Clinical Neurology and Neurosurgery 125 (2014) 19–23

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

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

Dramatic recovery after IV thrombolysis in anterior circulation ischemic stroke: Predictive factors and prognosis

João Rocha[a,*], João Pinho[a], Sara Varanda[a], José Amorim[b], Jaime Rocha[b], João Ramalho Fontes[a], Ricardo Maré[a], Carla Ferreira[a]

[a] Neurology Department of Hospital de Braga, Braga, Portugal
[b] Neuroradiology Department of Hospital de Braga, Braga, Portugal

ARTICLE INFO

Article history:
Received 12 June 2014
Received in revised form 30 June 2014
Accepted 7 July 2014
Available online 18 July 2014

Keywords:
Recovery
Thrombolysis
Ischemic stroke
Predictors
Prognosis

ABSTRACT

Background and purpose: Dramatic recovery (DR) after thrombolysis is dependent of vessel recanalization and is predictive of favorable clinical outcome. Successful recanalization is not equivalent to DR. Our objective was to assess its frequency and evaluate clinical and biochemical predictors and their prognosis.
Methods: We analyzed prospectively registered data from January 2007 to September 2012. All patients with anterior circulation stroke and NIHSS ≥ 10 were included. Improvement of ≥10 or a score ≤3 24 h after thrombolysis was defined as DR.
Results: In the 230 patients included, DR frequency was 23% (53 patients). DR group had lower admission NIHSS (14 vs 17, $p = 0.024$), less total anterior circulation infarcts ($p = 0.009$), more partial anterior circulation infarcts ($p = 0.003$) and lower blood glucose on admission (118 vs 128 mg/dL, $p = 0.013$). All patients with DR had an Alberta Stroke Program Early CT Score (ASPECTS) ≥7, vs 89.3% without DR ($p = 0.013$). Arterial recanalization, defined as hyperdense middle cerebral artery sign disappearance on control CT, was more frequent in the DR group (68.4% vs 14.1%, $p < 0.001$). Intracranial hemorrhage on 24 h-control CT scan was less frequent in the DR group ($p < 0.001$). Multinomial logistic regression analysis showed that ASPECTS score was an independent predictor of DR (OR = 2.35, 95%CI = 1.32–4.16, $p = 0.003$) and CT evidence of recanalization was independently associated with DR (OR = 11.60, 95%CI, 3.02–44.53, $p < 0.001$).
Conclusion: DR is a frequent occurrence. ASPECTS score is an independent predictor of DR, which is also independently associated with CT evidence of middle cerebral artery recanalization.

1. Introduction

Dramatic recovery (DR), the early and stable clinical improvement after recanalization therapies in the setting of acute ischemic stroke [1], has been reported to occur in 20–40% of patients with middle cerebral artery (MCA) stroke, submitted to intravenous (IV) thrombolysis [1–3]. Frequency varies depending on the definition of DR, hindering comparisons. Different time windows have been defined for improvement to be considered DR, from 1 h [1] to 24 h [2,4] or even 7 days after IV thrombolysis [2]. Additionally, the magnitude of improvement considered as DR varies, from an improvement of ≥40% on NIHSS [5] to the more consensual improvement of ≥10 points on NIHSS or NIHSS < 3 after treatment [1,2,4]. Most of the studies on DR are focused on MCA strokes, and studies analyzing DR after thrombolysis in all anterior circulation strokes, including anterior cerebral and internal carotid (ICA) arteries, are lacking.

Although recanalization is the major goal of acute ischemic stroke treatment, it is not a synonym of DR, since only 35.3% of patients who achieve recanalization have DR [4]. Previous studies have shown higher rates of DR with earlier and more complete recanalization [1,2,4,6], but other factors may have a role. Recognizing these predictive factors could help clinicians to anticipate early response after IV thrombolysis, and also prognosis on longer follow-up, since early improvement benefits are sustained [7], with 67.6% of patients being asymptomatic or minimally symptomatic at 3 months (compared to only 9.0% of patients without DR) [1].

