Cardiovasc Intervent Radiol (2018) 41:706–711
https://doi.org/10.1007/s00270-018-1902-7

Mechanical Thrombectomy in Patients with Acute Ischemic Stroke on Anticoagulation Therapy

David Černík[1,2] · Daniel Šaňák[1] · Petra Divišová[1] · Martin Köcher[3] · Filip Cihlář[4] · Jana Zapletalová[5] · Tomáš Veverka[1] · Andrea Prcúchová[1,2] · Dušan Ospalík[2] · Marie Černá[3] · Petra Janoušová[2,6] · Michal Král[1] · Tomáš Dorňák[1] · Vojtěch Prášil[3] · David Franc[1] · Petr Kaňovský[1]

Received: 12 January 2018 / Accepted: 7 February 2018 / Published online: 15 February 2018

Abstract

Introduction/Purpose Mechanical thrombectomy (MT) for acute ischemic stroke (IS) can be performed also in patients on anticoagulation therapy (AT); however, sufficient and reliable data about safety and efficacy of MT are still missing. Thus, we aimed to compare these parameters between patients treated on AT and without AT.

Materials and Methods All consecutive IS patients treated with MT using stent retrievers were included in the retrospective analysis. Neurological deficit was scored using National Institutes of Health Stroke Scale (NIHSS) and 90-day clinical outcome using modified Rankin scale with a score 0–2 for good outcome. Recanalization was rated using Thrombolysis in Cerebral Infarction (TICI) scale. Symptomatic intracerebral hemorrhage (SICH) was assessed according to the SITS-MOST criteria.

Results Out of 703 patients treated with MT, 88 (12.5%) patients (46% males, mean age 75.5 ± 11.8 years) were on AT with an admission median NIHSS of 17 points. Recanalization (TICI 2b-3) was achieved in 80% and complete (TICI 3) in 65% of patients on AT and in 80 and 65% of patients without AT (p—1.000). SICH after MT was detected in 9% of AT and 5% of non-AT patients (p—0.136). Good outcome was present in 36% of AT patients (p—0.03). AT patients with poor outcome had more frequently atrial fibrillation (93%, p—0.005), higher admission NIHSS (17, p—0.004) and higher rate of SICH (14.5%, p—0.047).

Conclusion MT seems to be safe also in patients on AT. Poor outcome may be related to higher admission NIHSS, higher rate of SICH and presence of atrial fibrillation.

Keywords Ischemic stroke · Mechanical thrombectomy · Anticoagulation therapy · Symptomatic intracerebral hemorrhage · Clinical outcome

✉ Daniel Šaňák
daniel.sanak@centrum.cz

[1] Department of Neurology, Comprehensive Stroke Center, Palacký University Medical School and Hospital, Olomouc, Czech Republic

[2] Department of Neurology, Comprehensive Stroke Center, Masaryk Hospital, Ústí nad Labem, KZ a.s., Ústí nad Labem, Czech Republic

[3] Department of Radiology, Palacký University Medical School and Hospital, Olomouc, Czech Republic

[4] Department of Radiology, Masaryk Hospital, Ústí nad Labem KZ a.s., Ústí nad Labem, Czech Republic

[5] Department of Medical Biophysics and Statistics, Palacký University Medical School, Olomouc, Czech Republic

[6] Department of Emergency, Masaryk Hospital, Ústí nad Labem KZ a.s., Ústí nad Labem, Czech Republic

Introduction

Mechanical thrombectomy (MT) of occluded middle cerebral artery (MCA) or distal internal carotid artery (ICA) is a standard treatment for acute ischemic stroke within the first six hours from stroke onset [1]. However, recently published results of the randomized trials DAWN (DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-UP and Late Presenting Strokes

Undergoing Neurointervention with Trevo) and DEFUSE-3 (The Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke) showed that time window for MT may be extended beyond 6 hours in patients carefully selected on basis of the brain imaging findings and clinical deficit [2, 3]. In case of basilar artery occlusion (BAO), the evidence from randomized trials is still missing; however, MT may be considered regarding a high risk of fatal outcome.

