Journal of the Neurological Sciences 396 (2019) 193–198

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Mechanical thrombectomy outcomes in large vessel stroke with high international normalized ratio

Abhi Pandhi[a], Georgios Tsivgoulis[a,b], Muhammad F. Ishfaq[a], Aristeidis Katsanos[b], Georgios Magoufis[c], Konark Malhotra[d], Rashi Krishnan[a], Adam Arthur[e], Daniel Hoit[e], Lucas Elijovich[a,e], Andrei V. Alexandrov[a], Ahmad Cheema[f], Nitin Goyal[a,*]

[a] Department of Neurology, University of Tennessee Health Science Center, United States
[b] Second Department of Neurology, National & Kapodistrian University of Athens, Athens, Greece
[c] Acute Stroke Unit, Metropolitan Hospital, Piraeus, Greece
[d] Department of Neurology, West Virginia University-Charleston Division, Charleston, WV, United States
[e] Department of Neurosurgery, University of Tennessee Health Science Center and Semmes Murphey Clinic, United States
[f] Department of Neurosurgery, University of Oklahoma-Health Sciences Center, Oklahoma City

ARTICLE INFO

Keywords:
Thrombectomy
Large vessel occlusion
Safety
Efficacy
International normalized ratio

ABSTRACT

Objective: Evaluating the safety and efficacy of mechanical thrombectomy (MT) in acute stroke patients due to emergent large vessel occlusion (ELVO) with high international-normalized-ratio (INR).

Methods: Consecutive ELVO patients treated with MT were evaluated from two centers. Outcome measures included symptomatic-intracranial-hemorrhage(sICH), three-month mortality, successful reperfusion(SR), and 3-month functional-independence(FI; mRS-scores of 0–2). Additionally, a meta-analysis of available cohort studies was performed to evaluate safety and efficacy of MT in ELVO patients with high INR.

Results: A total of 315 ELVO patients were evaluated. Of those 10 patients had INR > 1.7 [mean age 63.5 ± 15, median NIHSS-score: 17 points (IQR 14–22)],and remaining 305 ELVO patients had INR ≤ 1.7 ([mean age 62 ± 14.4, median NIHSS-score: 17 points (IQR 12–21)]. Patients with high INR did not differ in terms of sICH (10.0% vs. 6.9%; $p = .706$), 3-month mortality (20.0% vs. 24.2%; $p = .762$), SR (88.9% vs. 69.4%; $p = .209$) and 3-month FI (50% vs. 49.3%; p = .762) compared to the rest. Meta-analysis of available studies ($n = 5$) showed that high INR was not related to sICH (OR: 0.94, 95%CI: 0.42–2.07; $p = .88$), 3-month mortality (OR: 1.07, 95%CI: CI 0.72–1.60; $p = .73$) and 3-month FI (OR: 0.69, 95%CI: 0.34–1.40; $p = .30$).

Conclusions: MT can be performed safely and effectively in ELVO patients with high INR.

1. Introduction

Intravenous thrombolysis (IVT) administered within 4.5 h of symptom onset is standard of care for patients with acute ischemic stroke (AIS) [1]. Timely mechanical thrombectomy (MT) further improves outcomes of AIS patients due to emergent large vessel occlusion (ELVO). IVT is contraindicated in AIS patients pretreated with non-vitamin K oral antagonists (NOACs) and vitamin K antagonist (VKAs) with an elevated international normalized ratio (INR) of > 1.7 as well as in patients with coagulopathy and high INR [1]. Thus, it may be argued that MT in ELVO patients with high INR may be associated with a higher risk of hemorrhagic complications and worse clinical outcomes. However, the data evaluating the safety and efficacy of MT in ELVO patients with relative/absolute contraindications to IVT due to high INR are limited [2,3]. Moreover, only 2 out of 5 pivotal randomized-controlled clinical trials (RCTs) of MT in AIS demonstrated a beneficial effect of MT regardless of pretreatment with oral anticoagulants, while the remaining three RCTs excluded the ELVO patients who were on anticoagulants [4,5].

Recent small, single-center studies have provided preliminary evidence that MT appears to be safe in patients with high INR [3,6]. Nevertheless, firm conclusions cannot be drawn due to the limited number of ELVO patients with high INR that were treated with MT. In view of the former considerations, we conducted a multicenter study evaluating the safety and efficacy of MT in ELVO patients with high INR (> 1.7). We also performed a systematic review and meta-analysis of

* Corresponding author: Department of Neurology, University of Tennessee Health Science Center, 855 Monroe Avenue, Suite # 415, Memphis, TN 38163, United States.
E-mail address: ngoyal@uthsc.edu (N. Goyal).

https://doi.org/10.1016/j.jns.2018.11.019
Received 15 August 2018; Received in revised form 29 October 2018; Accepted 15 November 2018
Available online 19 November 2018
0022-510X/ © 2018 Elsevier B.V. All rights reserved.

available studies.

