Cerebral postischemic reperfusion injury

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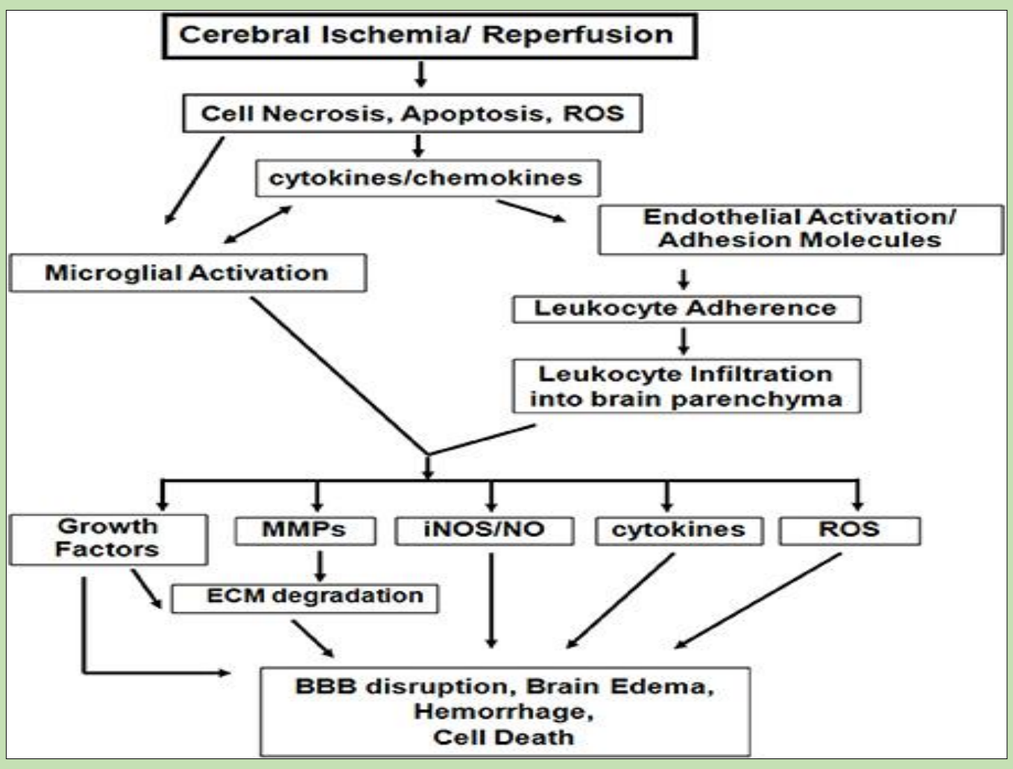
- ***Background and purpose:***