2. Objectives

Our objectives were to assess the frequency of DR in IV thrombolysis-treated patients with clinically severe anterior circulation stroke, to evaluate clinical, imaging and biochemical

* Corresponding author at: Neurology Department, Hospital de Braga, Sete Fontes, S. Victor, 4710-243 Braga, Portugal. Tel.: +351 916211539; fax: +351 253 027 999.
E-mail address: joaomrocha@gmail.com (J. Rocha).

http://dx.doi.org/10.1016/j.clineuro.2014.07.010
0303-8467/

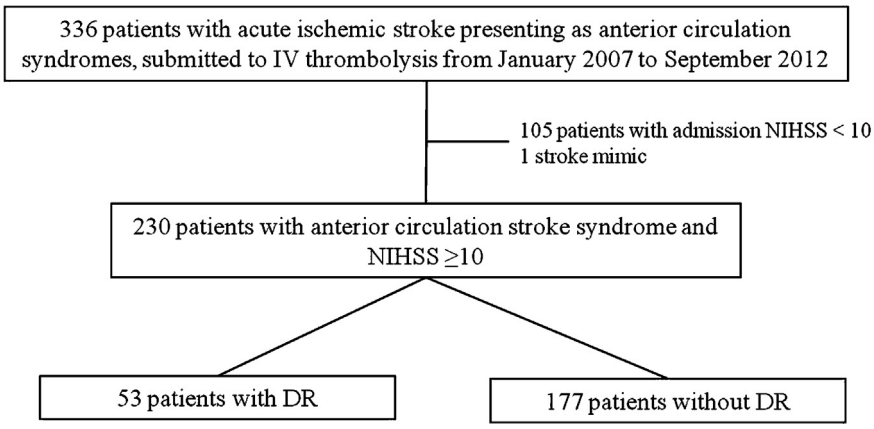

Fig. 1. Sample definition.

predictors of DR and to evaluate the clinical outcome of patients with and without DR.

3. Methods

Patients with anterior circulation stroke syndromes based on Oxfordshire Community Stroke Project (OCSP) [8] were identified from a prospective clinical registry of IV thrombolysis performed in acute ischemic stroke patients, from January 2007 to September 2012 in the supra-regional Stroke Unit of Hospital de Braga. Thrombolysis was performed using the standard rtPA protocol (0.9 mg/kg), according to the National Institute of Neurological Disorders and Stroke guidelines. Time window for IV thrombolysis was 3 h until late 2008, and 4.5 h since then. Age older than 80 years was a relative contraindication for thrombolysis in our center until May 2012. Alberta Stroke Program Early CT Score (ASPECTS) quantifies early ischemic CT changes in hyperacute MCA stroke patients [9], and lower scores are associated with poor functional outcomes and symptomatic hemorrhage in patients submitted to IV thrombolysis [10]. ASPECTS <7 was considered a relative contraindication for thrombolysis.

DR was defined as an improvement of ≥10 points on the National Institute of Health Stroke Scale (NIHSS) or an improvement to ≤3 points on NIHSS at 24 h evaluation after thrombolysis. Even though early clinical improvement consistent with DR has been initially described to occur until 1 h after rtPA, benefit is maintained at 24 h [1], leading us to adopt the more consensual 24 h time window for DR definition for the purpose of comparison with previous studies.

All patients with anterior circulation stroke and pre-treatment NIHSS ≥ 10 were included. This cutoff was chosen with the purpose of increasing the frequency of large-vessel occlusions and increasing sensitivity of DR diagnosis according to our definition.

We collected data from the prospective registry concerning demographic characteristics; vascular risk factors; previous antiplatelet treatment; stroke clinical classification using OCSP; NIHSS score at admission and 24 h after treatment; symptom-needle time; imaging findings and characteristics (pre-treatment ASPECTS and hyperdense middle cerebral artery (HMCA) sign presence; 24 h control CT presence of any intracranial hemorrhage and disappearance of HMCA). All admission and 24 h CT scans were independently reviewed by two neuroradiologists who were aware of the patients' clinical deficits. They classified ASPECTS on admission and evaluated the presence of HMCA (at admission and 24 h after thrombolysis) and the presence of any intracranial hemorrhage 24 h after thrombolysis. Cases in which there was a disagreement on imaging analysis were reviewed simultaneously by the two neuroradiologists and a consensus was achieved.