2. Methods

2.1. Study design (multicenter review and meta-analysis)

We performed a retrospective analysis of previously prospectively collected database of consecutive ELVO patients who underwent MT at two tertiary care stroke centers from January 2013 to June 2016. We included CT angiography (CTA) confirmed ELVO patients that presented within 6 h of symptom onset and subsequently treated with MT. For the patients presenting between 6 and 12 h from symptom onset, additional imaging selection criteria were used such as ASPECTS score ≥ 6 on CT head and/or good collaterals on CTA as previously reported in detail [7]. Baseline characteristics including demographics, vascular risk factors, admission NIHSS-scores, admission ASPECTS, pretreatment with IVT, admission serum glucose, admission INR, admission systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels were recorded as previously described [8–11]. All ELVO patients were stratified into two groups according to admission INR (INR > 1.7 vs. INR ≤ 1.7). Common causes of high INR (> 1.7) in our cohort were pretreatment with VKAs or coagulopathy due to liver disease or other blood disorders. The research protocol was approved by institutional IRB called iMedRIS (Integrated medical research information system).

The meta-analysis has adopted the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses [12]. The selection of eligible studies is detailed in the flowchart outlined in Fig. 1. We performed a computerized literature search on MEDLINE and SCOPUS databases on January 25, 2018, with the following search terms: “international normalized ratio”, “INR”, “mechanical thrombectomy”, “thrombectomy”, “endovascular reperfusion therapy”, “stent retriever”, “thromboaspiration”, “catheter”, “endovascular treatment”, “endovascular treatment”, “acute ischemic stroke”, “cerebral ischemia”, “stroke” and “large vessel occlusion”. No other search restrictions were applied. The complete search algorithm used in MEDLINE search is available in the Online Supplement. Two authors (AP and NG) did a literature search and extracted data from relevant studies. We excluded the studies for which the reported outcomes were not dichotomized or compared between INR > 1.7 and INR ≤ 1.7 groups. We assessed the quality of all eligible for the meta-analysis studies with the Newcastle-Ottawa Scale [13]. Quality control and bias identification were performed by two independent reviewers (AHK, GT) and all emerging conflicts were resolved with consensus.

2.2. Data availability statement

The data that support the findings of this study are available from the corresponding author on reasonable request.

2.3. Outcomes

The primary outcomes of our multicenter study were functional independence (FI) defined as modified Rankin scale (mRS) scores of 0–2 at 3 months, 3-month mortality, and symptomatic intracerebral hemorrhage (sICH) defined as presence of a parenchymal hematoma type 2 (PH2) on brain CT and/or MRI gradient recall echo (GRE) sequence