Anticoagulation therapy (AT) is generally used as a prevention of systemic or cerebral embolisation; however, the patients on AT may suffer an embolic event including acute ischemic stroke (AIS) [4–8]. In case of an occlusion of large cerebral vessel, MT may be performed also in the patients using AT, but it might be associated with a higher risk of symptomatic intracerebral hemorrhage or other bleeding events and poorer outcome due to affected coagulation. Published results from the positive randomized trials and following the Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials (HERMES) meta-analysis did not provide reliable data concerning the safety and efficacy of MT in these patients [9–14]. Moreover, anticoagulation agents including a "new" direct oral anticoagulants (DOAC) have different safety profile, and the number of treated patients has an increasing trend worldwide, especially due to the DOAC in a few lasts years.

Thus we aimed to compare safety and efficacy of MT performed in AIS patients using AT to those without AT.

Methods

All consecutive non-selected patients, who were treated with MT between years 2009 and 2016 in both centers, were enrolled in this retrospective bi-center study. In all patients, the symptomatic occlusion of cerebral artery was detected on computed tomographic angiography (CTA) or magnetic resonance angiography (MRA). MT was performed in case of occlusion of middle cerebral artery (MCA; M1 or M2 segment), or distal part of internal carotid artery (ICA) or in case of occlusion of basilar artery (BA). In case of arterial occlusion in anterior circulation, MT was initiated within first 6 h after stroke onset. In case of BA occlusion, MT was performed within first 24 h after stroke onset. The size of hypodense area corresponding to acute infarction larger than 2/3 of MCA territory present on admission CT in the patients with IS in the anterior circulation was only imaging exclusion criterion for MT. Prior severe disability and known fatal malignity were the clinical exclusion criteria. Patients with "wake-up" strokes in the anterior circulation were treated with MT if no hypodense area corresponding to acute infarction was present on admission CT or no hypersignal area corresponding to acute infarction was present on admission MRI sequence fluid attenuation inversion recovery (FLAIR). Admission clinical status was evaluated using the National Institutes of Health Stroke scale (NIHSS) by a certified neurologist. In patients without AT, intravenous thrombolysis (IVT) was administered within first 4.5 h from stroke onset prior MT. In patients with BAO, IVT was performed within first 24 h from stroke onset. No reversal agent was used for a normalization of coagulation parameters before the initiation of MT.

Mechanical thrombectomy was performed using stent retrievers (Solitaire®, Catch Device® and Trevo®). Achieved recanalization status was assessed according to the Thrombolysis in Cerebral Infarction Scale (TICI) on the final angiogram [15].

In all patients, the occurrence of intracerebral hemorrhage (ICH) was assessed on the control CT or MRI after 24 h. Symptomatic ICH was defined as a local remote parenchymal hematoma (type 2) or subarachnoid hemorrhage associated with at least four-point increase in NIHSS score or leading to death [16].

In the patients using AT, the anticoagulation was restarted after the control brain CT/MRI excluding ICH. In the patients without AT, antiplatelet therapy was initiated after the control brain imaging excluding ICH.

Neurological deficit was evaluated using the NIHSS after 24 h and clinical outcome after 3 months using the modified Rankin scale (mRS). A score 0–2 points was considered a good outcome. The mRS scoring was performed by an experienced certified neurologist and mostly during scheduled outpatient visits. In some patients, the scoring was performed using phone call with patient's relatives or caregivers.

The study protocol was in compliance with the Declaration of Helsinki (1975) and was approved by the ethical committee of our hospitals.

Statistical analysis

SPSS software (version 22.0; SPSS, Chicago, Illinois) was used for the statistical analysis. Fisher's exact test and Kruskal–Wallis test were used for nonparametric variables. Data normality was tested using Shapiro–Wilk test. Multivariate logistic regression analysis was used to identify possible predictors of ICH, SICH, and good clinical outcome. All tests used an α-level of 0.05 for significance.

Results

In total, 703 patients were treated with MT using stent retrievers in both centers during the investigated period (years 2009–2016). Demographic and baseline characteristics of these patients are shown in Table 1. Eighty-eight (12.5%) patients (46% of males, mean age 75.5 ± 11.8 years,) used AT in the time of AIS and had a median baseline NIHSS score of 17 points. Patients on AT were significantly older and had more frequently atrial fibrillation (AF), ischemic cardiopathy (ICD) and hypertension without medication (Table 1). IVT was performed before MT in 501 (81.5%) patients without AT and 114 (18.5%) patients without AT were treated with MT alone.

