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Effect of Workflow Improvements in Endovascular Stroke Treatment

A Systematic Review and Meta-Analysis

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Background and Purpose—Rapid initiation of endovascular stroke treatment is associated with better clinical outcome. The effect of specific improvements is not well known. We performed a systematic review and meta-analysis on the effectiveness of specific workflow improvements on time to treatment and outcome.

Methods—A random-effects meta-analysis was used to evaluate the difference in mean time to treatment between intervention group and control group. Secondary outcomes included good functional outcome at 90 days (modified Rankin Scale score 0–2).

Results—Fifty-one studies (3 randomized controlled trials, 13 prepost intervention studies, and 35 observational studies) with in total 8467 patients were included. Most frequently reported workflow intervention types concerned anesthetic management (n=26), in-hospital patient transfer management (n=14), and prehospital management (n=11). Patients in the intervention group had shorter time to treatment intervals (weighted mean difference, 26 minutes; 95% CI, 19–33; *P*<0.001) compared with controls. Subgroup meta-analysis of intervention types also showed a shorter time to treatment in the intervention group: a mean difference of 12 minutes (95% CI, 6–17; *P*<0.001) for anesthetic management, 37 minutes (95% CI, 22–52; *P*<0.001) for prehospital management, 41 minutes (95% CI, 27–54; *P*<0.001) for in-hospital patient transfer management, 47 minutes (95% CI, 28–67; *P*<0.001) for teamwork, and 64 minutes (95% CI, 24–104; *P*=0.002) for feedback. The mean difference in time to treatment of studies with multiple interventions implemented simultaneously was 50 minutes (95% CI, 31–69; *P*<0.001) in favor of the intervention group. Patients in the intervention group had increased likelihood of favorable outcome (risk ratio [RR], 1.39; 95% CI, 1.15–1.66; *P*<0.001).

Conclusions—Interventions in the workflow of endovascular stroke treatment lead to a significant reduction in time to treatment and results in an increased likelihood of favorable outcome. Acute stroke care should be reorganized by making use of the examples of workflow interventions described in this review to ensure the best medical care for stroke patients. **(*Stroke*. 2019;50:665-674. DOI: 10.1161/STROKEAHA.118.021633.)**

Key Words: anesthetic ■ patient transfer ■ stroke ■ thrombectomy ■ workflow

Multiple trials have shown the benefit of endovascular recanalization therapy in selected stroke patients.[1–3] Earlier treatment is associated with better functional outcome.[4] The time from symptom onset to treatment is influenced by prehospital and in-hospital processes. Healthcare systems are being reorganized to offer stroke patients rapid and effective medical care. Stroke services had already changed their workflow since intravenous tPA (tissue-type plasminogen activator) for selected stroke patients was proven effective.[5] Implementation of new strategies to improve the workflow process for treatment with intravenous tPA has led to a significant reduction of in-hospital delay.[6]

Providing an optimal diagnostic process and rapid endovascular stroke treatment requires close collaboration of the emergency medical service, emergency department team, stroke team, neurointerventional team, and anesthesia team. Diagnostic imaging and endovascular treatment facilities should be available in little time. Several strategies to reduce the time to endovascular stroke treatment have been proposed.[7–9] However, the effect of individual and combined strategies on reducing time to treatment is unclear. We performed a systematic review and meta-analysis on the effectiveness of specific workflow improvement interventions for rapid delivery of endovascular stroke treatment.

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Methods

This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines.[10] All data and supporting materials are available within the article and its online-only Data Supplement.

Search Strategy

Medline, EMBASE, Cochrane Central, and Web of Science were searched for studies that evaluated the effect of ≥1 workflow interventions on time to endovascular stroke treatment, from database inception to November 14th, 2017. Google Scholar and Google were searched on November 14th, 2017, and the first 200 hits were included. We developed a broad search strategy consisting of a combination of the 2 main topics of this study: endovascular stroke treatment and workflow intervention. The complete search strategy is available in the online-only Data Supplement. We restricted our search to studies published in English and excluded conference abstracts.

Eligibility Criteria

Studies were included if ≥1 (prehospital or in-hospital) interventions in the workflow of endovascular stroke treatment were assessed and effect on time to treatment intervals was reported. Endovascular stroke treatment was defined as mechanical thrombectomy or intra-arterial fibrinolysis in an acute stroke patient with an intracranial large vessel occlusion. Interventions only aimed at the duration of the endovascular treatment itself, for example, type of mechanical thrombectomy device used, were excluded. Interventions intended only to increase the accuracy of patient selection, for example, the introduction of a new imaging protocol, were also excluded. Studies were included in the systematic review when time to endovascular treatment was reported from symptom onset to start treatment or any time window between symptom onset and start treatment. Randomized and nonrandomized controlled trials and prepost intervention studies were included. Observational studies or post hoc analyses of observational data in trials were only included when a control group was reported. Reviews, editorials, and guidelines were excluded. Two authors (Drs Janssen and Venema) independently assessed the eligibility of all retrieved studies. Title and abstracts were first screened to identify potentially eligible articles and then full texts were read to confirm inclusion. Reference lists of identified eligible articles and review articles were scanned for additional relevant studies.

Risk of Bias Assessment

The risk of bias of each included study was assessed against the following key criteria: random sequence generation; allocation concealment; blinding of participants, personnel, and outcomes; incomplete outcome data; and selective outcome reporting; in accordance with the methods recommended by the Cochrane Library.[11] The following judgments were used: low risk, high risk, or unclear risk of bias (either lack of information or uncertainty on the potential for bias). Summary of risk of bias per key criterion was provided for all included articles separately.

Data Extraction and Outcome Variables

Data were extracted from published reports by 2 authors (Drs Janssen and Venema). Workflow interventions were described and divided into 6 predefined categories: (A) anesthetic management, (B) prehospital management, (C) in-hospital patient transfer management, (D) teamwork, (E) feedback, and (F) other workflow interventions. Other collected data on study characteristics included study design, study period, stroke type (anterior or posterior circulation stroke, or both), and sample size.

The primary outcome measure in this study was the difference in time to treatment between the intervention group and control group. Other study outcomes were good functional outcome, defined as modified Rankin Scale score 0 to 2 at 90 days after endovascular treatment, symptomatic intracranial hemorrhage, and mortality.

Statistical Analysis

Mean time to treatment with SD for the intervention group and control group was retrieved from each included study. When mean values with SD were not available in the publication nor obtained from the authors of the original publication, we used reported median time to treatment with interquartile range to estimate the sample mean and SD using the method described by Wan et al.[12] The absolute difference of mean time to treatment with 95% CIs was calculated for each study using a 2-sample *t* test.