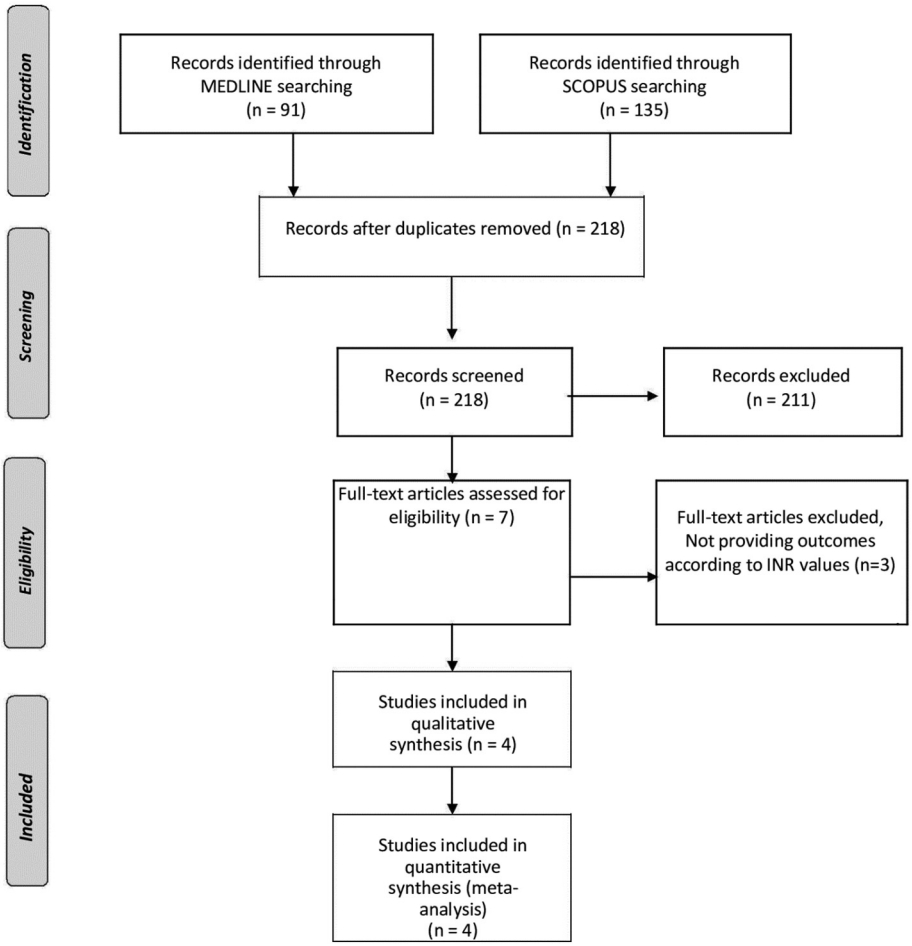

Fig. 1. Flowchart presenting the selection of eligible studies.

Table 1
Baseline characteristics of study population (n = 315).

Baseline Clinical Characteristics	INR > 1.7 (n = 10)	INR ≤ 1.7 (n = 305)	p value
Age (years, mean ± SD)	63.5 ± 15.0	62.0 ± 14.4	0.752
Males (%)	40.0%	52.1%	0.450
Race (%)	Caucasian: 60.0%	46.2%	–
	African American: 40.0%	53.5%	
	Asian: 0%	0.3%	
Hypertension (%)	70.0%	77.0%	0.603
Diabetes mellitus (%)	30.0%	32.9%	0.848
Hyperlipidemia (%)	50.0%	41.3%	0.583
Atrial fibrillation (%)	40.0%	25.4%	0.300
Heart Failure (%)	50.0%	20.9%	0.028
Coronary artery disease (%)	20.0%	25.3%	0.702
Smoking (%)	20.0%	29.8%	0.504
Prior stroke (%)	10.0%	22.8%	0.340
Prior anticoagulant use (%)	60.0%	15.1%	< 0.001
Anticoagulant type (n, %)	Coumadin: 5 (50.0%)	29 (9.5%)	–
	Apixaban: 0 (0%)	3 (1.0%)	
	Dabigatran: 0 (0%)	4 (1.3%)	
	Rivaroxaban: 1 (10.0%)	8 (2.6%)	
	Heparin/LMWH: 0 (0%)	2 (0.7%)	
Prior antiplatelet use (%)	30.0%	30.4%	0.980
SBP at baseline (mmHg, mean ± SD)	137.4 ± 13.3	158.4 ± 31.9	0.038
DBP at baseline (mmHg, mean ± SD)	80.1 ± 12.3	90.1 ± 22.0	0.155
Serum blood glucose at baseline (mg/dl, median, IQR)	146 (119–173)	127 (105–162)	0.424
LDL at baseline (mg/dl, median, IQR)	69 (41–146)	94 (71–120)	0.318
Baseline NIHSS score (median, IQR)	17 (14–22)	17 (12 − 21)	0.613
Disability (mRS > 1) prior to index event (%)	20.0%	12.8%	0.505
Baseline imaging characteristics			
ASPECTS score on baseline CT (median, IQR)	9 (8–10)	10 (8–10)	0.711
Presence of good collateral circulation on baseline CT (%)	70.0%	76.2%	0.650
Intracranial occlusion location (n, %)	Internal carotid artery: 0 (0%)	17 (5.6%)	
	M1 segment MCA: 4 (40%)	123 (40.3%)	
	M2 segment MCA: 3 (30%)	29 (9.5%)	
	Tandem occlusion: 2 (20%)	31 (10.2%)	
	Posterior circulation: 0 (0%)	43 (14.1%)	
	Multiple vessels: 1 (10%)	62 (20.3%)	
Treatment details and process times			
IVT pretreatment (%)	60.0%	68.8%	0.553
IA thrombolysis (%)	0	2.3%	0.628
Concomitant angioplasty (%)	10.0%	5.6%	0.556
Onset to groin puncture (min, median, IQR)	213 (182–258)	253 (185–369)	0.283

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; ASPECTS: Alberta stroke program early CT score; LDL: low density lipoprotein; IVT: intravenous thrombolysis; IA: intra-arterial; NIHSS: national institute of heath stroke scale.