The recanalization (TICI 2b and 3) was reached in 80% of AT patients and complete recanalization (TICI 3) in 65% of patients (p—1.000) (Table 2). Good 90-day clinical outcome (mRS 0–2) was present in 36% of AT patients and 35% of patients died within 3 months. ICH after MT was observed in 34% ($p = 0.38$) and SICH in 9% of patients on AT ($p = 0.136$, Table 2). In the group of patients without AT, no difference was found in the rate of ICH and SICH according to prior IVT; 29.1% of ICH and 5.0% of SICH in patients treated with prior IVT versus 25.4% of ICH and 5.3% of SICH in patients treated with MT alone.

Patients on AT had significantly poorer 90-day clinical outcome after MT than patients without AT ($p = 0.03$, Table 2, Fig. 1). Patients on AT with poor outcome after MT had more frequently AF (69 vs. 93%, p—0.005), higher admission NIHSS (13.5 vs. 17, p—0.004), and higher rate of SICH (0 vs. 14.5%, p—0.047) (Table 3).

Fifty (57%) of anticoagulated patients were on warfarin, 15 (17%) were on DOAC, and remaining 22 (26%) were on the therapeutic dose of low molecular weight heparin (LMWH). No significant difference was found in the recanalization rate, 90-day clinical outcome, and SICH occurrence among the individual types of AT (Table 4). In pooled analysis, no difference in the clinical outcome and rate of SICH was found between patients on warfarin with

Table 1 Patients' demographic and baseline clinical characteristics

	Non-AT patients	AT patients	p
N (males, %)	615 (51%)	88 (46%)	0.363
Age (years, mean ± SD)	70.0 ± 12.5	75.5 ± 11.8	0.001
Admission NIHSS—median (range)	17.0 (1–42)	16.5 (2–36)	0.523
Hypertension with medication (*n*, %)	416 (68%)	61 (69%)	1.000
Hypertension without medication (*n*, %)	43 (7%)	18 (21%)	< 0.0001
Diabetes mellitus (*n*, %)	160 (26%)	32 (36%)	0.052
Ischemic cardiomyopathy (*n*, %)	147 (24%)	46 (52%)	< 0.0001
Hyperlipidemia (*n*, %)	259 (42%)	42 (48%)	0.357
Atrial fibrillation (*n*, %)	230 (38%)	74 (84%)	< 0.0001
MCA occlusion (*n*, %)	503 (82%)	73 (83%)	0.883
ICA occlusion (*n*, %)	145 (24%)	16 (18%)	0.281
BA occlusion (*n*, %)	76 (12%)	12 (14%)	0.731

AT anticoagulation therapy, *BA* basilar artery, *ICA* internal carotid artery, *MCA* middle cerebral artery, *NIHSS* National Institute of Health Stroke Scale

Table 2 Results

	Non-AT patients	AT patients	p
"Onset to recanalization" interval (mean ± SD)	240 ± 98	225 ± 73	0.006
Recanalization (TICI ≥ 2b) (*n*, %)	492 (80%)	70 (80%)	1.000
Complete recanalization (TICI 3) (*n*, %)	394 (64%)	57 (65%)	1.000
ICH (*n*, %)	178 (29%)	30 (34%)	0.318
SICH (*n*, %)	31 (5%)	8 (9%)	0.136
Median of mRS at 90 days	3	5	1.000
mRS ≤ 2 at 90 days (*n*, %)	301 (49%)	32 (36%)	0.03
Mortality at 7 days (*n*, %)	55 (9%)	11 (13%)	1.000
Mortality at 90 days (*n*, %)	166 (27%)	31 (35%)	0.127

AT anticoagulation therapy, *ICH* intracerebral hemorrhage, *SICH* symptomatic intracerebral hemorrhage, *mRS* modified Rankin Scale, *SD* standard deviation, *TICI* Thrombolysis in Cerebral Infarction Scale

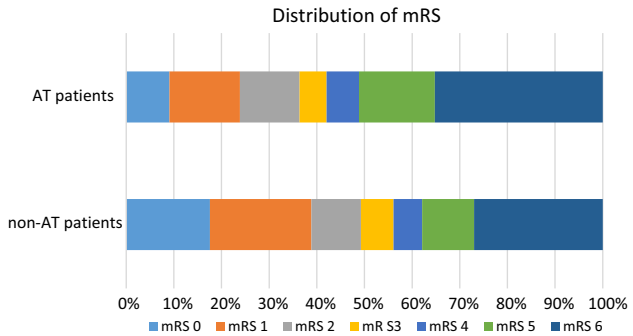

Fig. 1 Distribution of mRS in patients on AT and without AT

admission International normalized ratio (INR) < 1.7 and ≥ 1.7 (Table 5).

