RISK OF INTRACRANIAL HEMORRHAGE AND CLINICAL OUTCOME AFTER INTRAVENOUS THROMBOLYSIS IN POSTERIOR CIRCULATION STROKE: RESULTS FROM THE SITS-EAST REGISTRY

Roman Herzig [1], Jan Waishaupt [1], Silvie Bělašková [2], Eva Vítková [1], Kateřina Blejchařová [3], Petr Geier [3], Aleš Tomek [4], Michal Bar [5], Daniel Václavík [6], Robert Mikulík [7], Martin Vališ [1]

[1] Department of Neurology, Comprehensive Stroke Center, Charles University Faculty of Medicine and University Hospital, Hradec Králové; [2] St. Anne's University Hospital and International Clinical Research Center, Brno; [3] Department of Neurology, Charles University Faculty of Medicine, Hradec Králové; [4] Department of Neurology, Comprehensive Stroke Center, Charles University 2nd Faculty of Medicine and Motol University Hospital, Prague; [5] Department of Neurology, Comprehensive Stroke Center, University of Ostrava Faculty of Medicine and University Hospital, Ostrava; [6] Stroke Center, Department of Neurology, Vítkovice Hospital, Ostrava; [7] Department of Neurology, Comprehensive Stroke Center, St. Anne's University Hospital and International Clinical Research Center, Brno, Czech Republic

INTRODUCTION

Intravenous thrombolysis (IVT) represents a standard specific reperfusion therapy in acute ischemic stroke in both anterior and posterior cerebral circulation. Randomized trials showed that patients might benefit from IVT up to 4.5 h after symptoms onset [1]. Posterior circulation stroke (PCS) represents 12–19 % of all IVT-treated strokes and it is even more frequent in the non-IVT population (20–26 %) [2–7]. However, no randomized controlled trial or phase IV study is available for the evaluation of the safety and efficacy of IVT in PCS alone [6].

Previous studies demonstrated significantly lower risk of symptomatic intracranial hemorrhage (SICH) in PCS versus anterior circulation strokes (ACS) in patients treated with IVT – 0 vs. 5 % (P = 0.026) in the study including 883 patients (95 with PCS) [3], 5.1 vs. 17.2 % (P = 0.002) in the study including 882 Caucasian patients (100 with PCS) [6] and 3.2 vs 7.7 % (P = 0.03) in another study including 953 Chinese patients (124 with PCS) [7].

However, data regarding clinical outcomes are controversial [3,7–10]. For example, excellent 90-day clinical outcome, defined as 0–1 point on the modified Rankin scale (mRS), was significantly more frequent in PCS versus ACS patients in some of the mentioned studies – 66 vs. 47 % (P < 0.001) [3] and 55.7 vs. 41.6 % (P = 0.001) [7]. Similar findings were observed in the case of a good 90-day clinical outcome, defined as 0–2 points on the mRS, which was also found significantly more frequently in PCS versus ACS patients – 63.9 vs 53.0 % (P = 0.001) [7]. On the other hand, no significant differences were found in the clinical outcome of these particular patient groups in another study [8] and, also 90-day mortality did not significantly differ between PCS versus ACS patients [3,7,8] – 9 vs. 13 % (P = 0.243) [3] and 15.6 vs. 10.1 % (P = 0.07) [7].

The aim was to assess the SICH risk and 90-day clinical outcome in PCS versus ACS patients treated with IVT.

PATIENTS AND METHODS

Prospectively collected data in the Safe Implementation of Treatments in Stroke – Eastern Europe (SITS-EAST) registry between 2010 and 2015 were analyzed. SITS-EAST is an international study of implementation of evidence-based stroke care in Central and Eastern Europe using the SITS – International Stroke Thrombolysis Registry (SITS-ISTR) platform for data collection. The SITS-ISTR is an ongoing, prospective, academic-driven, multicenter international registry for centers using IVT for the treatment of acute ischemic stroke in clinical practice. The registry has been approved by local Ethics Committees of each participating country.