Table 2
Outcome variables following mechanical thrombectomy in two groups (high INR (> 1.7) vs. INR ≤1.7).

	INR > 1.7 (n = 10)	INR ≤ 1.7 (n = 305)	p-value
Outcomes			
Complete recanalization (%)	88.9%	69.4%	0.209
Time to recanalization (min, median, IQR)	70 (49–90)	48 (33–76)	0.249
sICH (%)	10.0%	6.9%	0.706
Serious complications (%)	20.0%	25.6%	0.689
NIHSS discharge (median, IQR)	7 (4–11)	7 (3–18)	0.828
mRS at discharge (median, IQR)	4 (2–5)	4 (2–5)	0.740*
In-hospital mortality (%)	10.0%	21.0%	0.398
mRS at 3-months (median IQR)	3 (1–4)	3 (1–6)	0.809*
FI (mRS ≤ 2) at 3 months (%)	50.0%	49.3%	0.966
3-month mortality (%)	20.0%	24.2%	0.762

* = non-significant difference in outcomes between the two groups.

accounting for deterioration with an increase in NIHSS-score of ≥4 points within 36 h from treatment. The rates of successful recanalization (SR) defined as modified thrombolysis in cerebral infarction grades of 2b or 3, time to recanalization, other serious complications (groin hematoma or vessel dissection/perforation), NIHSS at discharge, mRS at discharge, mRS at 3 months, and in-hospital mortality represented the secondary outcomes. The outcomes of our meta-analysis were sICH three-month FI and 3-month mortality.

2.4. Statistical analysis

Continuous variables are presented as mean ± SD (normal distribution) and as median with interquartile range (skewed distribution). Statistical comparisons between two groups (INR > 1.7 vs. INR ≤ 1.7) were performed using χ^2 test, or in case of small-expected frequencies, Fisher's exact test. Continuous variables were compared by the use of the unpaired t-test or Mann–Whitney U test, as indicated. The distribution on the mRS-score at discharge and at three months among ELVO patients was compared between two groups using Cochran Mantel-Haenszel test.

In the eligible for the meta-analysis studies we calculated the corresponding risk ratios (RRs) and 95% confidence intervals (CIs) on the reported outcomes of interest. A random-effects model (DerSimonian Laird) was used to calculate the pooled effect estimates. Heterogeneity between studies was assessed with the Cochran Q and I^2 statistics, with I^2 values of at least 50% considered to represent substantial heterogeneity and values of at least 75% indicative of considerable heterogeneity [14]. Pooled analyses were conducted using Review Manager (RevMan) Version 5.3 software (Copenhagen: The Nordic Cochrane

Table 3
Baseline characteristics of the studies included for the meta-analysis.

Trial Name	Nogueira et al.	Benavente et al	Mundiyanapurath et al..	Rozeman et al...
Study type	Pooled analysis of MERCI and Multi MERCI cohorts	Prospective	Prospective	Retrospective
Number of patients with INR > 1.7	19	12	21	18
Number of patients with INR ≤ 1.7	270	104	414	438
Age INR > 1.7/ INR < 1.7	72.8/67.6 (Mean)	n/a	n/a	61.5/62 (median)
Men (%) INR > 1.7/ INR < 1.7	39/51	n/a	n/a	89/58
Prior anticoagulant use (%) INR > 1.7/ INR < 1.7	100/10.1	n/a	n/a	n/a
NIHSS INR > 1.7/ INR < 1.7	18.94/19.5 (mean)	n/a	n/a	14.5 (5–38)/ 16 (1–42)
Location (%) INR > 1.7/ INR < 1.7	AC 100/AC 91, PC 9	n/a	AC 100/AC 100	AC 66, PC 34 / AC 71, PC 29
IVT used (%) INR > 1.7/ INR < 1.7	0/17.8	n/a	5/77	17/68

INR- International normalized ratio; IA- Intra-arterial; AC-Anterior circulation; PC-Posterior circulation; tPA- tissue plasminogen activator.

Table 4
Quality assessment of included studies with the Newcastle–Ottawa Scale.

