTs per interventionalist was not included in our analysis, let alone their competence in the intervention. Furthermore, we did not include the type of device used for EVT since this was not registered in the SITS-TBY. The influence of these factors on between-center differences in outcome after EVT need further study.

Our observation that between-center variation in time to reperfusion had a significant impact on the between-center variation in outcome is consistent with the observation from EVT trials that earlier treatment leads to a better functional outcome.[13] In our study, time from groin puncture to reperfusion had a significant effect on between-center variation in outcomes, independent of the other center characteristics. Earlier studies have shown that greater experience and steeper learning curves of interventionalists can contribute to faster recanalization times and are likely to lead to improved functional outcomes.[14–16] A meta-analysis showed that reducing time to treatment through interventions in the workflow of EVT, for example, by optimizing prehospital management, in-hospital transfer management, and teamwork, was associated with an increased likelihood of favorable outcome.[17] A previous study has shown a modest favorable linear time trend over time towards a shorter door to first pass time in clinical practice.[18] Future research should focus on the impact of interventions in the workflow of EVT, aimed at decreasing time to EVT, to improve outcome.

Our study has potential limitations. First, our results suggest that between-center variation in outcome after EVT for acute ischemic stroke could be partially explained by between-country differences. This between-country difference in outcome may be caused by our study design, since the 2 registries had a different method of data collection and had no blinding of outcome assessment. Furthermore, general differences between the 2 countries in organization of stroke health care before, during, and after hospital admission may have had an impact on the results. Second, our study cannot completely explain the observed between-center variation in outcomes in patients treated with EVT for acute ischemic stroke. Possibly other patient or center characteristics, not included in our study, also have an impact on between-center differences in outcomes. For example, low socioeconomic status is associated with a decreased survival and poor outcome in patients with ischemic stroke, independently of cardiovascular risk factors.[19–22] Between-center differences in socioeconomic status of patients were not evaluated in our study. Although

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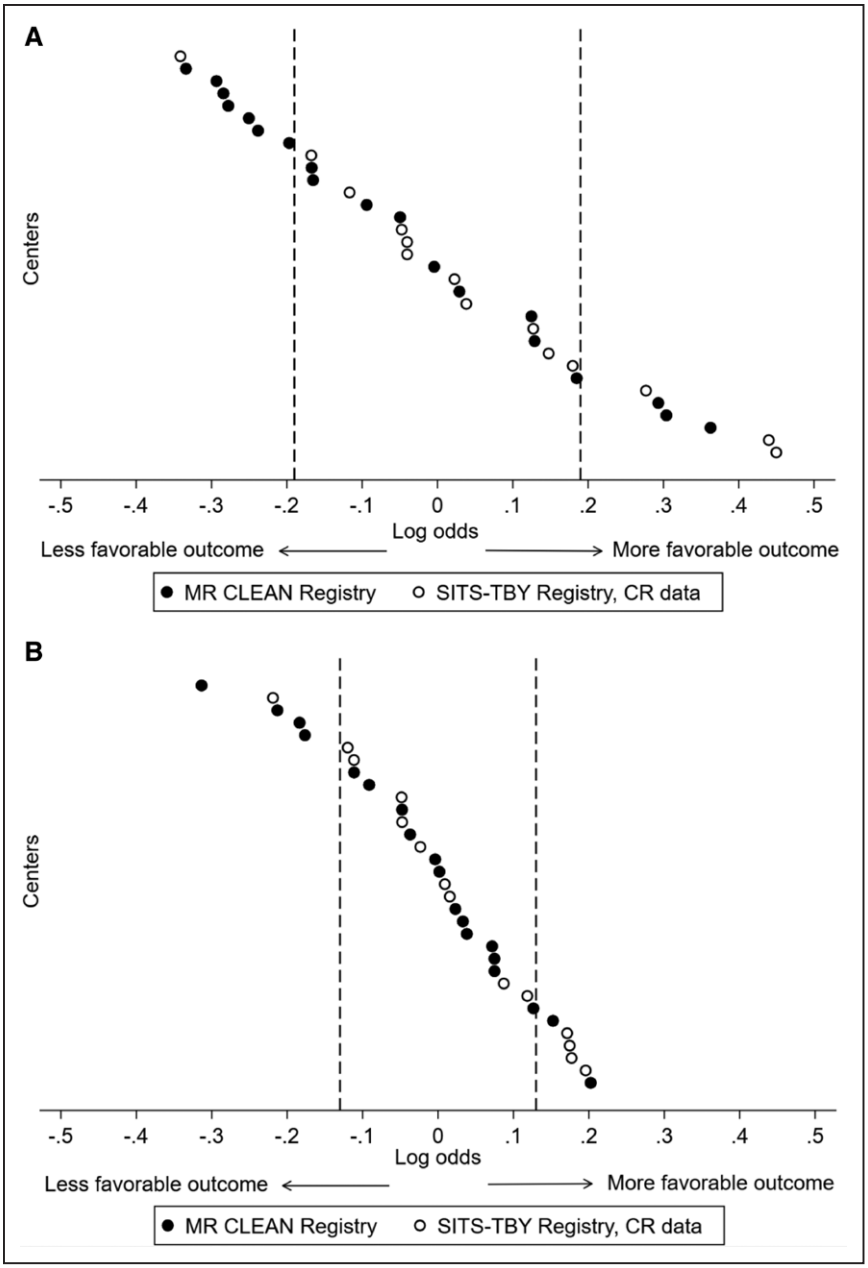