Studies were included in the meta-analysis when mean time to treatment with SD or median time to treatment with interquartile range was available for both groups. Weighted difference in mean time to treatment with 95% CI was calculated using a random-effects inverse variance model, with the estimate of heterogeneity being taken from the Mantel-Haenszel model. Subgroup analysis of the difference in mean time to treatment was performed for the predefined workflow intervention categories A to E and for studies implementing multiple interventions simultaneously.

Data on binary outcomes (good functional outcome, symptomatic intracranial hemorrhage, and mortality) were pooled using random-effects meta-analysis and expressed as RRs. Publication bias was assessed by constructing a funnel plot. All statistical analyses were conducted with Stata, version 15 (Statacorp LLC, College Station, TX).

Results

Our literature search identified 4127 potentially relevant unique articles; 211 articles were retained for full-text review (Figure 1). A total of 51 studies met the inclusion criteria and were included in the qualitative synthesis.[2,13–62] We contacted authors from 31 of 51 studies with requests for additional data necessary for our meta-analysis. These additional data were provided for 17 of 31 studies. The sample mean difference in time to treatment with SD could be estimated from published data from 8 of 31 studies. After exclusion of the remaining 6 studies because of lack of sufficient data, a total of 45 studies was included in the meta-analysis on effect of workflow interventions on the time to treatment.

Fifty-one studies with 8467 patients (4037 intervention group and 4430 control group) reported the effect of 25 different workflow interventions on the time to endovascular treatment (Tables 1 and 2). Two studies reported the effect on time to treatment of 2 interventions separately.[50,55] Most frequently reported workflow intervention types concerned anesthetic management (n=26), in-hospital patient transfer management (n=14), and prehospital management (n=11). Ten studies reported the effect on time to treatment of multiple interventions implemented simultaneously. Time to treatment was shorter in the intervention group in 48 of 53 interventions (91%) reported in the 51 included studies. Included studies differed in study design, with 3 studies randomizing patients for the workflow intervention of interest in our study, 13 prepost intervention studies, and the remaining 35 studies reporting observational data mostly from hospital stroke registries or randomized controlled trials investigating the effect of endovascular stroke treatment versus conservative treatment. Data collection was performed retrospectively in 34 studies, and 16 studies collected data from ≥1 center. Assessment of risk of bias is available in the online-only Data Supplement.

Random-effects meta-analysis of 45 studies (with 47 interventions), including 7482 patients (3480 intervention group and 4002 control group) showed a difference in mean time to

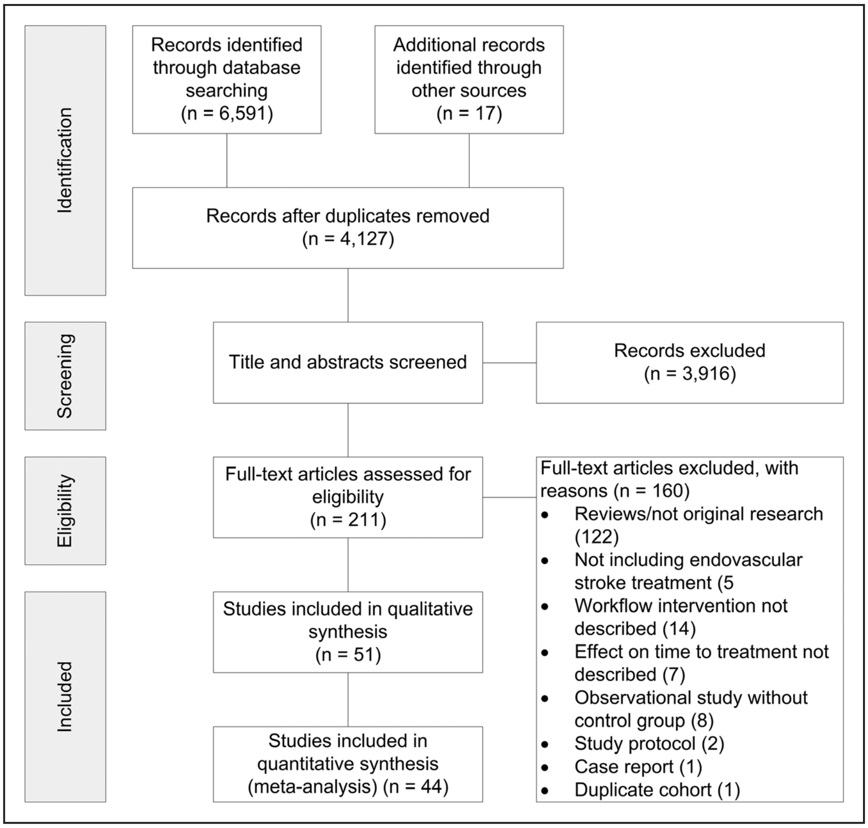

Figure 1. Flowchart of included and excluded articles, following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines

treatment of 26 minutes (95% CI, 19–32; *P*<0.001) in favor of the intervention group (Figure 2). I^2 value was 85.4%, and χ^2 value was 314.87 (df, 46; *P*<0.001), indicating considerable heterogeneity between studies.

The mean time to treatment was shorter in the intervention group compared with controls in the predefined workflow intervention categories (Table 3). The weighted difference in mean time to treatment was 12 minutes (95% CI, 6–17; *P*<0.001) for anesthetic management, 37 minutes (95% CI, 22–52, *P*<0.001) for prehospital management, 41 minutes (95% CI, 27–54, *P*<0.001) for in-hospital patient transfer management, 47 minutes (95% CI, 28–67, *P*<0.001) for teamwork, and 64 minutes (95% CI, 24–104, *P*=0.002) for feedback. The weighted difference in mean time to treatment of studies with multiple interventions implemented simultaneously was 50 minutes (95% CI, 31–69, *P*<0.001) in favor of the intervention group. Forest plots of the difference in mean time to treatment for each type of workflow intervention are available in the online-only Data Supplement. The description of used time intervals in the studies, mean (SD) estimates for each study group, and a subgroup analysis per time interval is provided in the online-only Data Supplement.