Multivariate logistic regression analysis did not show the age, hypertension, diabetes mellitus (DM), ICD, admission NIHSS, recanalization, and complete recanalization as predictors of SICH in patients on AT (Table 6).

Discussion

Ischemic stroke is not rare in the patients using anticoagulation therapy, especially in the presence of AF. Large randomized clinical studies showed a risk of AIS about 1–1.4%/year on warfarin and about 0.9 to 1.34/year on DOAC [4–6]. Li et al. [8] reported risk of AIS between 2.6–5.0%/year in the patients using warfarin, which depended on time in the therapeutic range. Sjögren et al. [7] recently reported the risk of AIS 1.03%/year in patients on warfarin and 1.04%/year in patients on DOAC.

The results of our study showed that MT might be safe and relatively effective also in patients using AT. The

Table 3 Comparison of patients on AT with good and poor 3-month clinical outcome after MT

	Pts with mRS 0-2	Pts with mRS 3-6	*p*
N	32 (36%)	56 (64%)	–
Age (years, mean ± SD)	69.5 ± 14.3	74.4 ± 9.9	0.116
AF (*n*, %)	22 (69%)	52 (93%)	0.005
Ischemic cardiomyopathy (*n*, %)	15 (47%)	31 (55%)	0.509
DM (*n*, %)	11 (34%)	21 (38%)	0.821
Hypertension (*n*, %)	26 (81%)	53 (95%)	0.067
Admission NIHSS (median)	13.5	17.0	0.004
BA occlusion (*n*, %)	2 (6%)	10 (18%)	0.198
TICI 3 (*n*, %)	24 (75%)	33 (59%)	0.166
SICH (*n*, %)	0 (0)	8 (14%)	0.047
"Onset to recanalization" interval (min, mean ± SD, median)	229 ± 79, 218	225 ± 70, 240	0.746

AF atrial fibrillation, *BA* basilar artery, *DM* diabetes mellitus, *mRS* modified Rankin Scale, *TICI* Thrombolysis in Cerebral Infarction Scale, *SD* standard deviation, *SICH* symptomatic intracerebral hemorrhage

Table 4 Comparison of results according to individual types of AT

	Warfarin	DOAC	LMWH	*p*
N (%)	50 (57%)	15 (17%)	22 (26%)	0.253
Age (years, mean ± SD)	76 ± 11	77 ± 6	74 ± 15	0.328
Onset to recanalization interval (mean ± SD)	217.5 ± 69.4	180 ± 68.8	240 ± 78.2	0.114
Overall recanalization (TICI ≥ 2b) (*n*, %)	41 (82%)	11 (73%)	17 (80%)	0.691
Complete recanalization (TICI 3) (*n*, %)	31 (62%)	10 (67%)	15 (68%)	0.950
ICH (*n*, %)	18 (36%)	6 (40%)	6 (27%)	0.630
SICH (*n*, %)	6 (12%)	0	2 (9%)	0.514
mRS ≤ 2 at 90 days (*n*, %)	18 (36%)	7 (47%)	7 (32%)	0.781
Mortality at 7 days (*n*, %)	4 (8%)	2 (13%)	5 (21%)	1.000
Mortality at 90 days (*n*, %)	19 (38%)	4 (27%)	7 (32%)	0.858

AT anticoagulation therapy, *DOAC* direct oral anticoagulants, *ICH* intracerebral hemorrhage, *mRS* modified Rankin Scale, *SD* = standard deviation, *SICH* symptomatic intracerebral hemorrhage, *TICI* Thrombolysis in Cerebral Infarction Scale

