

# Haemorrhagic risk after Intravenous Thrombolysis for ischemic stroke in patients with Cerebral Microbleeds and White Matter Disease

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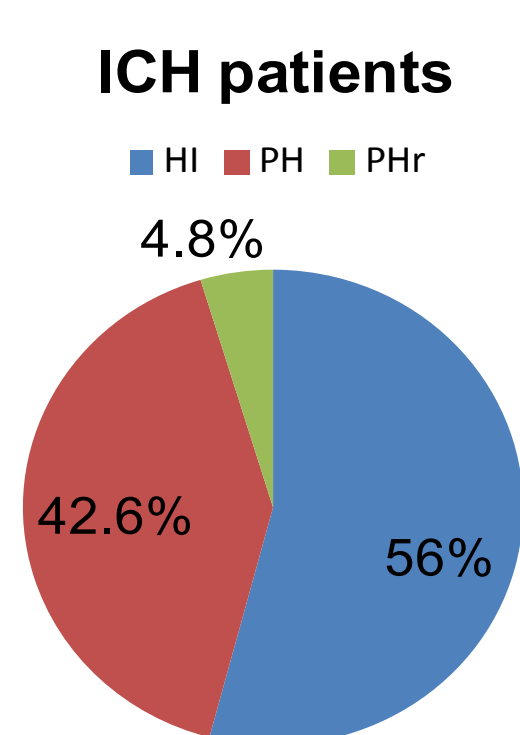
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**Objective.** Aim of this study is to evaluate the correlation of cerebral microbleeds (CMBs) and white matter disease (WMD) with intracerebral hemorrhage (ICH) after intravenous thrombolysis (IVT) for ischemic stroke. We also evaluated, if CMB and WMD burden and localization correlate with severity of ICH or the presence of symptomatic ICH (sICH).

**Material and methods.** We enrolled acute ischemic stroke patients treated with IVT. Number and location of CMBs as well as severity of WMD, were rated. We divided patients in ICH subgroups: [hemorrhagic infarction (HI), parenchymal hemorrhage (PH), remote parenchymal hemorrhage (PHr)]. Multivariable regression analysis was used to determine the impact of CMB and WMD on ICH subgroups and outcome.

**Results.** 291 patients (183 M, 108 F) underwent brain MR before or 24 h after rTPA infusion and were included in the study. A total of 111 CMBs were detected in 54 patients (18.5%). CMBs were lobar in 11.7% of patients and deep or infratentorial in 8.9% of them.



The number of CMBs ranged from 1 to 18 in individual patients.

**ICH** occurred in 82 (28.2%) patients, among which 22 (26.8%) had CMBs.

## Multivariate regression analysis

### Predictors of HI:

- diagnosis of diabetes ( $P=0.018$ ; odds ratio [OR], 2.832; 95% confidence interval [CI], 1.194–6.719)
- NIHSS > 7 ( $P=0.028$ ; OR, 2.256; 95% CI, 1.092–4.662)

### Predictors of PH:

- NIHSS > 7 ( $P=0.002$ ; OR, 5.227; 95% CI, 1.821–15.004)
- deep and infratentorial CMBs ( $P=0.007$ ; OR, 4.575; 95% CI, 1.502–13.932).

**WMD** is not significant correlated with HI and PH.

**Conclusion:** In our study ICH is not correlated with CMBs burden nor with WMD. Presence of deep CMBs, likely of hypertensive pathogenesis rather than related to cerebral amyloid angiopathy, seems to increase the risk of PH. CMBs cannot be considered a contraindication for thrombolytic therapy. Anyway, additional data through prospective multicentric studies are needed to evaluate the safety of tPA in patients carrying numerous microbleeds.

	All (n= 291)	No ICH (n=209)	HI (n=46)	PH (n= 35)	PHr (n=4)
<b>Age, y (mean±SD)</b>	67.7±13.9	67.2±14.27	68.1±13.7	70.6±11.4	61.2±17
<b>Vascular risk factors</b>					
Hypertension (%)	62.5	63.6	56.5	65.7	50
Diabetes mellitus (%)	17.2	15.7	<b>26.1*</b>	14.3	0
Atrial fibrillation (%)	14.1	11	21.7	22.9	25
Current smoking (%)	23	23.9	19.6	21.9	25
Previous smoking (%)	15	16.2	15.9	15.2	0
Hypercholesterolemia (%)	31.3	33.9	28.3	20	25
Previous stroke within 3 months (%)	0.3	0.3	0	0	0
Previous stroke earlier than 3 months (%)	10.7	10.5	8.7	14.3	0
Previous diagnosis of TIA / amaurosis (%)	2.1	0	2.2	<b>11.4**</b>	<b>25**</b>
Congestive heart failure (%)	2.4	1.4	<b>6.5*</b>	2.9	0
<b>Medication history</b>					
Prior antiplatelet therapy (%)	23.7	23.9	30.4	14.2	0
Prior oral anticoagulation (%)	3.4	2.3	4.3	8.5	0
Baseline NIHSS score (mean±SD)	9.3±6.5	8±6.4	<b>11.3±6.6*</b>	<b>14.8±6.4**</b>	10±5.2
Baseline systolic blood pressure (mm/hg) (mean±SD)	145.3±23.3	146.2±23.6	143.8±23.6	141.5±21.6	125±22.9
Baseline glucose level (mg/dl) (mean±SD)	86±45.4	134.4±45.7	139.2±35	140.7±47.3	123.6±17.7

	All (n=291)	No ICH n=209	HI (n=46)	PH (n= 35)	PHr (n=4)
<b>Fazekas WMD rating scale</b>					
0 (%)	39.9	37.3	50	42.9	50
1 (%)	40.2	43.5	32.6	28.6	25
2 (%)	16.5	17.2	8.7	22.9	25
3 (%)	3.4	1.9	<b>8.7*</b>	5.7	0
<b>Stroke territory</b>					
Anterior circulation (%)	82	80.8	80.4	91.4	75
Posterior circulation (%)	15.5	17.2	15.2	5.7	0
Both anterior and posterior (%)	2.4	1.9	4.3	0	25
<b>Stroke localization</b>					
Cortical (%)	20.3	27.7	4.3	0	0
Subcortical (%)	35.1	28.5	21.7	22.9	0
Cortico-subcortical (%)	44.7	32.5	<b>73.9*</b>	<b>77.1**</b>	100
<b>Cortical Siderosis (%)</b>	1.3	0	<b>6.5**</b>	0	0
<b>CMB burden (n.)</b>	111	56	14	<b>41**</b>	<b>23**</b>
<b>CMB localization</b>					
Lobar (%)	11.7	10.5	8.7	<b>22.9*</b>	<b>75**</b>
Deep and Infratentorial (%)	8.9	6.7	10.9	<b>20**</b>	0

	All (n= 291)	NoICH (n=209)	HI (n=46)	PH (n= 35)	PHr (n=4)
<b>mRS 7 days (mean±SD)</b>	2±1.8	1.56±1.8	2.7±2	3.6±1.6	4.2±0.9
<b>mRS 3 months (mean±SD)</b>	1.6±1.9	1.2±1.9	2.2±2.3	3.1±1.9	<b>3.6±0.5**</b>
<b>sICH (n,%)</b>	4 (1.4%)	0	0	<b>4 (11.4%)**</b>	<b>2 (50%)**</b>

\*  $p < 0.05$ , \*\*  $p < 0.01$

## References:

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