Twenty studies reported the occurrence of favorable outcome, defined as score 0–2 on the modified Rankin Scale at 90 days (in the online-only Data Supplement). Meta-analysis showed that patients in the intervention group had a higher likelihood of favorable outcome (absolute risk difference, 12.2%; RR, 1.39; 95% CI, 1.15–1.66; *P*<0.001) in comparison with controls. Data from 21 studies reporting the prevalence of symptomatic intracranial hemorrhage showed no difference between patients in the intervention groups and controls (RR, 0.88; 95% CI, 0.71–1.09; *P*=0.239). Mortality was assessed in 25 studies. Twelve studies reported in-hospital mortality, 2 studies reported mortality at 30 days, and 11 studies reported mortality at 3 months. Patients in the intervention groups had a lower risk of overall mortality (absolute risk difference, 7.4%; RR, 0.74; 95% CI, 0.63–0.87; *P*<0.001) compared with controls.

We found no evidence of potential publication bias in the funnel plot that was constructed after exclusion of 2 studies with a very large absolute difference in time to treatment between intervention group and controls (Figure 3).[34,36]

Discussion

Our systematic review and meta-analysis showed that interventions in the workflow of endovascular treatment for acute ischemic stroke led to a significant reduction in time to treatment. This applied to all categories of studied interventions, which were interventions aimed at using local anesthesia or conscious sedation, optimizing prehospital management, reducing in-hospital patient transfer, improving teamwork, and supplying feedback on achieved time intervals to the team. These workflow interventions led to higher likelihood of favorable functional outcome after 3 months.

The favorable effect of workflow interventions on the time to treatment is consistent with previous studies, including acute stroke patients treated with intravenous tPA. Implementation of a national quality improvement initiative organized by the American Heart Association/American Stroke Association, including >70 000 patients, resulted in significantly shorter door-to-needle time and significantly higher percentage of patients treated with intravenous tPA within 60 minutes.[63]

Table 1. Studies Included in Systematic Review

Author	Country	Study Design	Study Period*	Anterior, Posterior Circulation Stroke or Both	Intervention Group (n)	Control Group (n)	Type of Intervention
Abou-Chebl et al[13]	United States	Retrospective cohort study; multicenter	2005–2009	Anterior	552	428	A
Abou-Chebl et al[14]	United States	Post hoc analysis retrospective NASA Registry; multicenter	2012–2013	Both	68	159	A
Abou-Chebl et al[15]	Canada, Europe, United States	Post hoc analysis IMS III trial; multicenter	2006–2012	Both	269	147	A
Aghaebrahim et al[16]	United States	Prospective prepost study; single center	2012–2013/ 2013–2014	Both	108	178	B1, C1–3, D1–2, E1, F1
Alotaibi et al[17]	Canada	Retrospective prepost study; single center	2011–2014/ 2014–2016	Both	28	17	E2
Van den Berg et al[18]	The Netherlands	Retrospective cohort study; multicenter	2002–2010	Anterior	278	70	A
Berkhemer et al[19]	The Netherlands	Post hoc analysis MR CLEAN trial; multicenter	2010–2014	Anterior	137	79	A
Bracard et al[2]	France	Post hoc analysis THRACE trial; multicenter	2010–2014	Both	74	69	A
Cerejo et al[20]	United States	Retrospective cohort study; single center	2014	Anterior	5	5	B2
Davis et al[21]	Canada	Retrospective cohort study; single center	2003–2009	Both	37	39	A
Eesa et al[22]	Canada	Retrospective cohort study; single center	2005–2009	Both	71	30	A
Frei et al[23]	United States	Retrospective prepost study; single center	2012–2013/ 2013–2015	Both	267	113	B1, D2–4, F1–3
Goyal et al[24]	Canada, Europe, United States	Post hoc analysis IMS III trial; multicenter	2006–2012	Both	17	64	B3
Goyal et al[25]	Europe, United States	Post hoc analysis SWIFT PRIME trial; multicenter	2012–2014	Anterior	61	35	A
Hassan et al[26]	United States	Retrospective cohort study; multicenter	2006–2010	Both	83	53	A
Henden et al[27]	Sweden	Randomized controlled trial; single center	2013–2016	Anterior	45	45	A
Herrmann et al[28]	Germany	Prepost study; retrospective data preintervention, prospective data post-intervention; single center	2006–2009/ 2009–2010	Both	23	48	F4
Jadhav et al[29]	United States	Retrospective cohort study; single center	2013–2016	Both	111	150	C2
Jagani et al[30]	United States	Retrospective cohort study; single center	2008–2015	Both	61	38	A
Janssen et al[31]	Germany	Retrospective cohort study; single center	2012–2014	Anterior	31	53	A
Jeon et al[32]	Korea	Retrospective prepost study; single center	2014–2016/ 2016	Not specified	19	93	B1, C3, D2, E1, F1-2
John et al[33]	United States	Retrospective cohort study; single center	2008–2012	Anterior	99	91	A
Jumaa et al[34]	United States	Retrospective cohort study; single center	2006–2009	Anterior	73	53	A
Just et al[35]	Canada	Retrospective cohort study; single center	2000–2013	Both	67	42	A
Kamper et al[36]	Germany	Retrospective prepost study; single center	2002–2006/ 2007–2010	Posterior	20	18	F5
Koge et al[37]	Japan	Retrospective prepost study; single center	2008–2014/ 2014–2016	Not specified	23	19	D3–4, E1
Komatsubara et al[38]	Japan	Prepost study; retrospective or prospective data collection not specified; single center	2012–2014/ 2014–2015	Both	14	14	E1, F1, F6
Li et al[39]	United States	Retrospective cohort study; single center	2006–2012	Both	74	35	A
Liang et al[40]	United States	Retrospective cohort study; single center	2015–2016	Not specified	22	17	B4
Mascitelli et al[41]	United States	Retrospective prepost study; single center	2014/ 2014–2015	Both	29	27	B1, E1–2, F1
McTaggart et al[42]	United States	Retrospective cohort study; multicenter	2015–2016	Anterior	22	48	B4–5, C2, D2

(*Continued*)

