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UNIVERSITÄT BERN

Media release

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Stroke therapy:

Study shows additional positive effect of Urokinase

Mechanical removal of blood clots is the therapy of choice for stroke patients. Peripheral, small blood vessels with reduced or blocked patency are, however, problematic. The study by the Department of Neurology and the University Institute for Diagnostic and Interventional Neuroradiology at Inselspital, Bern University Hospital, and the University of Bern demonstrates clear advantages of a simultaneous intra-arterial administration of Urokinase, a blood-clot-dissolving substance (thrombolytic).

Since 2015, the mechanical removal of the blood clot (endovascular mechanical thrombectomy) has been the standard procedure for treating patients with an occluded cerebral artery (stroke). Several randomized studies have shown that there is a relevant reduction in the degree of disability among stroke patients with this therapy.
Endovascular mechanical thrombectomy has been routinely performed at Inselspital since 2010. Between 300-400 patients are treated at Neurozentrum every year. Currently, the scientific focus in the area of endovascular stroke therapy lies primarily on expanding the area of use for the procedure, organizing stroke networks as well as improving the restoration of blood flow (reperfusion).

Objective: To improve the patency of blood vessels
In a meta-analysis published in 2018 (doi: 10.1136/jnnp-2017-317602), the research team led by Dr. Kaesmacher, Prof. Gralla and Prof. Fischer was able to show that there was a statistically significant and relevant difference for the patient as to whether the brain tissue is completely (so-called TICI3 result) or almost completely refused (so-called TICI2b result) with mechanical thrombectomy. Therefore, intensive research is being conducted into ways of further improving reperfusion when no further mechanical improvements can be achieved. Apart from invasive rescue treatments such as inserting a permanent stent into a cerebrovascular vessel, a recently published study in Bern showed that the administration of coagulation-dissolving medicines (thrombolytics) through the catheter could improve the reperfusion result and thus reduce the degree of disability, without increasing the risk of bleeding. Dr. Kaesmacher reports: “Until now, the significance of administering intra-arterial thrombolytic medicines following mechanical thrombectomy has not been clarified. Accordingly, the

recommendation of the American Stroke Association regarding its use has been cautious. The published results of the study thus constitute an important component in defining the future significance of the intra-arterial administration of fibrinolytics."

Intra-arterial dissolution of blood clots has potential for improvement

The patients analyzed in the study (doi: 10/1001/jamaneurol.2019.4192) published in JAMA Neurology showed residual peripheral occlusions subsequent to mechanical thrombectomy, which led to an almost complete rather than a complete reperfusion. The authors of the study were able to show that these peripheral occlusions could often be dissolved with the intra-arterial administration of a special thrombolytic (Urokinase) and thereby further improve reperfusion. This was also reflected in a better outcome among the patients. In particular, it is important to note that the study found no increased risk of bleeding following the additional intra-arterial administration of Urokinase. The risk of symptomatic bleeding after the intra-arterial administration of Urokinase was 5.2% and 6.9% in the control group.

"Further studies are still needed for a widespread use of this procedure, and a pan-European, multicenter study is already well under way," explains Prof. Dr. Jan Gralla, the neuroradiological senior author of the study. Co-supervisor of the study, Prof. Dr. Urs Fischer, summarizes: "The chosen approach constitutes a promising therapeutic strategy with which the therapeutic benefit of endovascular stroke treatment can be further improved. For patients with a low risk of bleeding, this means it is now more important than ever to do everything possible to further improve the reperfusion result."

Publications:

- Kaesmacher J, Bellwald S, Dobrocky T. 2019: Safety and Efficacy of Intra-arterial Urokinase After Failed, Unsuccessful or incomplete Mechanical Thrombectomy in Anterior Circulation Large-Vessel Occlusion Stroke; doi: 10/1001/jamaneurol.2019.4192
- Kaesmacher J, Dobrocky T, Heldner MR, Bellwald S, Mosimann PJ, Mordasini P, et al. 2018: Systematic review and meta-analysis on outcome differences among patients with TICI2b versus TICI3 reperfusions: success revisited. *J. Neurol. Neurosurg. Psychiatry*. 2018;89:910–917; doi: 10.1136/jnnp-2017-317602

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