Study name	Selection	Comparability	Outcome	Overall	Comments
Nogueira et al	***	*	***	7/9	1, 2
Benavente et al	***	*	***	7/9	1, 2
Mundiyanapurath et al	****	*	***	8/9	2
Rozeman et al	***	**	***	8/9	1
Pandhi et al	****	*	***	8/9	2
Overall	17/20	6/10	15/15	38/45	

[1]Consecutivity of included patients not explicitly reported.
[2]Not adjusting for potential confounders.

Centre, The Cochrane Collaboration, 2014).

3. Results

Our study population consisted of 315 consecutive AIS patients with ELVO. Of those, 10 patients had INR > 1.7 [mean age 63.5 ± 15, 40% men, median NIHSS-score: 17 points (IQR 14–22)], while the remaining 305 ELVO patients had INR ≤ 1.7 ([mean age 62 ± 14.4, 52.1% men, median NIHSS-score: 17 points (IQR 12–21)]. The baseline clinical, imaging and treatment characteristics of the study population are presented in Table 1. Of 10 patients with INR > 1.7, five were on VKAs, one on rivaroxaban and remaining 4 patients had INR > 1.7 caused by general medical condition. The two groups (INR > 1.7 vs. INR ≤ 1.7) were well balanced in terms of baseline clinical and imaging variables except for the the history of congestive heart failure (50% vs. 20.9%, $p = .028$) and prior anticoagulation use (60% vs. 15.1%, $p < .001$) that were more common in the high INR group, while mean SBP levels at baseline were lower in high INR group (137.4 ± 13.3 mmHg vs. 158.4 ± 31.9 mmHg, $p = .038$).

Table 2 depicts the various primary and secondary outcomes in the two INR subgroups. The two groups did not differ in terms of rates of sICH (10% vs. 6.9%, $p = .249$), 3-month FI (50% vs. 49.3%, $p = .966$), 3-month mortality (20% vs. 24.2%, $p = .762$), SR (88.9% vs 69.4%, $p = .209$), and median groin puncture to recanalization [70 min (IQR: 49–90) vs. 48 min (IQR: 33–76), p = .249)]. The remaining secondary outcomes were similar in the two groups.

Our search strategy initially identified 7 eligible studies for inclusion in our meta-analysis. Ultimately, 3 studies were excluded for not providing outcomes of interest according to INR levels (Supplementary Table 1) and the 4 studies that met the inclusion criteria were included in the meta-analysis (Table 3) [3,6,15,16]. The selected studies were published between 2009 and 2017. Baseline characteristics and quality assessment of included studies are presented in Tables 3 and 4, respectively. A total of 1627 ELVO treated with MT were included in the present meta-analysis involving 4 studies identified from the literature search and our multicenter study; 80 (4.9%) patients had INR > 1.7, while in the remaining 1547 (95.1%) INR levels were ≤ 1.7. High INR was not associated with an increased likelihood of sICH (5 studies; OR: 0.94, 95%CI: 0.42–2.07, $p = .88$). There was no heterogeneity across included studies (Cochran's Q statistic 1.89, df = 4; $p = 0$ 0.76, $I^2 = 0\%$). High INR was also not related with higher odds of 3-month mortality (4 studies; OR: 1.07, 95%CI: 0.72–1.60, $p = .73$) without any heterogeneity across included studies (Cochran's Q statistic 0.28, df = 3; $p = .96$, $I^2 = 0\%$). There was no association between high INR and 3-month FI (4 studies; OR: 0.69, 95%CI: 0.34–1.40, $p = .30$) without substantial heterogeneity across included studies (Cochran's Q statistic 0.29, df = 3; $p = 0$ 0.08, $I^2 = 56\%$). These results are represented in the Forest plots in Fig. 2.

4. Discussion

The present multicenter study and meta-analysis indicate that MT in ELVO patients with high INR is safe and is not associated with higher risk of sICH and 3-month mortality. Additionally, INR levels were not associated with efficacy outcomes including three-month FI, SR and groin puncture to recanalization time. These observations underscore that the efficacy of MT for AIS patients due to ELVO appears not to be moderated by pretreatment with VKAs or coagulopathy resulting in high INR.

There are theoretical concerns regarding a potentially higher risk of hemorrhagic complications post-MT in ELVO patients with higher INR. A couple of proposed explanation can be given for observed comparable safety and efficacy of MT in two INR groups. The most contributing explanation is direct relationship of collateral status to clinical outcomes in ELVO patients with poor collaterals with higher risk of hemorrhagic complications and poor efficacy outcomes as well.

