FIBRINOGEN DEGRADATION COAGULOPATHY: A MIRROR OF THROMBOLYSIS EFFECTIVENESS IN STROKE PATHOLOGY?

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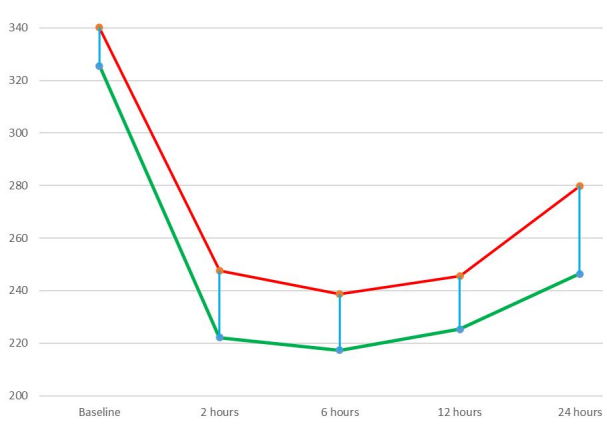
Background and aims - Thrombolysis during ischaemic stroke degradates fibrin matrix of occluding vascular thrombus, reperfunding cerebral tissue; its effect is extended to circulating fibrinogen because of its incomplete specificity, resulting in fibrinogen depletion. Recent studies demonstrated importance of monitoring fibrinogen levels after thrombolysis to reduce intracerebral haemorrhage risk. Beyond this, our aim was to investigate if there was a different fibrinogen dynamic profile between patients who underwent high successful thrombolysis and patients who experimented low response to endovenous treatment.

Materials - We retrospectively collected ischemic stroke patients admitted to Trieste Stroke Unit and acutely treated with thrombolysis or bridge thrombectomy between January 1st, 2018 and December 31st, 2021 who underwent to a complete fibrinogen monitoring: peripheral blood samples were drawn at baseline and at predefined time-points of 2, 6, 12 and 24 hours after thrombolysis. Intracerebral haemorrhages were excluded. We divided patients into two groups. Group H ("High" successful thrombolysis) included patients with absolute ≥4 points-difference, relative ≥50%-difference between admission- and 24 hours-NIHSS score or 24h-NIHSS=0; remaining patients filled Group L ("Low" successful thrombolysis). We evaluated differences using Mann-Whitney U test for numeric or Chi-square test for nominal variables (statistically significance when p <0.05). Inferential analyses were performed.

Results

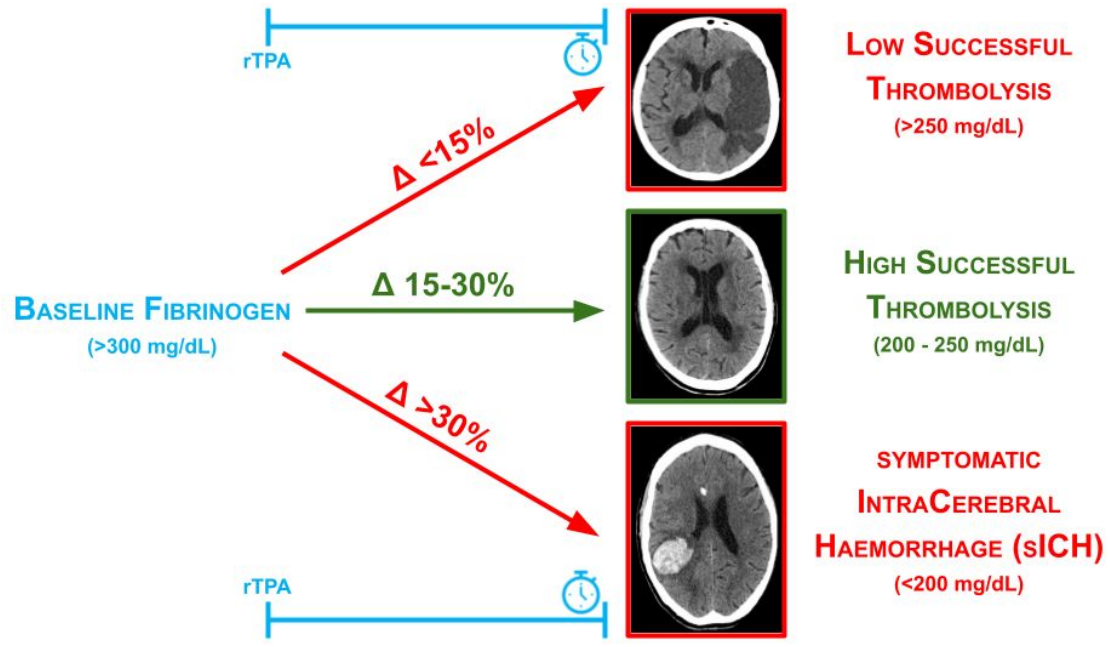


Thrombolysis and Bridge Thrombectomies

Only Thrombolysis

Multivariate for NIHSS at discharge	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age	0.995	0.993 to 0.998	**0.0012**
Fibrinogen delta 0-2 hours	1.001	1.001 to 1.001	**<0.00001**