We assumed the presence of HMCA as a sign of vessel occlusion and its disappearance as an indirect sign of recanalization. The modified Rankin Scale (mRS) at 3 months follow-up was assessed by direct observation in the outpatient clinic or by a structured telephone interview. Good clinical outcome was defined as a 3-month mRS of 0–2. Patients who had missing follow-up information were only excluded from the 3 month analysis (six patients on the DR group and 34 patients on the group without DR).

Distribution of continuous variables was analyzed using the Kolmogorov–Smirnov test. Interobserver agreement for HMCA sign on admission and 24 h CT and ASPECTS on admission CT was calculated using Cohen's kappa. Independent sample *T*-, Mann–Whitney or Chi-square tests were used to determine group differences in demographic and clinical variables, depending on the comparison and test assumptions. We developed a binary logistic regression model, using categorical and continuous variables found to be significant in group difference analysis. The standard non-corrected significance level of $p < 0.05$ was used. Statistical analysis was performed using IBM SPSS Statistics version 20.0.

4. Results

During the inclusion period 336 patients with anterior circulation stroke syndromes were consecutively submitted to IV thrombolysis, of which 105 were excluded for having NIHSS < 10 and one patient who had a stroke mimic. Final study population consisted of 230 patients, 53 with DR and 177 without DR (Fig. 1). The baseline characteristics of patients with and without DR are described in Table 1, and no differences were found on demographic characteristics, vascular risk factors, previous anti-platelet treatment or time to thrombolytic treatment.

Patients with DR had a lower median admission NIHSS, lower frequency of total anterior circulation infarct (TACI) and higher frequency of partial anterior circulation infarct (PACI) (Table 2). Frequencies of documented cardioembolic etiology were not different between groups. Although there was only a non-significant trend for higher frequency of diabetes in the group without DR (Table 1), patients with DR had lower median blood glucose on admission (Table 2). Mean arterial blood pressure at admission was similar in both groups.

Interobserver agreement was considered good for both HMCA sign on admission CT ($\kappa = 0.704$) and HMCA sign on 24 h CT ($\kappa = 0.760$), and moderate for ASPECTS on admission CT ($\kappa = 0.602$).

Concerning imaging characteristics we found that ASPECTS ≥ 7 was more frequent in patients with DR and, in fact, only patients with ASPECTS ≥ 7 had DR. At baseline, HMCA presence on admission CT scan was similar in the two groups but its disappearance was significantly higher in DR patients (Fig. 2). Also, intracranial

Table 1
Pre-thrombolysis patients characteristics.

	Dramatic recovery		*p* value
	Yes (*n* = 53) 23.0%	No (*n* = 177) 77.0%	
Men (%)	50.9	53.7	0.727
Age, y, median ± SD	72 ± 11.0	72 ± 10.6	0.942
Vascular risk factors (%)			
Diabetes mellitus	11.3	22.6	0.072
Hypertension	64.2	66.7	0.734
Dyslipidemia	37.7	41.8	0.597
Current smoker	9.4	7.9	0.724
Previous anti-platelet treatment (%)	41.5	29.9	0.115
Symptoms-needle time (mean, min)	151.1	154.0	0.750
Symptoms-needle time			
Symptoms-needle time > 90 min (%, *n*)	86.8% (46)	94.4% (167)	0.065
Symptoms-needle time < 90 min (%, *n*)	13.2% (7)	5.6% (10)	

Table 2
Clinical and imaging characteristics.

	Dramatic recovery		*p* value
	Yes (*n* = 53) 23.0%	No (*n* = 177) 77.0%	
Clinical evaluation			
Admission NIHSS (median, IQR)	14 (11–17)	17 (13–19.5)	0.024
Admission blood glucose (median, IQR, mg/dL)	118 (105–137.5)	128 (111.8–160)	0.013
Mean arterial pressure on admission (mean, mm Hg)	105.1	103.9	0.602
Cardioembolic stroke (%)	45.2	47.2	0.800
Stroke classification (%)			
OCSP			0.014
TACI	67.9	84.2	
PACI	30.2	13.0	
LACI	1.9	2.8	
Image evaluation			
ASPECTS ≥ 7 (%)	100.0	89.3	0.013
Hyperdense MCA on admission CT (%, n)	35.8 (19)	47.5 (84)	0.136
MCA revascularization on CT 24 h after thrombolysis (%[a], *n*)	68.4 (13)	14.1 (12)	<0.001
Any intracranial hemorrhagic complication 24 h after thrombolysis (%)	5.7 (3)	31.1 (55)	<0.001

IQR, interquartile range; MCA, middle cerebral artery.
[a] % refers to the number of patients with HMCA on admission whose sign disappeared on control CT.

hemorrhagic complications were over five times more frequent in patients without DR (Table 2).