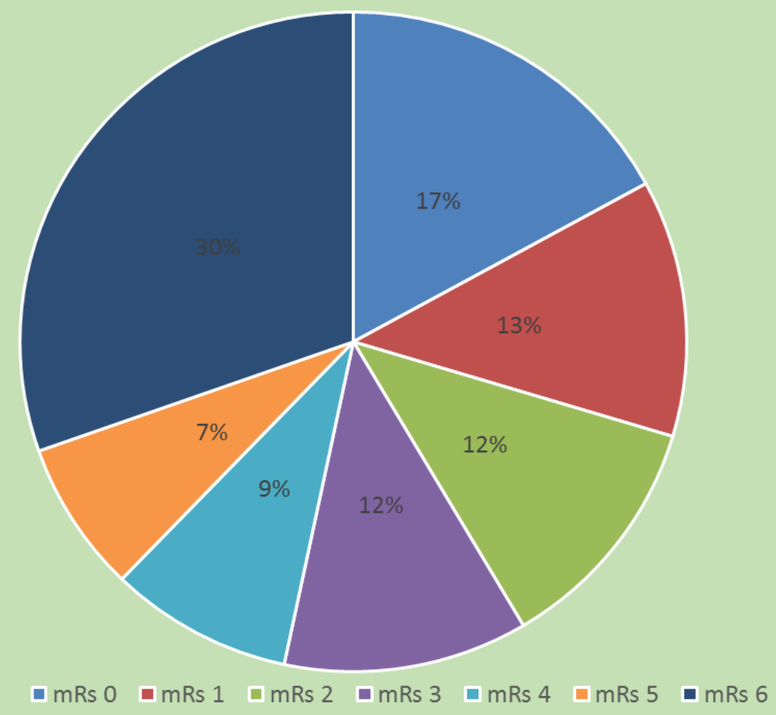
Ischaemic stroke is one of major cause of death and serious disability. The target of stroke treatments aiming at recanalisation of the occluded vessel is the reperfusion of ischaemic brain tissue. Although the restauration of blood flow is a major goal in acute treatment , if this occurs too late, or reperfusion of acutely ischaemic tissue may result clinically futile , or even detrimental because of so-called repefusion injury. Reperfusion injury **(RI)** is a pathofysiological term that describes complex biochemical mechanisms that may damage the ischaemic tissue even with successful recanalisation of the occluded vessel. Haemorrhagic transformation and malignant brain oedema may by considered as clinical expression of reperfusion injury .Preliminary evidence showed that the disruption of the blood-brain barrier (BBB) wich can be investigated by MR techniques or CT as a key phenomenon of the repefusion injury. Experimental studies of cerebral ischaemia have demonstrated that a number of biological factors , including inflammatory mediators , matrix metalloproteinases (MMP) and endothelial function mediators may contribute to reperfusion injury. Activated endothelial cells produce more reactive oxygen species, but less nitric oxide following reperfusion and the imbalance results in a subsequent inflammatory response. The inflammatory response is partially responsible for damage of reperfusion injury. White blood cells release inflammatory factors such as interleukins as well free radicals in response of tissue damage.The restored blood flow reintroduces oxygen within cells that damages cellular proteins, DNA, and the plasma membrane. Damage to the cell´s membrane may in turn cause the release of more free radicals. Such reactive species may also act indirectly in signaling to turn on apoptosis. White blood cells may also bind to the endothelium of small capilaries, obstructing them and leading to more ischaemia. Ischaemic tissue would also have decreasing function of these free oxygen radicals scavengers because of cell injury. Once blod flow is reestablished , oxygen species contained in the blood will damage the ischaemic tissue . Especifically unbalance of MMP levels and their natural inhibitors seem to be associated with disruption of BBB and increased risk of haemorrhagic transformation of malignant oedema . Next to text is FIGURE in which the main mechanisms are outlined.



- ***Methods :***

After approval by the Ethics committee of our institution (University Hospital, Trnava, Slovakia) we analysed retrospectivelly all patients who underwent endovascular treatment for stroke during 12 monts of 2017, which was 146 patients. We had mRs data after 3 months from just 135 patients from them. Beside is diagram with available patients data. We assumed that the patient's profile with axonal injury after stroke were following : severe neurologic deficit with strong vessel patology, fast recanalisation (TICI 2b-3) after short duration of endovascular mechanical trombectomy with range (min to hours) of improvement of patient´s state after treatment.

Revisiting cerebral postischemic reperfusion injury: new insights in understanding reperfusion failure, hemorrhage, and edema.
Int J Stroke. 2015 Feb;10(2):143-52 Bai J[1], Lyden PD