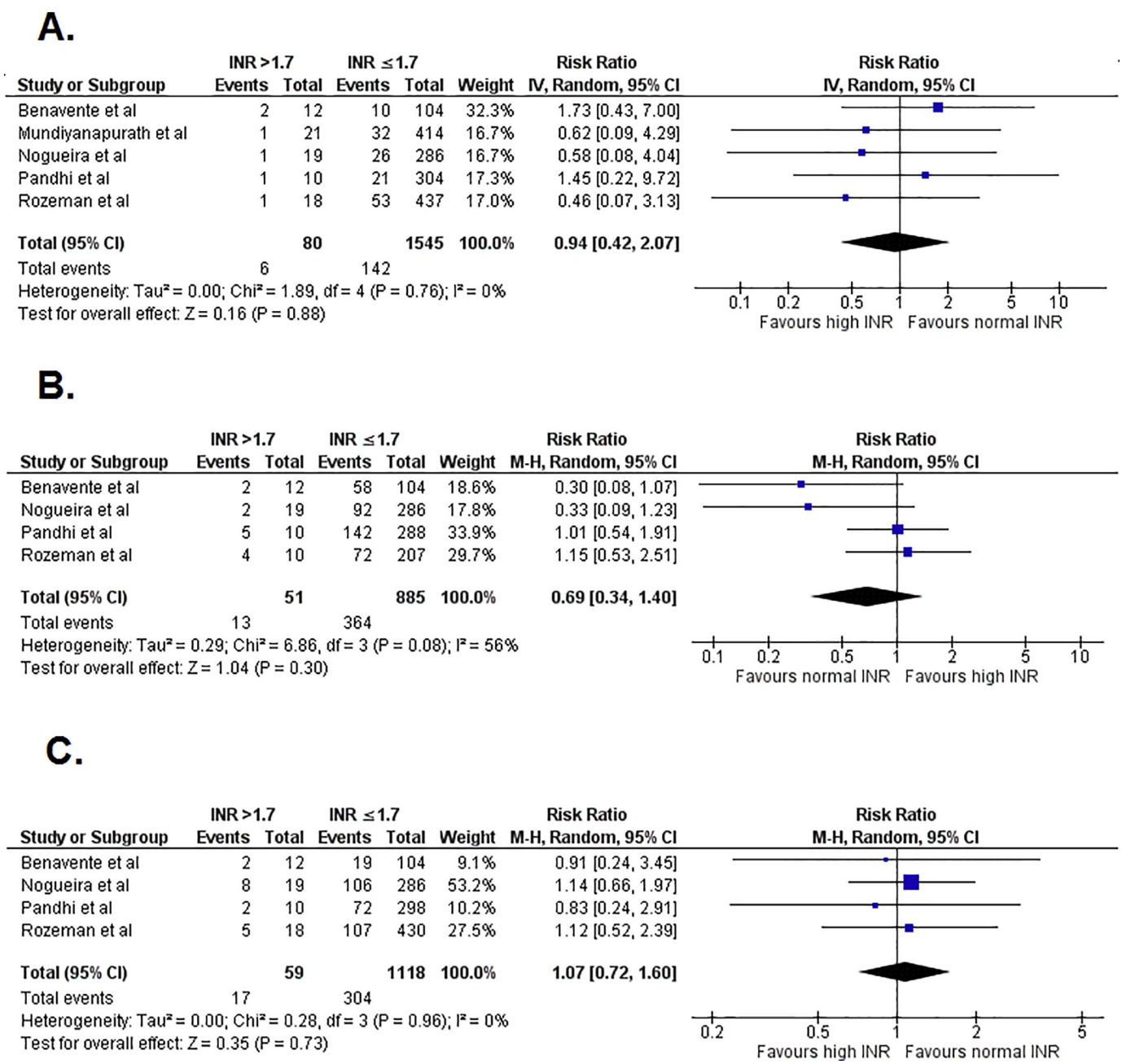

Fig. 2. Forrest plots depicting the association of high INR (> 1.7) (compared to INR ≤ 1.7) with symptomatic intracranial hemorrhage (sICH- panel A), three-month functional independence (FI- panel B), and three-month mortality (panel C) in patients with acute ischemic stroke due to large vessel occlusion.

Theoretically it is possible that higher atherosclerotic burden can cause impaired autoregulation and thus higher hemorrhagic complications [15] and even smaller contribution related to delays in onset to groin leading to bigger strokes and higher poor outcomes [17]. Collateral status and onset to groin times were comparable between both groups. Status of atherosclerosis and final infarct volumes were not available in our dataset to draw further conclusions either.