Binary logistic regression model using admission NIHSS, admission blood glucose, ASPECTS (as a continuous variable), OCSP as PACI or non-PACI and vessel recanalization, revealed that only ASPECTS (odds ratio OR = 2.35, 95%CI = 1.32–4.16, $p = 0.003$) and the indirect evidence of vessel recanalization (OR = 11.6, 95%CI = 3.02–44.53, $p < 0.001$) were independently associated with DR.

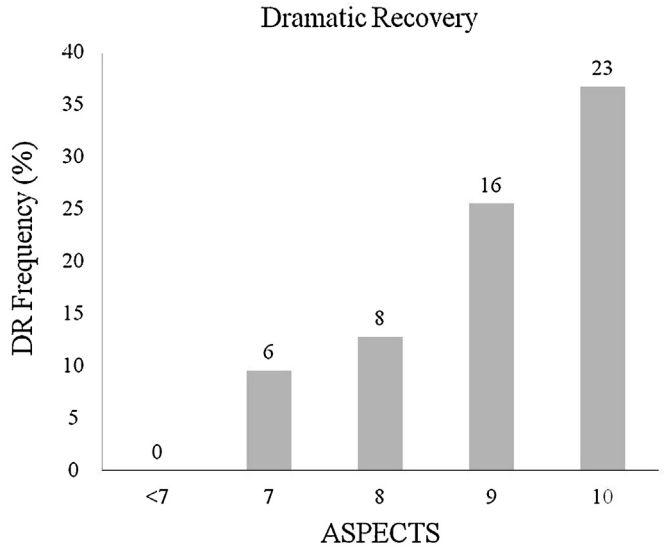

Fig. 2. Frequency of dramatic recovery according to ASPECTS on admission CT (*numbers on graph are total number of patients in the ASPECTS category).

On 3 months follow-up, good functional outcome (mRS 0–2) was achieved in 89.4% of patients with DR and 31.5% of patients without DR ($p < 0.001$) and no patient died in the DR group vs 28 patients (19.6%) without DR ($p = 0.001$). Patients' distribution of mRS scores at 3 months is described in Fig. 3.

5. Discussion

DR after IV thrombolysis for anterior circulation stroke occurred in 23.0%, reinforcing the notion that DR is not infrequent. Previous studies found DR in 20–40% of patients with MCA strokes submitted to IV thrombolysis [1–3], and we hypothesize the DR frequency we found is in the lower end of this range because we also included patients with ICA occlusions.

Concerning clinical characteristics, we found that DR patients had less severe strokes with median NIHSS score of 14 vs 17 in patients without DR (Table 2). Classically, NIHSS has been described as an independent predictor of clinical improvement after recanalization therapies [11–13] and a long term clinical outcome predictor [14]. In previous studies, NIHSS values have consistently been demonstrated to be lower in DR patients, [2,4,5]

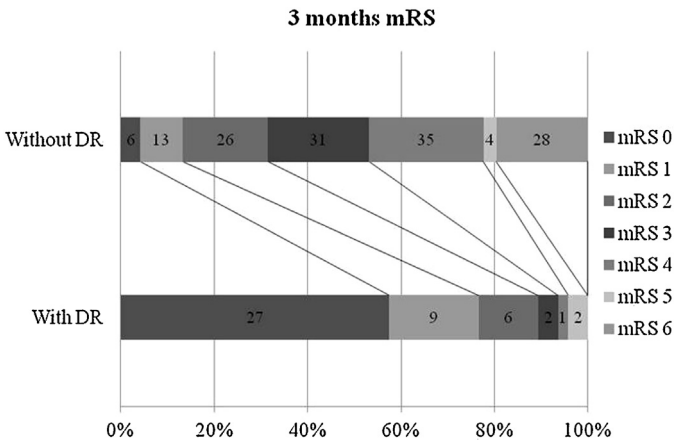

Fig. 3. Distribution of modified Rankin scale (mRS) at 3 months follow-up.

and clinical severity in our study population was similar to these studies.