Multivariate for mRS 0-2 at 3 months	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age	0.994	0.990 to 0.997	**0.0010**
Gender	1.007	0.922 to 1.099	0.8741
Treatment	1.041	0.922 to 1.175	0.5091
Premorbid mRS score	0.906	0.862 to 0.952	**0.0001**
NIHSS score on admission	0.969	0.960 to 0.977	**<0.00001**
TOAST classification	1.001	0.999 to 1.003	0.2431
Bamford classification	0.995	0.941 to 1.053	0.8835
Atrial fibrillation	1.011	0.918 to 1.113	0.8224
Diabetes mellitus	0.909	0.818 to 1.012	*0.0819*
Arterial hypertension	0.999	0.899 to 1.110	0.9942
Smoking	1.017	0.910 to 1.138	0.7552
Dyslipidemia	0.943	0.833 to 1.067	0.3549
Fibrinogen delta 0-2 hours	1.001	1.001 to 1.001	**0.0136**



Personal characteristic	Group H (n=304)	Group L (n=74)	p-value
Age	77 (63;82)	80 (73;85)	**0.003**
Female (n) [%]	159 [52%]	37 [50%]	0.410
Treatment (n) [%]			0.319
- Thrombolysis	240 [79%]	56 [76%]	
- Bridge Thrombectomy	64 [21%]	18 [24%]	
NIHSS score			
- on admission	6 (3;11)	6 (4;15)	0.138
- at discharge	0 (0;2)	7 (3;16)	**< 0.001**
mRS score 0-2 [%]			
- premorbid	284 [93%]	68 [92%]	0.492
- three months later	207 [68%]	15 [20%]	**< 0.00001**
TOAST classification (n) [%]:			0.618
- cardioembolic	115 [38%]	28 [38%]	
- atherothrombotic	30 [10%]	12 [16%]	
- small-vessel occlusion	48 [16%]	12 [16%]	
- other	9 [3%]	1 [1%]	
- cryptogenic	87 [29%]	19 [26%]	
- stroke mimic	15 [5%]	2 [3%]	
Cardiovascular risk factors (n) [%]			
- atrial fibrillation	109 [36%]	30 [41%]	0.453
- smoking	63 [21%]	12 [16%]	0.383
- arterial hypertension	223 [73%]	54 [73%]	0.947
- diabetes mellitus	60 [20%]	22 [30%]	*0.061*
- dyslipidemia	184 [61%]	43 [58%]	0.703
- ischemic cardiopathy	39 [13%]	15 [20%]	0.101
Time onset-to-needle (min)	158 (120-210)	150 (125-186)	0.490
Bamford classification			0.691
- TACI	60 [20%]	18 [24%]	
- PACI	130 [43%]	33 [45%]	
- LACI	79 [26%]	15 [20%]	
- POCI	35 [12%]	8 [11%]	

Fibrinogen time-point	Group H (n=304)	Group L (n=74)	p-value
Baseline Fibrinogen	325.5 ± 99.6	340.2 ± 104.5	0.2581
2h-Fibrinogen	222.1 ± 74.4	247.5 ± 85.2	**0.0104**
6h-Fibrinogen	217.3 ± 72.4	238.6 ± 78.5	**0.0253**
12h-Fibrinogen	225.3 ± 76.1	245.5 ± 72.5	**0.0372**
24h-Fibrinogen	246.4 ± 76.4	279.9 ± 91.8	**0.0012**

Thrombolysis alone	Group H (n=240)	Group L (n=56)	p-value
Baseline Fibrinogen	331.9 ± 104.9	346.9 ± 116.5	0.3462
2h-Fibrinogen	222.8 ± 78.4	254.3 ± 91.4	**0.0093**
6h-Fibrinogen	218.1 ± 76.4	245.8 ± 84.0	**0.0171**
12h-Fibrinogen	223.6 ± 79.9	246.6 ± 77.2	**0.0520**
24h-Fibrinogen	242.2 ± 75.5	272.9 ± 86.7	**0.0084**

Discussion and conclusion - Our study suggests a different fibrinogen profile between ischaemic patients who underwent high or low successful treatment. Monitoring step-by-step fibrinogen levels in the first 24 hours after thrombolysis, we noted steady lower values in patients with higher improvement from stroke symptoms: even if fibrinogen drop occurs especially in the first 2 hours, it maintains this trend in all following time-points. In this way, rTPA-related fibrinogen degradation coagulopathy could be a mirror of thrombolysis strength in dissolving local cerebral thrombus. In conclusion, in addition to preventing intracerebral haemorrhage risk, monitoring the fibrinogen levels curve in the first 24 hours could be useful to follow thrombolysis efficacy in stroke patients.

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