Table 5 Mechanical thrombectomy in patients on warfarin

	INR > 1.7	INR ≤ 1.7	*p*
N (%)	21 (41%)	29 (59%)	1.000
Age (years, mean ± SD)	71.6 ± 13.7	75.2 ± 7.1	0.594
Overall recanalization (TICI ≥ 2b) (*n*, %)	15 (71%)	25 (86%)	0.391
Complete recanalization (TICI 3) (*n*, %)	12 (59%)	18 (63%)	1.000
ICH (*n*, %)	10 (46%)	9 (30%)	0.372
SICH (*n*, %)	4 (18%)	2 (7%)	0.388
mRS ≤ 2 at 90 days (*n*, %)	6 (27%)	13 (44%)	0.248
Mortality at 7 days (*n*, %)	2 (10%)	2 (7%)	1.000
Mortality at 90 days (*n*, %)	7 (32%)	12 (41%)	0.565

ICH intracerebral hemorrhage, *INR* International normalized ratio, *mRS* modified Rankin Scale, *SD* standard deviation, *SICH* symptomatic intracerebral hemorrhage, *TICI* Thrombolysis in Cerebral Infarction Scale

Table 6 Multivariate logistic regression analysis for prediction of SICH after MT in AT patients

Variable	*p*	95% CI
Age	0.781	0.944–1.079
Admission NIHSS	0.179	0.819–1.038
Diabetes mellitus	0.944	0.235–4.739
Ischemic cardiomyopathy	0.893	0.211–3.871
"Onset to recanalization" interval	0.994	0.990–1.010
Complete recanalization (TICI 3)	0.529	0.323–9.007
Hypertension	0.999	N/A

AT anticoagulation therapy, *CI* confidential interval, *MT* mechanical thrombectomy, *NIHSS* National Institute of Health Stroke Scale, *SICH* symptomatic intracerebral hemorrhage, *TICI* Thrombolysis in Cerebral Infarction Scale

higher rate of poor 90-day clinical outcome and higher 3-month mortality (35%) in the presented study may be related to higher rate of AF, higher admission NIHSS and higher rate of SICH after MT in these patients (Table 3). Presence of AF is generally associated with a poor outcome and with a higher mortality after IS [17].

Up to date, only very limited data are available in terms of MT performed in AIS patients treated with anticoagulants; however, MT is being performed in some patients on AT in experienced centers. Benavente et al. [18] analyzed retrospectively 30 patients on warfarin treated with MT. Good outcome was present in 46.7% of patients with the rate of 3-month mortality 6.7% in the analyzed group and SICH was detected in 16.7% of cases [18].

Patients using AT have generally a higher risk of ICH, and thus the occurrence of SICH after MT in our AT patients (9%) exceeded reported numbers from previous positive randomized trials (4.4%) [14], but the difference in the SICH rate between patients on AT and without AT was found not significant in our cohort (Table 2). A trend of low SICH rate was observed in subgroup of patients on DOAC (Table 4), which may correspond to a known better safety profile of DOAC with lower incidence of ICH compared to warfarin [19]. Moreover, a specific antidotum for immediate reversal of anticoagulant effect of dabigatran was approved recently [20] and may be considered to use before MT in patients with high risk of bleeding complications [21].

Interestingly, no difference was found in the rate of ICH, SICH, and mortality between subgroups of patients using warfarin according to the admission INR (Table 5), even though Benavente et al. [18] reported significantly higher mortality in the patients with admission INR ≥ 1.7. Our results showed no difference in the recanalization rate between both groups. Moreover surprisingly, none of the analyzed baseline, clinical, and recanalization parameters was found as a predictor of SICH after MT including the value of INR (Table 6).

Our study has some limitations. Retrospective bi-center study was conducted with a relatively small sample size; however, the risk of ischemic stroke is generally low in patients on AT, and only very limited data about MT in these patients are available up to now. We present retrospective patients' cohort for 7 years, but all patients were treated with stent retrievers and were enrolled for the treatment according to the same criteria during whole analyzed period (see "Methods" section).

In conclusion, MT performed in patients using AT was not associated with a significantly higher rate of SICH. Patients on AT with poor outcome after MT had more frequently AF, higher admission NIHSS, and higher rate of SICH. Further large multicenter prospective studies are strongly needed, because of an increasing number of patients on AT worldwide.