Less severe clinical deficits in DR patients were accompanied by a higher ASPECTS score (assessing the early ischemic changes on pre-treatment CT studies), consistent with a lower infarct volume at admission, which is also a known predictor of good clinical outcome after thrombolysis [9,15]. In accordance with this evidence, in our study, only patients with ASPECTS ≥ 7 presented DR. In non-DR patients, the frequency of ASPECTS ≥ 7 was significantly lower (89.3%, $p = 0.013$). However, interpretation of these results have to be cautious, given that ASPECTS < 7 was a relative exclusion criteria for thrombolysis and few patients with lower scores were included. Lower post-treatment infarct volume in diffusion weighted imaging on magnetic resonance imaging (DWI-MR) was associated with DR [15], but only recently, the cutoff of ASPECTS ≥ 7 has been identified as an independent predictor of DR using DWI-MR sequences [5]. To the best of our knowledge, this is the first study to identify CT based ASPECTS as an independent predictor of DR, and although few patients with a score lower than 7 were included, our results have sufficient statistical power to draw this conclusion. Our data suggests that not only the CT-ASPECTS score is an independent predictor of DR but also that higher ASPECTS scores are associated with increased frequency of DR occurrence (Fig. 2). In logistic regression analysis, each increment of one point on ASPECTS was associated with a 2.35-fold increased probability of DR. In sum, clinical improvement consistent with DR occurred in patients with less severe strokes, which is supported by the fact that these patients had a lower NIHSS score on admission, higher ASPECTS and, as expected, higher frequency of PACI syndromes.

Furthermore in our imaging analysis, we found no differences in baseline prevalence of HMCA, but disappearance of HMCA in control CT scan was significantly more frequent in patients with DR, and was independently associated with DR. The HMCA sign is found on non-contrast CT scan, presenting as a spontaneous middle cerebral artery density increment, and although its sensitivity is not high, it is very specific for vessel occlusion [16]. Cerebral angiography observational studies confirmed that HMCA disappearance after thrombolysis reflects vessel recanalization [17]. Patients with more severe strokes (NIHSS ≥ 10) have a higher probability of presenting a large vessel occlusion, and we think this population was suitable to analyze the relation of HMCA with DR. Although CT was performed using the same equipment, and imaging analysis was performed by the same observers, minimizing possible errors, we must reinforce that this sign has a low sensitivity and should be addressed with caution. Nevertheless, as previously pointed out, HCMA is a frequently observed sign in every-day practice which has been demonstrated to correlate with vessel occlusion by studies using angiographic methods [16,17].

Cardioembolic strokes are more frequently associated with large vessel occlusions and have been described to be more responsive to IV thrombolysis [18]. In our sample TOAST etiological classification was not predictive of DR (data not shown) and we think it is not a confounder in the analysis.

Recanalization was one of the first described independent predictors of DR, confirmed by transcranial Doppler (TCD) [1,3], angiography and MR-angiography studies [2,4], but not every patient with successful vessel recanalization after stroke achieves DR or even a good clinical outcome. Early TCD studies showed a trend for DR patients to be treated earlier [1]. This trend was later confirmed by angiography [2,4] and vessel recanalization proved to be a time-dependent predictor of good clinical outcome [6,12,19,20].

In our patients, symptom needle time was not significantly different between the two groups, even when considering a 90 min cut-off point sub-analysis. We must emphasize that only 17 patients were treated in this time window, and that demonstration of symptom-needle time as a predictor for DR could be limited due to lack of statistical power.

We must also address that although the frequency of diabetic patients was not different in both groups, there was a non-significant tendency for patients without DR to have a higher frequency of diabetes (Table 1), and pre-treatment blood glucose was lower in DR patients. Baseline hyperglycemia is found more commonly in patients with preexisting diabetes but is also present in a significant proportion of non-diabetic stroke patients [21]. In stroke patients treated with IV-rtPA, admission hyperglycemia is independently associated with increased risk of death, symptomatic intracranial hemorrhage, poor functional status at 90 days [22], and its association with lower DR frequency as been suggested. Higher admission blood glucose and lower recanalization rates have also been described in IV thrombolysis [13].