Figure 2. Effect of center characteristics on between-center variation in outcomes after endovascular treatment for acute ischemic stroke.
Log odds of outcome, measured with the modified Rankin Scale at 90 d, calculated for each center and compared with the average, with adjustment for patient characteristics (**A**), and again with adjustment for patient and center characteristics (**B**). Each dot represents one center and centers are ranked from relatively worse to better performance. The dashed lines represent the 25th and 75th percentile of the outcome distribution. Log odds of −0.19 and 0.19 refer to odds ratios of 0.83 and 1.21, respectively (**A**), and log odds of −0.13 and 0.13 refer to odds ratios of 0.88 and 1.14, respectively (**B**). CR indicates Czech Republic; MR CLEAN, Multicenter Randomized Controlled Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; and SITS-TBY, Safe Implementation of Treatments in Stroke-Thrombectomy.

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socioeconomic status could possibly explain between-center differences in outcome, this is a nonmodifiable patient characteristic. Adherence to stroke guidelines, however, is to some extent modifiable. Analysis of received, guideline-recommended, secondary stroke prevention treatments in 991 995 patients with stroke showed that almost one-quarter of patients received suboptimal care.[23] This was also seen in a smaller study on quality of care parameters in acute stroke care, which showed that execution of recommended diagnostic investigations and medical treatment in the acute phase, subacute care, and performance of secondary prevention varied considerably between centers.[4] To analyze the effect of guideline adherence, we could only include the percentage of patients treated >390 minutes after stroke onset, which was the recommended time window for EVT during the study period. Further research is needed to evaluate the influence of guideline adherence on between-center variation in outcome after EVT for acute ischemic stroke. A third limitation is the amount of loss to follow-up at 90 days resulting in missing mRS scores in 18% of patients. By performing multiple imputation using multiple variables including NIHSS at 24 to 48 hours, we tried to minimize bias in the estimates. Another variable with a relative large amount of missing data concerned the time of arrival at the primary stroke center. Therefore, missing arrival times were imputed, and the center characteristic concerning the time from first door to groin puncture was then computed.

Between-center variation in outcomes has not only been described in stroke, but also in other acute

Table 4. Effect of Each Center Characteristic on Between-Center Variation in Outcome After EVT for Acute Ischemic Stroke

	Common odds ratio (95% CI)*	Effect on between-center variation in outcome†
Slightly modifiable center characteristics		
Mean number of treated patients per 3 mo (per 10 patients)	0.82 (0.65-1.04)	*P*=0.10
Type of center‡	1.05 (0.92-1.21)	*P*=0.48
Availability of endovascular treatment for intracranial aneurysms§	1.01 (0.74-1.39)	*P*=0.92
Percentage of patients treated with onset-to-groin puncture time >390 min	0.99 (0.95-1.02)	*P*=0.47
Percentage of transferred patients (per 10%)	1.03 (0.93-1.15)	*P*=0.54
Percentage of patients receiving intravenous alteplase treatment (per 10%)	0.96 (0.83-1.10)	*P*=0.54
Largely modifiable center characteristics		
Median time from onset to door intervention center (per 10 min)	0.96 (0.90-1.02)	*P*=0.90
Median time from first door to groin puncture (per 10 min)	1.00 (0.94-1.07)	*P*=0.21
Median time from groin puncture to reperfusion (per 10 min)	0.88 (0.80-0.98)	*P*=0.02
Additional center characteristic		
Country‖	1.31 (0.96-1.78)	*P*=0.10

EVT indicates endovascular thrombectomy; and mRS, modified Rankin Scale.