Table 1. Continued

Author, Year	Country	Study Design	Study Period*	Anterior, Posterior Circulation Stroke or Both	Intervention Group (n)	Control Group (n)	Type of Intervention
Mehta et al[43]	United States	Prepost study; retrospective data preintervention, prospective data post-intervention; single center	2007–2011/ 2011–2013	Anterior	51	93	C3, D2–4
Menon et al[44]	Canada, Ireland, South Korea, United Kingdom, United States	Prespecified secondary analysis ESCAPE trial; multicenter	2013–2014	Anterior	136	15	A
Miley et al[45]	United States	Retrospective cohort study; multicenter	2005–2008	Both	52	39	A
Mundiyanapurath et al[46]	Germany	Prospective cohort study; single center	2013–2014	Both	15	29	A
Nichols et al[47]	United States	Post hoc analysis IMS II trial; multicenter	2003–2006	Anterior	40	17	A
Pedragosa et al[48]	Spain	Prospective cohort study; multicenter	2008–2010	Not specified	25	20	B6
Pfaff et al[49]	Germany	Prospective cohort study with historical controls; single center	2014	Both	3	16	C4
Pfaff et al[50]	Germany	Prospective cohort study with historical controls; single center	2014–2016	Anterior	22	28	A
Pfaff et al[50]	Germany	Prospective cohort study with historical controls; single center	2014–2016	Anterior	28	28	C4
Psychogios et al[51]	Germany	Retrospective cohort study; single center	2016	Not specified	30	44	C4
Qureshi et al[52]	United States	Retrospective cohort study; multicenter	2007–2012	Not specified	66	117	C3
Ragoschke et al[53]	Germany	Prepost study; retrospective data preintervention, prospective data post-intervention; single center	2006–2010/ 2010–2014	Both	174	81	C5
Rai et al[54]	United States	Prospective prepost study; single center	2011–2014/ 2015	Both	30	64	B1, D2–4, F2
Ribo et al[55]	Spain	Retrospective cohort study; single center	2015–2016	Not specified	74	87	C1
Ribo et al[55]	Spain	Retrospective cohort study; single center	2015–2016	Not specified	40	87	C2
Schonenberger et al[56]	Germany	Randomized controlled trial; single center	2014–2016	Anterior	77	73	A
Schregel et al[57]	Germany	Retrospective prepost study; single center	2008–2014/ 2014–2015	Both	90	278	C3, D2, E1
Simonsen et al[58]	Denmark	Randomized controlled trial, single center	2015–2017	Anterior	63	65	A
Singer et al[59]	Austria, Germany	Post hoc analysis ENDOSTROKE registry; both retrospective and prospective data collection; multicenter	2011–2012	Both	36	691	A
Slezak et al[60]	Switzerland	Prospective cohort study; single center	2010–2015	Anterior	135	266	A
Sugg et al[61]	United States	Retrospective cohort study; single center	2007–2009	Both	57	9	A
Tsujimoto et al[62]	Japan	Retrospective cohort study; single center	2011–2013	Both	6	16	B7

ENDOSTROKE, Endovascular Stroke Treatment; ESCAPE, Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times; IMS, Interventional Management of Stroke; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; NASA, North American Solitaire Stent-Retriever Acute Stroke; SWIFT PRIME, Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke; and THRACE, Thrombectomie des Artères Cerebrales.

*Study period for pre/postintervention group.

Workflow improvement strategies were promoting prenotification of hospitals by emergency medical service, rapid activation of the entire stroke team, rapid acquisition of brain imaging, and provision of feedback to the stroke team on performance. A single center study showed that the introduction of multiple concurrent strategies aimed at reducing in-hospital delay in treatment of acute stroke patients with intravenous tPA led to a remarkable time reduction and final median door-to-needle of 20 minutes.[6]

Our results are also consistent with studies on workflow improvement for reperfusion treatment of patients with myocardial infarction with ST-segment elevation. A study on time-saving strategies in the workflow for patients with acute myocardial infarction, including 365 hospitals, showed that

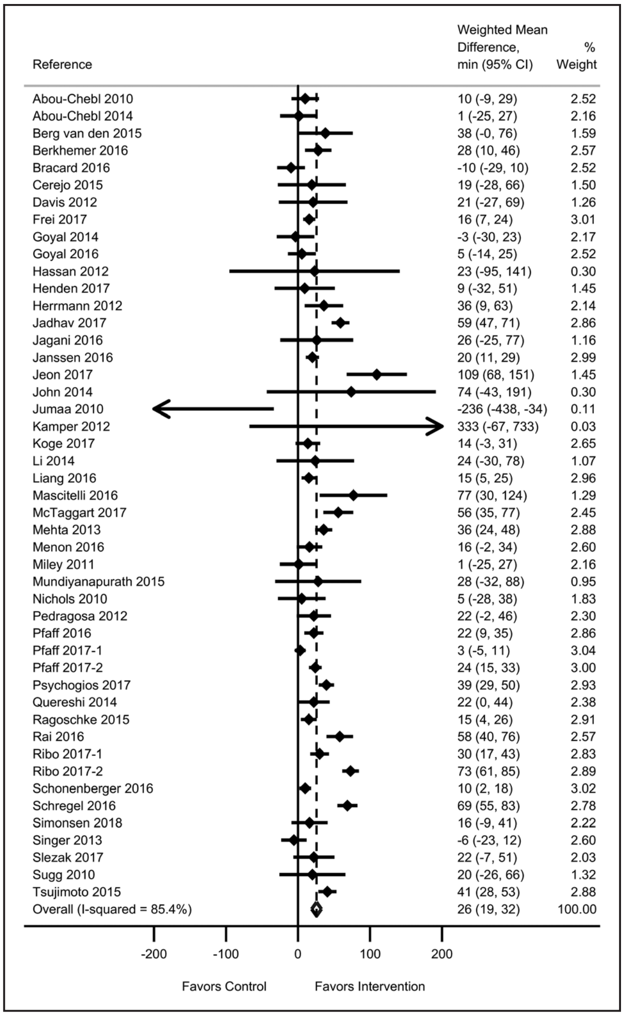

Figure 2. Forest plot of weighted difference in mean time to treatment for workflow interventions in endovascular stroke treatment, using random-effects meta-analysis

rapid activation and availability of the entire team and use of real-time data feedback by the staff in the emergency department and angiography suite, reduced mean door-to-balloon time with 8 to 19 minutes.[64]

The workflow interventions in this review can easily be implemented in any intervention center. A time-saving effect of >1 hour could be achieved by providing feedback on time intervals to the entire team. Implementation of regular feedback in the 4 included studies in this meta-analysis was executed by supplying time intervals and outcome to the entire team daily using an online bulletin or email, reviewing each patient during weekly or monthly meetings, or comparing actually achieved times to target times every 3 months.[32,37,41,57] Evaluation of time intervals can simply be added to existing regular meetings at intervention hospitals. Optimizing in-hospital teamwork by using parallel processing instead of sequential processing in the workflow, and by early activation of all team members, requires multidisciplinary protocols or standard operating procedures. The time-investment to draft and implement such protocols seems well worthwhile because our meta-analysis showed a mean time reduction of 47 minutes.[23,32,37,42,43,54,57] Effects of multiple interventions cannot be simply added, but implementing multiple interventions at the same time still led to a very large time reduction of 50 minutes and is probably preferred above implementing 1 intervention at a time.