Criteria of the National Institute of Neurological Disorders and Stroke (NINDS) were used for SICH definition: any ICH on any posttreatment imaging and any deterioration in National Institutes of Health Stroke Scale (NIHSS) or death within 7 days. 90-day outcome was assessed using mRS with good clinical outcome defined as 0–2 points.

For all calculations, SAS software version 9.2 and 9.3 were used. For generalized linear mixed models estimates, PROC GLIMMIX was applied with Newton-Raphson optimization method. The P-value for fixed effect testing were calculated from t-distribution with df = 2718 degrees of freedom.

RESULTS

The set consisted of 2738 patients – 363 (13.3 %) with PCS and 2375 (86.7 %) with ACS. As presented in *Figure 1,* SICH occurred insignificantly less frequently in PCS patients and, PCS patients reached significantly more frequently good 90-day clinical outcome. Independent predictors of the SICH occurrence and of a good 90-day clinical outcome are shown in *Table 1.*

Table 1. Independent predictors of the occurrence of symptomatic intracranial hemorrhage and of a good 90-day clinical outcome (mRS 0-2)

Observed factor	OR	95% CI	P value
Predictors of the SICH occurrence			
Age	1.025	1.008 – 1.043	0.004
Baseline diastolic blood pressure	1.016	1.002 – 1.030	0.02
Intravenous antihypertensive therapy before/during IVT	1.632	1.101 – 2.421	0.01
Predictors of a good 90-day clinical outcome			
Age	0.953	0.943 – 0.964	< 0.0001
Pre-stroke mRS value	0.611	0.526 – 0.709	< 0.0001
Baseline glycemia	0.927	0.889 – 0.968	0.0005
Intravenous antihypertensive therapy before/during IVT	0.526	0.401 – 0.690	< 0.0001
SICH occurrence	0.096	0.056 – 0.166	< 0.0001
Posterior circulation stroke	1.413	1.037 – 1.926	0.03

CI, confidence interval; IVT, intravenous thrombolysis; mRS, modified Rankin scale; OR, odds ratio; SICH, symptomatic intracranial hemorrhage

CONCLUSION

In patients treated with IVT, data from SITS-EAST registry showed that localization of stroke in the posterior circulation was associated with better 90-day clinical outcome than in the anterior circulation. Nevertheless, the SICH risk was only statistically insignificantly lower in PCS versus ACS patients.

Age, baseline diastolic blood pressure and the use of intravenous antihypertensive therapy before/during IVT were identified as independent predictors of the SICH occurrence. Age, pre-stroke mRS value, baseline glycemia, the use of intravenous antihypertensive therapy before/during IVT and SICH occurrence were identified as independent negative predictors and, localization of stroke in the posterior cerebral circulation as an independent positive predictor of the achievement of a good 90-day clinical outcome.

REFERENCES

[1] Lees KR, et al. Lancet 2010; 375: 1695–703.
[2] Bogousslavsky J, et al. Stroke 1988; 19: 1083–92.
[3] Sarikaya H, et al. Stroke 2011; 42: 2498–502.
[4] Santalucia P. Front Neurol Neurosci 2012; 30: 176–80.
[5] Sung SF, et al. J Neurol Sci 2013; 335: 96–100.
[6] Dorňák T, et al. Int J Stroke 2015; 10: 1224–8.
[7] Tong XU, et al. Medicine 2016; 95: e3848.
[8] Forster A, et al. Cerebrovasc Dis 2011; 32: 349–53.
[9] De Marchis GM, et al. J Neurol Neurosurg Psychiatry 2011; 82: 33–7.
[10] Sarraj A, et al. Int J Stroke 2015;10: 672–8.

FIGURE 1. SICH OCCURRENCE AND GOOD 90-DAY CLINICAL OUTCOME.

SICH OCCURRENCE: PCS 0.55%, ACS 5.51%, P > 0.05. GOOD 90-DAY CLINICAL OUTCOME (mRS 0-2): PCS 68.60%, ACS 58.90%, P = 0.02.