The present meta-analysis provides reassurance to stroke physicians that MT is safe and effective in ELVO patients with high INR due to pretreatment with oral anticoagulants or underlying coagulopathy. Since IVT is strictly contraindicated in this subgroup of AIS MT remains the only available acute reperfusion therapy in patients with high INR. Notably, none of the ELVO patients in our multicenter cohort received reversal therapy for high INR in form of fresh frozen plasma or prothrombin complex concentrates. Potential attempts to reverse high INR may lead to unacceptable time delays in the initiation of MT and may induce a pro-thrombotic state that can, in turn result in further neurological deterioration due to stroke progression.

Another important implication of our study findings is related to the pre-hospital management of ELVO patients. If the diagnosis of ELVO is suspected en route to the hospital and a history of coagulopathy with high INR is suspected, then the patients can be taken directly to centers with endovascular capabilities avoiding unnecessary transfer delay to primary stroke centers. This could potentially decrease substantially the onset to groin puncture time [18].

Certain limitations of the present report need to be acknowledged. First, the number of studies included in our meta-analyses is small so the lack of documented associations may be attributed to type II error caused by small sample size. Second, the majority of the included studies were non-randomized creating the possibility of selection bias. Third, the upper high cut off of INR was not defined in our study. Fourth, our sample size is small (n – 10) thus lower power of the results.

Even 60% of these received intravenous thrombolysis. The decision to give IV tPA to these patients was based on clinical history of no coagulopathy or no anticoagulant use without INR results being available until after tPA administration. Another limitation of our study included non-availability of final infarct volumes from our study. Low sample size limited us to do further subgroup analysis to study whether there was difference accounted due to background and natural history of the disease or treatment that led to increased INR. It is not a common practice at our hospital to obtain Eccarin Clotting Time (ECT) or DOAC level and the compliance for the patient on DOAC was verified by the patient and family and pharmacy.

In conclusion, our multicenter study coupled with the findings of this meta-analysis indicates that MT is deemed relatively safe and effective in ELVO patients with high INR due to pretreatment with oral anticoagulants or underlying coagulopathy. Thus, ELVO patients with high INR should be considered for timely MT.

Conflict of interest disclosure statement

Dr. Pandhi reports no disclosures.
Dr. Tsivgoulis reports no disclosures.
Dr. Ishfaq reports no disclosures.
Dr. Katsanos reports no disclosures.
Dr. Magoufis reports no disclosures.
Dr. Malhotra reports no disclosures.
Dr. Krishnan reports no disclosures.
Dr. Arthur: consultant for Codman, Medtronic, Microvention, Penumbra, Sequent, Siemens, Stryker and has received research support from Sequent and Siemens
Dr. Hoit: consultant for Codman Neurovascular, Medtronic, MicroVention, Penumbra, Sequent, and Stryker.
Dr. Elijovich: consultant for Codman Neurovascular, Medtronic, MicroVention, Penumbra, Sequent, and Stryker.
Dr. A. V. Alexandrov reports no disclosures.
Dr. Cheema reports no disclosures.
Dr. Goyal reports no disclosures.

Author contributions

Dr. Pandhi: Study concept and design, Acquisition of Data, Analysis and interpretation, critical revision of the manuscript for important intellectual content.
Dr. Tsivgoulis: Analysis and interpretation, critical revision of the manuscript for important intellectual content.
Dr. Ishfaq: Acquisition of Data, critical revision of the manuscript for important intellectual content.
Dr. Katsanos: Acquisition of Data, critical revision of the manuscript for important intellectual content.
Dr. Magoufis: Acquisition of Data, critical revision of the manuscript for important intellectual content.
Dr. Malhotra: Acquisition of Data, critical revision of the manuscript for important intellectual content.
Dr. Krishnan: critical revision of the manuscript for important intellectual content.
Dr. Arthur: Acquisition of Data, critical revision of the manuscript for important intellectual content.
Dr. Hoit: Acquisition of Data, critical revision of the manuscript for important intellectual content.
Dr. Elijovich: Critical revision of the manuscript for important intellectual content.
Dr. A. V. Alexandrov: Acquisition of Data, critical revision of the manuscript for important intellectual content.
Dr. Cheema: critical revision of the manuscript for important intellectual content.
Dr. Goyal: Study concept and design, Acquisition of Data, Analysis and interpretation, critical revision of the manuscript for important intellectual content.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2018.11.019.