Table 2. Categories of Workflow Interventions in Endovascular Stroke Treatment

Anesthetic Management
A=Nongeneral anesthesia vs general anesthesia
Prehospital Management*
B1=Prenotification ED team, CT technologist, and stroke team by EMS
B2=Mobile stroke treatment unit with CT scanner, point of care laboratory testing, vascular neurologist available via telemedicine
B3=Ship and drip for transfer patients vs drip and ship
B4=CTA at PSC vs at CSC
B5=Cloud based image sharing between PSC and CSC
B6=Use of telemedicine assessment by a stroke neurologist at PSC
B7=Air transfer vs ground transfer
In-hospital Patient Transfer
C1=Transporting patients directly to CT scanner by EMS
C2=Transporting (transfer) patients directly to angiosuite by EMS
C3=No turn around approach (not returning to ED after imaging for decision-making)
C4=Single room used for CT, angiography, and EVT
C5=Single room for patient evaluation, CT, angiography, and EVT
Teamwork
D1=Early communication between ED team and stroke team about plan of care
D2=Early activation neurointerventional team
D3=Parallel processing from ED/hospital ward to CT: clinical assessment, laboratory tests, imaging, patient/family education by the teams in a parallel workflow
D4=Parallel processing from CT to angiosuite: neurointerventional team meets patient at CT, teams evaluate CT/CTA and make treatment decision while angiosuite is set up, patient/family education
Feedback
E1=Education and feedback all teams
E2=Smartphone application/digital system for real-time window from stroke onset to puncture for all teams, visualizing performance metrics
Other
F1=Limiting nonessential interventions (eg, ECG, chest X-ray, additional venous access, bladder catheter placement)
F2=Standard angiography set for all of the devices needed for EVT
F3=No groin shaving
F4=Standard operating procedure for intubation at the intensive care unit before EVT
F5=Standard operating procedure for EVT
F6=Not waiting for effect IV tissue-type plasminogen activator vs waiting for 1 h

CT indicates computed tomography; CTA, computed tomography angiography; CSC, comprehensive stroke center; ED, emergency department; EMS, emergency medical service; EVT, endovascular treatment; IV, intravenous; and PSC, primary stroke center.*Prehospital management includes all interventions performed before the patient arrives at the CSC.

Table 3. Random-Effects Meta-Analysis of Difference in Mean Time to Treatment for Categories of Workflow Interventions in Endovascular Stroke Treatment

	No. of Studies	No. of Patients (Intervention/ Control Group)	Weighted Mean Difference, min (95% CI)
All interventions	47	3480/4002	26 (19–32); *P*<0.001
Anesthetic management	23	2283/2445	12 (6–17); *P*<0.001
Prehospital management	10	442/463	37 (22–52); *P*<0.001
In-hospital patient transfer management	13	730/1150	41 (27–54); *P*<0.001
Teamwork	7	502/708	47 (228–67); *P*<0.001
Feedback	4	161/417	64 (24–104); *P*=0.002
Multiple interventions simultaneously	8	531/735	50 (31–69); *P*<0.001

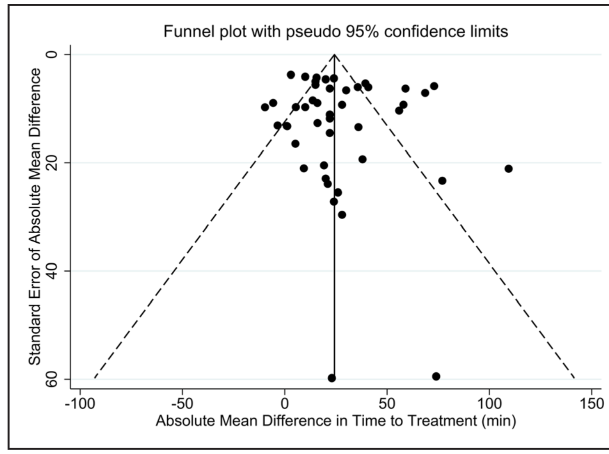

Figure 3. Funnel plot to detect potential publication bias in 43 studies of workflow interventions improvements in endovascular stroke treatment

Anesthetic management in endovascular stroke treatment is a much-discussed topic because it possibly influences both time to treatment intervals as cerebral perfusion and thereby indirect functional outcome. A meta-analysis, including 4716 patients undergoing endovascular stroke treatment, showed a difference in time to treatment of 14 minutes in favor of patients receiving local anesthesia or conscious sedation compared with general anesthesia and a higher odds of good functional outcome.[65] Which studies were used for comparing time to treatment by type of anesthesia management and the way missing data was handled was not disclosed. Our meta-analysis included additional studies on anesthetic management and showed a comparable difference in time to treatment of 12 minutes in favor of patients receiving local anesthesia or conscious sedation. Both meta-analyses included many observational studies with possible selection bias. Only 3 randomized controlled trials, randomizing patients for local anesthesia or conscious sedation versus general anesthesia, were included in our meta-analysis, showing a nonsignificant difference in treatment intervals in 2 studies,[27,58] and a significant difference in time to treatment in 1 study of 10 minutes in favor of conscious sedation (95% CI, 2–18).[56] We did not find studies comparing conscious sedation with local anesthesia. Regarding anesthetic management in endovascular stroke treatment and its effect on time to treatment, results of included randomized and nonrandomized studies in our analysis varied between a significant positive effect or a significant negative effect of local anesthesia or conscious sedation and a nonsignificant difference compared with general anesthesia. By combining these results in a meta-analysis, we showed a potential positive effect of nongeneral anesthesia on workflow.

The favorable effect of reducing time to treatment on functional outcome as described in previous studies is confirmed by our study.[4,66] Analysis of 5 endovascular stroke treatment trials showed a 4% absolute risk difference for a good functional outcome per hour of delay between symptom onset and reperfusion.[4] Our meta-analysis showed a difference in time to treatment effect of 26 minutes, with a total absolute risk difference of good functional outcome of 12%, which is higher compared with the ≈2% absolute risk difference per half hour as seen in the meta-analysis of 5 endovascular stroke treatment trials. However, selection bias could have occurred in the nonrandomized studies included in our meta-analysis and differences in baseline characteristics might have influenced our results. The effect of time to treatment on functional outcome might be stronger in clinical practice compared with a selected patient population from randomized controlled trials.[67] Furthermore, some workflow improvements, such as anesthetic management, have an effect on functional outcome which is not completely explained by the difference in time to treatment.[1]

A meta-analysis of 5 large endovascular stroke trials showed no effect of time to treatment on rates of mortality and symptomatic intracranial hemorrhage.[4] Our study showed no difference in rate of symptomatic intracranial hemorrhage, but significantly lower mortality among patients in the intervention group. However, possible selection bias in the nonrandomized studies included in our meta-analysis could have influenced the effect of time to treatment on mortality.