Hemorrhagic complications were infrequent in DR patients, with an approximately 5.5-fold increased frequency of any kind of hemorrhage in patients without DR (Table 2). There was no difference in type of hemorrhage according to SITS-MOST definition [23], and the majority corresponded to type II hemorrhagic infarcts (data not shown). Intracranial hemorrhage of any type and DR have also been found to be independently associated with DR patients having a 55% lower risk of bleeding after revascularization therapies [1]. Although our results are similar, comparison with the previous study is difficult since it included not only IV thrombolysis but also intra-arterial thrombolysis and thrombectomy procedures.

Our data confirm that DR patients have a significant better outcome at 3 months follow-up, with almost 90% of patients being asymptomatic or minimally symptomatic (mRS 0–2) (Fig. 3). Mortality was also significantly lower. None of the DR patients died during follow-up and almost 20% died in the non-DR group. These results confirm the notion that DR benefits are stable and maintained at long term [1,4,7].

These results must be regarded with caution: by excluding patients with less severe strokes, we are precluded to extrapolate data for patients with less severe strokes, which may include patients with small infarct from small vessel disease, distal vessel occlusions and large vessel occlusion with good collateral circulation. Good collateral circulation was also described as a predictor of recanalization and good prognosis [9,24].

Our study was not able to determine other pre-treatment independent predictors of DR in addition to ASPECTS. Although not a true predictor, indirect sign of vessel recanalization was independently associated with DR, and to the best of our knowledge this has been the first study to associate DR with HMCA sign and also to infarct volume using CT based ASPECTS. Additionally, we included

all anterior circulation stroke syndromes submitted to IV thrombolysis only, and not only patients with documented large vessel occlusion or submitted to combination therapies, which characterized the largest DR studies in previous years. Since CT scan and IV thrombolysis are the most available resources in worldwide Stroke Units, we think that this study is an important contribution to centers where MRI, angiography and invasive recanalization techniques are not readily available in emergency settings. Inclusion of all anterior circulation stroke syndromes limits a direct comparison with previous studies, which included only MCA strokes, but represents more closely the daily clinical practice in the emergency department and stroke units. In the future, a consensual definition of DR must be achieved for the purpose of a more precise assessment of this phenomenon and its predictive factors and comparison between recanalization strategies.

6. Conclusion

Dramatic recovery is a frequent occurrence. ASPECTS is an independent predictor of DR in patients with anterior circulation stroke submitted to IV thrombolysis, and DR is independently associated with indirect CT evidence of vessel recanalization. Patients with lower clinical severity and lower blood glucose on admission also seem to benefit the most with IV thrombolysis. DR patients have a better clinical prognosis at 3 months than patients without DR.

Source of funding

To conduct this study the authors have not received any financial support.