*A common odds ratio <1 means that a higher value of the variable leads to a less favorable mRS score at 90 d, and a common odds ratio >1 means that a higher value of the variable leads to a more favorable mRS score.

†*P* value of likelihood ratio test comparing the difference in between-center variation in outcomes between a complete model with patient characteristics and all center characteristics against the same model with one specific variable taken out.

‡Values of the variable type of center: 0=academic center, 1=teaching, nonacademic center, and 2=nonteaching nonacademic center.

§Values of the variable availability of endovascular treatment for intracranial aneurysms: 0=no and 1=yes.

‖Values of the variable country: 0=the Netherlands and 1=Czech Republic.

diseases, such as traumatic brain injury and myocardial infarction.[10,24–27] A study of 9578 patients with moderate or severe traumatic brain injury showed that risk-adjusted odds of unfavorable outcome differed 3.3-fold between centers at the 2.5th and 97.5th percentile of the outcome distribution.[10] A large observational study of 2 million patients with ST-segment–elevation myocardial infarction showed significant regional differences in in-hospital mortality, independent of patient characteristics and treatment selection.[24] This study emphasized that our research focus should not only be directed on developing improved treatments but also on implementation of current evidence and guidelines in clinical practice.

The baseline characteristics of our included patients, with higher age and more frequent cardiovascular comorbidity than in the EVT trials, suggest that our study population reflects the acute ischemic stroke population eligible for EVT of many centers and countries. The large study population, treated in 33 interventions centers with varying center characteristics, makes the results of our study applicable to many centers and countries. This means that between-center variation in outcome after EVT for acute ischemic stroke needs to be acknowledged. We hope that addressing and visualizing differences between centers in outcome and in center characteristics may help to improve stroke care. This is already being applied in the European Stroke Organisation Enhancing and Accelerating Stroke Treatment program,[28] and in the Dutch PERFEQTOS trial.[29] To optimize the implementation of EVT, we need to determine the optimal combination of center characteristics, for example, balancing center size and time from onset to arrival at the intervention center. The optimal implementation differs between geographic countries and between regions, and thus is most easily addressed with modeling studies.[30] However, we think that the association between the center characteristics we studied, such as time to treatment and volume, and outcome are generalizable to other settings. These association and their magnitudes should be taken into account when redesigning stroke systems.

We conclude that the proportion of patients with good functional outcome after EVT for acute ischemic stroke varies substantially between centers. This between-center variation in outcomes could be largely explained by center-specific characteristics, such as time to reperfusion. Improvement of these parameters may likely result

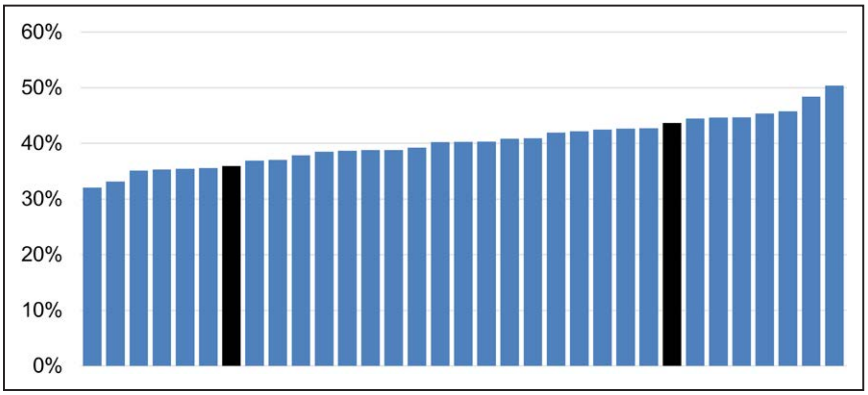

Figure 3. Estimated frequency of good functional outcome (modified Rankin Scale [mRS] score 0–2) for an average patient for each center. Each bar represents one center. The black bars represent the centers at the 25th and 75th percentile of the outcome distribution, corresponding to an interquartile range of the relative frequencies to achieve good functional outcome of 36%–44%, adjusted for patient characteristics.

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in a decrease in center-specific differences, and an overall improvement in outcome of patients with acute ischemic stroke.

ARTICLE INFORMATION

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Supplemental Material

Table S1

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