This study has several limitations. To perform the meta-analysis, we estimated the mean time to treatment for 8 studies using the median time to treatment, interquartile range, and sample size. Because the meta-analysis is aimed at the difference in time to treatment between groups, rather than the actual time intervals per group, we assume that using the estimation of the mean time to treatment has no significant effect on the primary outcome. Considerable heterogeneity between included studies was observed. Therefore, we used a random-effects inverse variance model for our meta-analysis and categorized the interventions to perform separate analyses for each intervention type. Forty-eight of 51 included studies used a nonrandomizing study design, with a high risk of selection bias. Furthermore, most data were collected retrospectively in a single center, without blinding of personnel and participants, possibly leading to performance bias. Multiple prepost intervention studies were included in our meta-analysis, in which learning effect over time can also effect time to treatment. Therefore, generalizability is difficult to assess for the individual studies. However, because we included multiple studies on the same subject, these results can give us valuable insight on the possible effects in general practice, which is very promising. One of the purposes of a systematic review is to identify gaps in our knowledge and point out clinical areas that would benefit from more research. The 7 subcategories of prehospital intervention with only a limited number of studies suggest that more work can be done in this area. Intervention studies and modeling of prehospital workflow may provide more insights, and effective prehospital management strategies may have a relatively large effect on outcome.

In conclusion, interventions in the workflow of endovascular stroke treatment lead to a significant reduction in time to treatment. Reduction of any delay in time to treatment, by workflow interventions aimed at any interval between symptom onset and treatment, leads to a higher chance of good functional outcome for each individual patient. Acute stroke care should be reorganized by making use of the examples of workflow interventions described in this review to ensure the best medical care for patients with acute ischemic stroke.

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Disclosures

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References

1. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al; HERMES Collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723–1731. doi: 10.1016/S0140-6736(16)00163-X
2. Bracard S, Ducrocq X, Mas JL, Soudant M, Oppenheim C, Moulin T, et al; THRACE Investigators. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial. *Lancet Neurol*. 2016;15:1138–1147. doi: 10.1016/S1474-4422(16)30177-6
3. Muir KW, Ford GA, Messow CM, Ford I, Murray A, Clifton A, et al; PISTE Investigators. Endovascular therapy for acute ischaemic stroke: the Pragmatic Ischaemic Stroke Thrombectomy Evaluation (PISTE) randomised, controlled trial. *J Neurol Neurosurg Psychiatry*. 2017;88:38–44. doi: 10.1136/jnnp-2016-314117
4. Saver JL, Goyal M, van der Lugt A, Menon BK, Majoie CB, Dippel DW, et al; HERMES Collaborators. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA*. 2016;316:1279–1288. doi: 10.1001/jama.2016.13647
5. The National Institute of Neurological Disorders and Stroke rt-PA Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med*. 1995;333:1581–1588. doi: 10.1056/NEJM199512143332401
6. Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindsberg PJ, Kaste M. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. *Neurology*. 2012;79:306–313. doi: 10.1212/WNL.0b013e31825d6011
7. Asif KS, Lazzaro MA, Zaidat O. Identifying delays to mechanical thrombectomy for acute stroke: onset to door and door to clot times. *J Neurointerv Surg*. 2014;6:505–510. doi: 10.1136/neurintsurg-2013-010792
8. Assis ZA, Menon BK, Goyal M. Imaging department organization in a stroke center and workflow processes in acute stroke. *Eur J Radiol*. 2017;96:120–124. doi: 10.1016/j.ejrad.2017.06.014
9. Goyal M, Menon BK, Hill MD, Demchuk A. Consistently achieving computed tomography to endovascular recanalization <90 minutes: solutions and innovations. *Stroke*. 2014;45:e252–e256. doi: 10.1161/STROKEAHA.114.007366
10. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6:e1000097. doi: 10.1371/journal.pmed.1000097
11. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343.d5928.
12. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14:135. doi: 10.1186/1471-2288-14-135
13. Abou-Chebl A, Lin R, Shazam Hussain M, Jovin TG, Levy EI, Liebeskind DS, et al. Conscious sedation versus general anesthesia during endovascular therapy for acute anterior circulation stroke: preliminary results from a retrospective, multicenter study. *Stroke*. 2010;41:1175–1179.
14. Abou-Chebl A, Zaidat OO, Castonguay AC, Gupta R, Sun CHJ, Martin CO, et al. North American SOLITAIRE stent-retriever acute stroke registry: choice of anesthesia and outcomes. *Stroke*. 2014;45:1396–1401.
15. Abou-Chebl A, Yeatts SD, Yan B, Cockroft K, Goyal M, Jovin T, et al. Impact of general anesthesia on safety and outcomes in the endovascular arm of Interventional Management of Stroke (IMS) III Trial. *Stroke*. 2015;46:2142–2148.
16. Aghaebrahim A, Streib C, Rangaraju S, Kenmuir CL, Giurgiutiu DV, Horev A, et al. Streamlining door to recanalization processes in endovascular stroke therapy. *J Neurointervent Surg*. 2017;9:340–345.
17. Alotaibi NM, Sarzetto F, Guha D, Lu M, Bodo A, Gupta S, et al. Impact of smartphone applications on timing of endovascular therapy for ischemic stroke: a preliminary study. *World Neurosurg*. 2017;107:678–683.
18. van den Berg LA, Koelman DL, Berkhemer OA, Rozeman AD, Fransen PS, Beumer D, et al. Type of anesthesia and differences in clinical outcome after intra-arterial treatment for ischemic stroke. *Stroke*. 2015;46:1257–1262.
19. Berkhemer OA, van den Berg LA, Fransen PS, Beumer D, Yoo AJ, Lingsma HF, et al. The effect of anesthetic management during intra-arterial therapy for acute stroke in MR CLEAN. *Neurology*. 2016;87:656–664.
20. Cerejo R, John S, Buletko AB, Taqui A, Itrat A, Organek N, et al. A Mobile Stroke Treatment Unit for field triage of patients for intraarterial revascularization therapy. *J Neuroimaging*. 2015;25:940–945.
21. Davis MJ, Menon BK, Baghirzada LB, Campos-Herrera CR, Goyal M, Hill MD, et al. Anesthetic management and outcome in patients during endovascular therapy for acute stroke. *Anesthesiology*. 2012;116:396–405.
22. Eesa M, Menon BK, Hill MD, Demchuk A, Goyal M. Achieving faster recanalization times by IA thrombolysis in acute ischemic stroke: where should we direct our efforts? *Interv Neuroradiol*. 2011;17:228–234.
23. Frei D, McGraw C, McCarthy K, Whaley M, Bellon RJ, Loy D, et al. A standardized neurointerventional thrombectomy protocol leads to faster recanalization times. *J Neurointervent Surg*. 2017;9:1035–1041.
24. Goyal M, Almekhlafi MA, Fan L, Menon BK, Demchuk AM, Yeatts SD, et al. Evaluation of interval times from onset to reperfusion in patients undergoing endovascular therapy in the Interventional Management of Stroke III trial. *Circulation*. 2014;130:265–272.
25. Goyal M, Jadhav AP, Bonafe A, Diener H, Mendes Pereira V, Levy E, et al. Analysis of workflow and time to treatment and the effects on outcome in endovascular treatment of acute ischemic stroke: results