Acknowledgements The study was supported by the grant of the IGA LF UP_010_2017, IGA-KZ-2016-1-2 and partially by the grant of Ministry of Health Czech Republic, No. 17-30101A.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, American Heart Association Stroke Council, et al. 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2015;46:3020–35. https://doi.org/10.1161/STR.0000000000000074.
2. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, for the DAWN Trial Investigators, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med. 2018;378:11–21. https://doi.org/10.1056/nejmoa1706442.
3. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, for the DEFUSE 3 Investigators, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. N Engl J Med. 2018. https://doi.org/10.1056/nejmoa1713973 (**Epub 2018 Jan 24**).
4. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, RE-LY Steering Committee and Investigators, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361:1139–51. https://doi.org/10.1056/NEJMoa0905561.
5. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, ROCKET AF Investigators, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365:883–91. https://doi.org/10.1056/NEJMoa1009638.
6. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, ARISTOTLE Committees and Investigators, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981–92. https://doi.org/10.1056/NEJMoa1107039.
7. Sjögren V, Byström B, Renlund H, Svensson PJ, Oldgren J, Norrving B, et al. Non-vitamin K oral anticoagulants are non-inferior for stroke prevention but cause fewer major bleedings than well-managed warfarin: a retrospective register study. PLoS ONE. 2017;12(7):e0181000. https://doi.org/10.1371/journal.pone.0181000.
8. Li W-H, Huang D, Chiang C-E, Lau C-P, Tse H-F, Chan EW, et al. Efficacy and safety of dabigatran, rivaroxaban, and warfarin for stroke prevention in Chinese patients with atrial fibrillation: the Hong Kong Atrial Fibrillation Project. Clin Cardiol. 2017;40:222–9. https://doi.org/10.1002/clc.22649.
9. Berkhemer OA, Fransen PPS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med. 2015;372(1):11–20.
10. Goyal M, Demchuk AM, Menon BK, for the ESCAPE Trial Investigators, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med. 2015;372(11):1019–30.
11. Saver JL, Goyal M, Bonafe A, for the STAR Investigators, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med. 2015;372(24):2285–95.
12. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med. 2015;372:2296–306.
13. Campbell BC, Mitchel PJ, Kleinig HM, et al. Endovascular treatment for ischemic stroke with perfusion-imaging selection. N Engl J Med. 2015;372(11):1009–18.
14. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, HERMES collaborators, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet. 2016;387:1723–31. https://doi.org/10.1016/S0140-6736(16)00163-X.
15. Higashida RT, Furlan AJ. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. Stroke. 2003;34:109–37.
16. Wahlgren N, Ahmed N, Eriksson N, Aichner F, Bluhmki E, Dávalos A, Safe Implementation of Thrombolysis in Stroke-MOnitoring STudy Investigators, et al. Multivariable analysis of outcome predictors and adjustment of main outcome results to baseline data profile in randomized controlled trials: Safe Implementation of Thrombolysis in Stroke-MOnitoring STudy (SITS-MOST). Stroke. 2008;39:3316–22. https://doi.org/10.1161/strokeaha.107.510768.
17. Liang J, Liu W, Sun J, Gu X, Ma Q, Tong W. Analysis of the risk factors for the short-term prognosis of acute ischemic stroke. Int J Clin Exp Med. 2015;8:21915–24 (**eCollection 2015**).
18. Benavente L, Larrosa D, García-Cabo C, Pérez ÁI, Rico M, Vega P, et al. Safety and efficacy of mechanical thrombectomy in acute ischemic stroke of anticoagulated patients—a prospective observational study. J Stroke Cerebrovasc Dis. 2016;25:2093–8. https://doi.org/10.1016/j.jstrokecerebrovasdis.2016.06.006.
19. Alberts MJ, Eikelboom JW, Hankey GJ. Antithrombotic therapy for stroke prevention in non-valvular atrial fibrillation. Lancet Neurol. 2012;11:1066–81. https://doi.org/10.1016/S1474-4422(12)70258-2.
20. Pollack CV Jr, Reilly PA, Eikelboom J, Glund S, Verhamme P, Bernstein RA, et al. Idarucizumab for dabigatran reversal. N Engl J Med. 2015;373:511–20. https://doi.org/10.1056/NEJMoa1502000.
21. Diener HC, Kleinschnitz C. Non-vitamin K oral anticoagulants in stroke patients: practical issues. J Stroke. 2016;18:138–45. https://doi.org/10.5853/jos.2016.00157.