References

[1] W.J. Powers, A.A. Rabinstein, T. Ackerson, et al., Guidelines for the early Management of Patients with Acute Ischemic Stroke: a Guideline for Healthcare professionals from the American Heart Association/American Stroke Association, Stroke (2018), https://doi.org/10.1161/STR.0000000000000158 (pii: STR.0000000000000158). (Epub ahead of print).
[2] J.C. Purrucker, M. Wolf, K. Haas, et al., Safety of endovascular thrombectomy in patients receiving non-vitamin K antagonist oral anticoagulants, *Stroke* 47 (2016) 1127–1130.
[3] S. Mundiyanapurath, A. Tillmann, M.A. Möhlenbruch, et al., Endovascular stroke therapy may be safe in patients with elevated international normalized ratio, J Neurointerv Surg 9 (2017) 1187–1190.
[4] M. Goyal, A.M. Demchuk, B.K. Menon, et al., Randomized assessment of rapid endovascular treatment of ischemic stroke, N. Engl. J. Med. 372 (2015) 1019–1030.
[5] O.A. Berkhemer, P.S. Fransen, D. Beumer, et al., A randomized trial of intraarterial treatment for acute ischemic stroke, N Engl J Med. 372 (2015) 11–20.
[6] R.G. Nogueira, W.S. Smith, MERCI and Multi MERCI Writing Committee. Safety and efficacy of endovascular thrombectomy in patients with abnormal hemostasis: pooled analysis of the MERCI and multi MERCI trials, Stroke 40 (2009) 516–522.
[7] N. Goyal, G. Tsivgoulis, A. Pandhi, et al., Admission hyperglycemia and outcomes in large vessel occlusion strokes treated with mechanical thrombectomy, J Neurointerv Surg. 10 (2018) 112–117.
[8] N. Goyal, G. Tsivgoulis, C. Nickele, et al., Posterior circulation CT angiography collaterals predict outcome of endovascular acute ischemic stroke therapy for basilar artery occlusion, J Neurointerv Surg. 8 (2016) 783–786.
[9] R. Bhole, N. Goyal, K. Nearing, et al., Implications of limiting mechanical thrombectomy to patients with emergent large vessel occlusion meeting top tier evidence criteria, J Neurointerv Surg. 9 (2017) 225–228.
[10] A. Pandhi, G. Tsivgoulis, R. Krishnan, et al., Antiplatelet pretreatment and outcomes following mechanical thrombectomy for emergent large vessel occlusion strokes, *J Neurointerv Surg.* (2017), https://doi.org/10.1136/neurintsurg-2017-013532 pii: neurintsurg-2017-013532. (Epub ahead of print).
[11] N. Goyal, G. Tsivgoulis, A. Pandhi, et al., Blood pressure levels post mechanical thrombectomy and outcomes in large vessel occlusion strokes, Neurology 89 (2017) 540–547.
[12] A. Liberati, D.G. Altman, J. Tetzlaff, et al., The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration, Ann. Intern. Med. 151 (2009) W65–W94.
[13] G.A. Wells, B. Shea, D. O'Connell, et al., The Newcastle-Ottawa Scale (NOS) for Assessing the Quality if Nonrandomized Studies in Meta-Analyses, Available from: http://wwwohrica/programs/clinical_epidemiology/oxfordasp.
[14] J.J. Deeks, J. Higgins, D.G. Altman, J. Higgins, S. Green (Eds.), Analysing Data and Undertaking Meta-Analyses. In Cochrane handbook for Systematic Reviews of Interventions, Wiley-Blackwell, Hoboken, NJ, USA, 2008, pp. 243–296.
[15] L. Benavente, D. Larrosa, C. García-Cabo, et al., Safety and Efficacy of Mechanical Thrombectomy in Acute Ischemic Stroke of Anticoagulated Patients-a prospective Observational Study, J. Stroke Cerebrovasc. Dis. 25 (2016) 2093–2098.
[16] A.D. Rozeman, M.J. Wermer, Lycklama à Nijeholt GJ et al. MR CLEAN pre-trial study group. Safety of intra-arterial treatment in acute ischaemic stroke patients on oral anticoagulants. A cohort study and systematic review, Eur. J. Neurol. 23 (2016) 290–296.
[17] M.G. Lansberg, G.W. Albers, C.A. Wijman, Symptomatic intracerebral hemorrhage following thrombolytic therapy for acute ischemic stroke: a review of the risk factors, Cerebrovasc. Dis. 24 (2007) 1–10.
[18] A.P. Jadhav, C.L. Kenmuir, A. Aghaebrahim, et al., Interfacility transfer Directly to the Neuroangiography Suite in Acute Ischemic Stroke patients Undergoing Thrombectomy, Stroke 48 (2017) 1884–1889.