from the SWIFT PRIME Randomized Controlled Trial. *Radiology*. 2016;279:888–897.
26. Hassan AE, Chaudhry SA, Zacharatos H, Khatri R, Akbar U, Suri MF, et al. Increased rate of aspiration pneumonia and poor discharge outcome among acute ischemic stroke patients following intubation for endovascular treatment. *Neurocrit Care*. 2012;16:246–250.
27. Henden PL, Rentzos A, Karlsson JE, Rosengren L, Leiram B, Sundeman H, et al. General anesthesia versus conscious sedation for endovascular treatment of acute ischemic stroke: the AnStroke Trial (Anesthesia During Stroke). *Stroke*. 2017;48:1601–1607.
28. Herrmann O, Hug A, Bosel J, Petersen JJ, Hartmann M, Rohde S, et al. Fast-Track intubation for accelerated interventional stroke treatment. *Neurocrit Care*. 2012;17:354–360.
29. Jadhav AP, Kenmuir CL, Aghaebrahim A, Limaye K, Wechsler LR, Hammer MD, et al. Interfacility transfer directly to the neuroangiography suite in acute ischemic stroke patients undergoing thrombectomy. *Stroke*. 2017;48:1884–1889.
30. Jagani M, Brinjikji W, Rabinstein AA, Pasternak JJ, Kallmes DF. Hemodynamics during anesthesia for intra-arterial therapy of acute ischemic stroke. *J Neurointerv Surg*. 2016;8:883–888.
31. Janssen H, Buchholz G, Killer M, Ertl L, Bruckmann H, Lutz J. General anesthesia versus conscious sedation in acute stroke treatment: the importance of head immobilization. *Cardiovasc Intervent Radiol*. 2016;39:1239–1244.
32. Jeon SB, Ryoo SM, Lee DH, Kwon SU, Jang S, Lee EJ, et al. Multidisciplinary approach to decrease in-hospital delay for stroke thrombolysis. *J Stroke*. 2017;19:196–204.
33. John S, Thebo U, Gomes J, Saqqur M, Farag E, Xu J, et al. Intra-arterial therapy for acute ischemic stroke under general anesthesia versus monitored anesthesia care. *Cerebrovasc Dis*. 2014;38:262–267.
34. Jumaa MA, Zhang F, Ruiz-Ares G, Gelzinis T, Malik AM, Aleu A, et al. Comparison of safety and clinical and radiographic outcomes in endovascular acute stroke therapy for proximal middle cerebral artery occlusion with intubation and general anesthesia versus the nonintubated state. *Stroke*. 2010;41:1180–1184.
35. Just C, Rizek P, Tryphonopoulos P, Pelz D, Arango M. Outcomes of general anesthesia and conscious sedation in endovascular treatment for stroke. *Can J Neurol Sci*. 2016;43:655–658.
36. Kamper L, Meyn H, Rybacki K, Nordmeyer S, Kempkes U, Piroth W, et al. Workflow optimization in vertebrobasilar occlusion. *Cardiovasc Intervent Radiol*. 2012;35:491–497.
37. Koge J, Matsumoto S, Nakahara I, Ishii A, Hatano T, Sadamasa N, et al. Improving treatment times for patients with in-hospital stroke using a standardized protocol. *J Neurol Sci*. 2017;381:68–73.
38. Komatsubara K, Dembo T, Sato E, Sasamori H, Torii M, Shiokawa Y, et al. Does reducing the duration from symptom onset to recanalization improve the results of intracranial mechanical thrombectomy in the elderly? *Neurol Med Chir*. 2017;57:107–114.
39. Li FH, Deshaies EM, Singla A, Villwock MR, Melnyk V, Gorji R, et al. Impact of anesthesia on mortality during endovascular clot removal for acute ischemic stroke. *J Neurosurg Anesthesiol*. 2014;26:286–290.
40. Liang JW, Stein L, Wilson N, Fifi JT, Tuhrim S, Dhamoon MS. Timing of vessel imaging for suspected large vessel occlusions does not affect groin puncture time in transfer patients with stroke. *J Neurointerv Surg*. 2018;10:22–24.
41. Mascitelli JR, Wilson N, Shoirah H, De Leacy RA, Furtado SV, Paramasivam S, et al. The impact of evidence: evolving therapy for acute ischemic stroke in a large healthcare system. *J Neurointervent Surg*. 2016;8:1129–1135.
42. McTaggart RA, Yaghi S, Cutting SM, Hemendinger M, Baird GL, Haas RA, et al. Association of a primary stroke center protocol for suspected stroke by large-vessel occlusion with efficiency of care and patient outcomes. *JAMA Neurol*. 2017;74:793–800.
43. Mehta BP, Leslie-Mazwi TM, Chandra RV, Bell DL, Sun CHJ, Hirsch JA, et al. Reducing door-to-puncture times for intra-arterial stroke therapy: a pilot quality improvement project. *J Am Heart Assoc*. 2014;3:e000963.
44. Menon BK, Sajobi TT, Zhang Y, Rempel JL, Shuaib A, Thornton J, et al. Analysis of workflow and time to treatment on thrombectomy outcome in the endovascular treatment for small core and proximal occlusion ischemic stroke (ESCAPE) randomized, controlled trial. *Circulation*. 2016;133:2279–2286.
45. Miley JT, Memon MZ, Hussein HM, Valenta DA, Suri MFK, Vazquez G, et al. A multicenter analysis of "time to microcatheter" for endovascular therapy in acute ischemic stroke. *J Neuroimaging*. 2011;21:159–164.
46. Mundiyanapurath S, Schonenberger S, Rosales ML, Carrilho Romeiro AM, Mohlenbruch M, Bendszus M, et al. Circulatory and respiratory parameters during acute endovascular stroke therapy in conscious sedation or general anesthesia. *J Stroke Cerebrovasc Dis*. 2015;24:1244–2149.