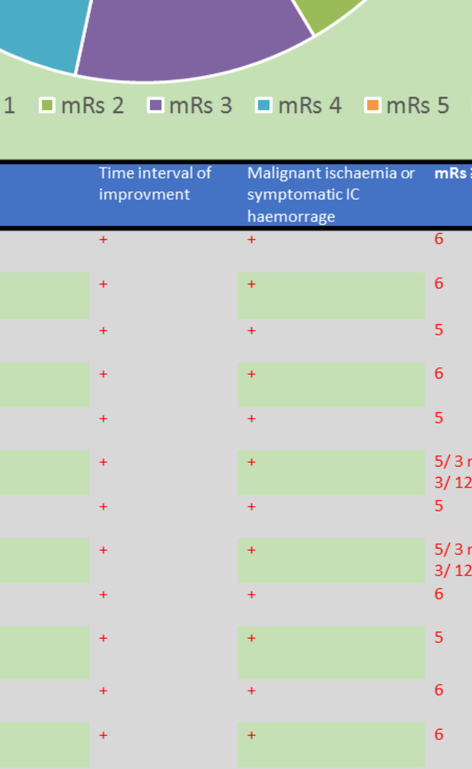


- ***Results:***

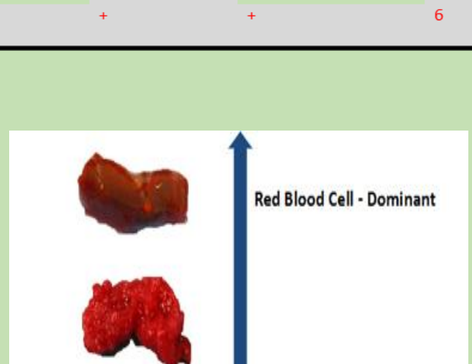
№	Age Town	Etiology	Vessel pathology	i.v. rt-PA yes/no	TICI grade after EVT	Oncet to treatment (IVT) min	Oncet to puncture min	Oncet to EVL recanalisation min	Time interval of improvment	Malignant ischaemia or symptomatic IC haemorrage	mRs ≥ 3m
1. men	76 Trencin	AF (atrial fibrilation)	Left tandem occlusion	no	3	_	330	338	+	+	6
2. men	57 Galanta	AT (atherotrombotic)	M1 occlusion right	yes	3	135	230	250	+	+	6
3. woman	59 Levice	AT	M1 occlusion left	yes	3	195	310	320	+	+	5
4. woman	83 Trnava	AF	M1 occlusion right	no	3	_	253	263	+	+	6
5. woman	77 Trencin	AT	M1 occlusion left	yes	3	100	204	220	+	+	5
6. men	41 Trencin	Disection	Right tandem occlusion	no	3	90	293	335	+	+	5/ 3 monts 3/ 12 monts
7. men	75 Trnava	Af	M1 occlusion right	no	3	_	130	145	+	+	5
8. men	57 Trencin	AF	Left tandem occlusion	yes	3	170	260	305	+	+	5/ 3 montsds 3/ 12 monts
9. woman	71 Trencin	AT	M1 occlusion left A1 occlusion left	no	3	75	130	190	+	+	6
10. Woman	81 Levice	AT	M2 occlusion left	yes	3	80	315	355	+	+	5
11. woman	82 Trencin	AF	M1 occlusion left	no	3	_	210	239	+	+	6
12. men	85 Trnava	AF	T occlusion left	no	3	_	Wake up		+	+	6
13. men	88 Trnava	AF	M1 occlusion right	yes	3	70	154	174	+	+	6
14. woman	76 Trnava	AF	T occlusion left	yes	3	240	285	295	+	+	6
15. woman	91 Komarno	AF	T occlusion left	yes	3	112	260	308	+	+	6

- ***Conclusions :***

- We have sufficient information and evidence on the mechanisms of postischemic reperfusion injury, but without the possibility of affecting it in daily routine practice
- Limited diagnostic options of specific imaging modalities or tests
- Unavailability of effective treatment
- There is with high probability a high number of patients (more than 10%) with reperfusion postischemic injury with poor outcome despite technical "successful" EVT (so called "unexplained deterioration of the patient,,)
- ***What´s most likely profile of patient with reperfusion injury according to results in our patient group?***



- Average of therapeutic "time window" in EVT does not deviate from standard guidelines
- Very good reperfusion effect after EVT - TICI 3 (100%)
- Clinical improvement time interval after EVT (100% of patients) with subsequent, often severe, deterioration of the state of the patient
- "Catastrophic state" as a result of malignant infarction, haemorrhagic transformation, or sICH after EVT (100%)
- A large percentage of RI patients group have atrial fibrillation (60%) and have received IV Alteplase (67%), also with high percentage of mRs 6 (60%)
- A high percentage (67%) of patients are from referral departments



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