References

[1] Felberg RA, Okon NJ, El-Mitwalli A, Burgin WS, Grotta JC, Alexandrov AV. Early dramatic recovery during intravenous tissue plasminogen activator infusion: clinical pattern and outcome in acute middle cerebral artery stroke. Stroke 2002;33:1301–7.
[2] Khatri P, Abruzzo T, Yeatts SD, Nichols C, Broderick JP, Tomsick TA. Good clinical outcome after ischemic stroke with successful revascularization is time-dependent. Neurology 2009;73:1066.
[3] Mazighi M, Meseguer H, Labreuche J, Serfaty JM, Laissy JP, Lavallée PC, et al. Dramatic recovery in acute ischemic stroke is associated with arterial recanalization grade and speed. Stroke 2012;43:2998–3002.
[4] Labiche LA, Al-Senani F, Wojner AW, Grotta JC, Malkoff M, Alexandrov AV. Is the benefit of early recanalization sustained at 3 months: a prospective cohort study. Stroke 2003;34:695–8.
[5] Aoki J, Kimura K, Shibazaki K, Sakamoto Y. DWI-ASPECTS as a predictor of dramatic recovery after intravenous recombinant tissue plasminogen activator administration in patients with middle cerebral artery occlusion. Stroke 2013;44:534–7.
[6] Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. Lancet 1991;337:1521–6.
[7] Bang OY, Liebeskind DS, Saver JL, Kim GM, Chung CS, Lee KH. Stunned brain syndrome: serial diffusion perfusion MRI of delayed recovery following revascularization for acute ischaemic stroke. J Neurol Neurosurg Psychiatry 2011;82:27e32.
[8] Alexandrov AV, Demchuk AM, Felberg RA, Christou I, Barber PA, Burgin WS, et al. High rate of complete recanalization and dramatic clinical recovery during tPA infusion when continuously monitored with 2-MHz transcranial Doppler monitoring. Stroke 2000;31:610–4.
[9] Pexman JHW, Barber PA, Hill MD, Sevick RJ, Demchuk AM, Hudon ME, et al. Use of the Alberta Stroke Program Early CT Score (ASPECTS) for assessing CT scans in patients with acute stroke. Am J Neuroradiol 2001;22:1534–42.
[10] Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. Lancet 2000;355:1670–4.
[11] Galimanis A, Jung S, Mono ML, Fischer U, Findling O, Weck A, et al. Endovascular therapy of 623 patients with anterior circulation stroke. Stroke 2012;43:1052–7.
[12] Nogueira RG, Liebeskind DS, Sung G, Duckwiler G, Smith WS. Predictors of good clinical outcomes, mortality, and successful revascularization in patients with acute ischemic stroke undergoing thrombectomy: pooled analysis of the mechanical embolus removal in cerebral ischemia (MERCI) and multi MERCI trials. Stroke 2009;40:3777–83.
[13] Saqqur M, Uchino K, Demchuk AM, Molina CA, Garami Z, Calleja S, et al. Site of arterial occlusion identified by transcranial Doppler predicts the response to intravenous thrombolysis for stroke. Stroke 2007;38:948–54.
[14] Fischer U, Mono ML, Zwahlen M, Nedeltchev K, Arnold M, Galimanis A, et al. Impact of thrombolysis on stroke outcome at 12 months in a population: the Bern stroke project. Stroke 2012;43:1039–45.
[15] Sanak D, Herzig R, Zapletalova J, Horak D, Kral M, Skoloudik D, et al. Predictors of good clinical outcome in acute stroke patients treated with intravenous thrombolysis. Acta Neurol Scand 2011;123:339–44.
[16] Muir KW, Buchan A, Von Kummer R, Rother J, Baron JC. Imaging of acute stroke. Lancet Neurol 2006;5:755–68.
[17] Leys D, Pruvo JP, Godefroy O, Rondepierre P, Leclerc X. Prevalence and significance of hyperdense middle cerebral artery in acute stroke. Stroke 1992;23:317–24.
[18] Rha JH, Saver JL. The impact of recanalization on ischemic stroke outcome: a meta-analysis. Stroke 2007;38:967–73.
[19] Molina CA, Montaner J, Arenillas JF, Ribo M, Rubiera M, Alvarez-Sabín J. Differential pattern of tissue plasminogen activator-induced proximal middle cerebral artery recanalization among stroke subtypes. Stroke 2004;35:486–90.
[20] Mazighi M, Serfaty JM, Labreuche J, Laissy JP, Meseguer E, Lavallée PC, et al. Comparison of intravenous alteplase with a combined intravenous–endovascular approach in patients with stroke and confirmed arterial occlusion (RECANALISE study): a prospective cohort study. Lancet Neurol 2009;8:802–9.
[21] Poppe AY, Majumdar SR, Jeerakathil T, Ghali W, Buchan AM, Hill MD. Admission hyperglycemia predicts a worse outcome in stroke patients treated with intravenous thrombolysis. Diabetes Care 2009;32:617–22.
[22] Wahlgren N, Ahmed N, Dávalos A, Ford GA, Grond M, Hacke W, et al. Thrombolysis with alteplase for acute ischaemic stroke in the safe implementation of thrombolysis in stroke-monitoring study (SITS-MOST): an observational study. Lancet 2007;369(9558):275–82.
[23] Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. Stroke 2001;32:2426–32.
[24] Lima FO, Furie KL, Silva GS, Lev MH, Camargo ECS, Singhal AB, et al. The pattern of leptomeningeal collaterals on CT angiography is a strong predictor of long-term functional outcome in stroke patients with large vessel intracranial occlusion. Stroke 2010;41:2316–22.