47. Nichols C, Carrozzella J, Yeatts S, Tomsick T, Broderick J, Khatri P. Is periprocedural sedation during acute stroke therapy associated with poorer functional outcomes? *J Neurointerv Surg*. 2010;2:67–70.
48. Pedragosa A, Alvarez-Sabín J, Rubiera M, Rodriguez-Luna D, Maisterra O, Molina C, et al. Impact of telemedicine on acute management of stroke patients undergoing endovascular procedures. *Cerebrovasc Dis*. 2012;34:436–442.
49. Pfaff J, Herweh C, Pham M, Schönenberger S, Bösel J, Ringleb PA, et al. Mechanical thrombectomy using a combined CT/C-arm X-ray system. *J Neurointervent Surg*. 2016;8:621–625.
50. Pfaff J, Schönenberger S, Herweh C, Pham M, Nagel S, Ringleb PA, et al. Influence of a combined CT/C-arm system on periprocedural workflow and procedure times in mechanical thrombectomy. *Eur Radiol*. 2017;27:3966–3972.
51. Psychogios MN, Behme D, Schregel K, Tsogkas I, Maier IL, Leyhe JR, et al. One-stop management of acute stroke patients: minimizing door-to-reperfusion times. *Stroke*. 2017;48:3152–3155.
52. Qureshi AI, Egila H, Adil MM, Siddiqi H, Mian N, Hassan AE, et al. "No turn back approach" to reduce treatment time for endovascular treatment of acute ischemic stroke. *J Stroke Cerebrovasc Dis*. 2014;23:e317–e323.
53. Ragoschke-Schumm A, Yilmaz U, Kostopoulos P, Lesmeister M, Manitz M, Walter S, et al. Stroke Room': diagnosis and treatment at a single location for rapid intraarterial stroke treatment. *Cerebrovasc Dis*. 2015;40:251–257.
54. Rai AT, Smith MS, Boo S, Tarabishy AR, Hobbs GR, Carpenter JS. The pit-crew model for improving door-to-needle times in endovascular stroke therapy: a Six-Sigma project. *J Neurointervent Surg*. 2016;8:447–452.
55. Ribo M, Boned S, Rubiera M, Tomasello A, Coscojuela P, Hernandez D, et al. Direct transfer to angiosuite to reduce door-to-puncture time in thrombectomy for acute stroke. *J Neurointerv Surg*. 2018;10:221–224.
56. Schonenberger S, Uhlmann L, Hacke W, Schieber S, Mundiyanapurath S, Purrucker JC, et al. Effect of conscious sedation vs general anesthesia on early neurological improvement among patients with ischemic stroke undergoing endovascular thrombectomy: a randomized clinical trial. *JAMA*. 2016;316:1986–1996.
57. Schregel K, Behme D, Tsogkas I, Knauth M, Maier I, Karch A, et al. Effects of workflow optimization in endovascularly treated stroke patients - A pre-post effectiveness study. *PLoS ONE*. 2016;11:e0169192.
58. Simonsen CZ, Yoo AJ, Sorensen LH, Juul N, Johnsen SP, Andersen G, et al. Effect of general anesthesia and conscious sedation during endovascular therapy on infarct growth and clinical outcomes in acute ischemic stroke: a randomized clinical trial. *JAMA Neurol*. 2018:75;470–477.
59. Singer OC, Haring HP, Trenkler J, Nolte CH, Bohner G, Neumann-Haefelin T, et al. Periprocedural aspects in mechanical recanalization for acute stroke: data from the ENDOSTROKE registry. *Neuroradiology*. 2013;55:1143–1151.
60. Slezak A, Kurmann R, Oppliger L, Broeg-Morvay A, Gralla J, Schroth G, et al. Impact of anesthesia on the outcome of acute ischemic stroke after endovascular treatment with the Solitaire stent retriever. *Am J Neuroradiol*. 2017;38:1362–1367.
61. Sugg RM, Jackson AS, Holloway W, Martin CO, Akhtar N, Rymer M. Is mechanical embolectomy performed in nonanesthetized patients effective? *Am J Neuroradiol*. 2010;31:1533–1535.
62. Tsujimoto M, Yoshimura S, Enomoto Y, Yamada N, Matsumaru N, Kumada K, et al. Preliminary experience with air transfer of patients for rescue endovascular therapy after failure of intravenous tissue plasminogen activator. *Neurol Med Chir*. 2015;55:248–252.
63. Fonarow GC, Zhao X, Smith EE, Saver JL, Reeves MJ, Bhatt DL, et al. Door-to-needle times for tissue plasminogen activator administration and clinical outcomes in acute ischemic stroke before and after a quality improvement initiative. *JAMA*. 2014;311:1632–1640. doi: 10.1001/jama.2014.3203
64. Bradley EH, Herrin J, Wang Y, Barton BA, Webster TR, Mattera JA, et al. Strategies for reducing the door-to-balloon time in acute myocardial infarction. *N Engl J Med*. 2006;355:2308–2320. doi: 10.1056/NEJMsa063117
65. Brinjikji W, Pasternak J, Murad MH, Cloft HJ, Welch TL, Kallmes DF, et al. Anesthesia-related outcomes for endovascular stroke revascularization: a systematic review and meta-analysis. *Stroke*. 2017;48:2784–2791. doi: 10.1161/STROKEAHA.117.017786

66. Khatri P, Yeatts SD, Mazighi M, Broderick JP, Liebeskind DS, Demchuk AM, et al; IMS III Trialists. Time to angiographic reperfusion and clinical outcome after acute ischaemic stroke: an analysis of data from the Interventional Management of Stroke (IMS III) phase 3 trial. *Lancet Neurol*. 2014;13:567–574. doi: 10.1016/S1474-4422(14)70066-3

67. Mulder MJHL, Jansen IGH, Goldhoorn RB, Venema E, Chalos V, Compagne KCJ, et al; MR CLEAN Registry Investigators. Time to endovascular treatment and outcome in acute ischemic stroke: MR CLEAN registry results. *Circulation*. 2018;138:232–240. doi: 10.1161/CIRCULATIONAHA.117.032600