M U N I

COMMENTARY TO HABILITATION THESIS[1]

[*Introduction*

This habilitation thesis is conceived as a collection of 6 articles published by the author and his colleagues. It contains chapters describing modern Acute Ischemic Stroke (AIS) treatment. Where relevant, it is followed by commentaries introducing topic of each publication with the description of the author's contribution to knowledge in this field.

Background

Intravenous thrombolysis (IVT) represents AIS treatment of choice if indicated. In cases of large intracranial vessel occlusion, IVT leads to revascularization only in 13–33 % of cases. **Endovascular mechanical thrombectomy (MT)** significantly improves the efficacy of brain revascularization and patient's clinical outcome. Recently, MT´s therapeutic window has been widened to 24 hours based on the CT perfusion studies performed with the automatic value calculation. IVT is followed by MT as a second-tier treatment in indicated cases. It is the best available treatment of AIS with middle cerebral artery (MCA) occlusion. This combined management fails in 5-10% of cases. **Microsurgical MCA revascularization** using microsurgical embolectomy or EC-IC bypass represents a historically available treatment option. There is a lack of data on the benefit of microsurgery in modern AIS treatment.

Aim of this work

is to prove safety and efficacy of open microsurgery in the settings of standard AIS therapy failure and MCA occlusion.

Methods

Systhemic review evaluating open brain revascularization just after IVT was defined. Institutional protocol of the open microsurgery as an "ultimum refugium" treatment of an acute MCA occlusion in patients with failed IVT and/or MT and with a persisting viable penumbra was defined and approved by local ethical committee. The protocol of a **bicentric randomized prospective study** (Comprehensive Stroke Centers České Budějovice and Ostrava) evaluating the results of an urgent microsurgical MCA recanalization was registered and study was performed.

[1] The commentary must correspond to standard expectations in the field and must include a brief characteristic of the investigated matter, objectives of the work, employed methodologies, obtained results and, in case of co-authored works, a passage characterising the applicant's contribution in terms of both quality and content.

Results

Our systemic review detected 3267 potential studies evaluating microsurgery in AIS treatment. Twelve studies evaluating 13 AIS patients with urgent open MCA revascularizaton surgery after IVT were found using a three-staged selection. České Budějovice and Ostrava Comprehensive Stroke Centeres treated 2175 patients using IVT and 1121 patients with MT from 2016 till 2020. IVT and MT failed in 22 patients (4.5%) in České Budějovice, while it failed in 25 patients (4.3 %) in Ostrava. The surgical group of patients showed a significantly better clinical outcome: 58.3% of microsurgically treated patients were independent (defined as mRS 0-2) at 3 months after surgery in comparison with 10% and 12% in the non-surgical groups.

Conclusion and future work directions

Our bicentric randomized study produced pilot data on the safety and efficacy of an urgent microsurgical MCA recanalization. Approximately 1350 patients were treated with mechanical thrombectomy in 2021 in Czech Republic. It is estimated that there are at least 50 patients after standard IVT and MT treatment failure who are still within the therapeutic window, in Czechia annually. We are working on multicentric trial.

Author´s statement

All the urgent brain microsurgeries presented in this thesis were performed by the author. Standard AIS treatment was delivered by the whole Comprehensive stroke center´s teams. Author initiated all the studies mentioned in this thesis. His rate of participation in the 6 published works is mentioned next]

[1]*FIEDLER Jiří *(corresponding author)**, Vladimir PRIBAN, Ondrej SKODA, Ivo SCHENK, Vera SCHENKOVA a Simona POLAKOVA. Cognitive outcome after EC-IC bypass surgery in hemodynamic cerebral ischemia. *Acta Neurochirurgica* [online]. 2011, **153**(6), 1303–1312. ISSN 0001-6268. Dostupné z: doi:10.1007/s00701-011-0949-x
Document Type: Article; IF = 1,520; Quartile by IF: SURGERY Q2; Quartile by AIS: SURGERY Q2

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
70%		100%	100%

[2] *FIEDLER, Jiri*, Martin REISER, Petr KOSTAL, Jiri KUBALE, Svatopluk OSTRY, Tomas HRBAC, Petra KESNEROVA, Tana FADRNA, Katerina LANGOVA, Roman HERZIG a David SKOLOUDIK. Blood Flow Volume Measurement in Cervical and Intracranial Arteries using Quantitative Magnetic Resonance Angiography and Duplex Sonography (Bocaccia) - A Prospective Observational Study. *Ultraschall in Der Medizin* [online]. 2021, **42**(01), 65–74. ISSN 0172-4614. Dostupné z: doi:10.1055/a-1113-7343

Document Type: Article; IF = 5,445; Quartile by IF: RADIOLOGY Q1; Quartile by AIS: RADIOLOGY Q1

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20%	20%	20%	30%

[3] ***FIEDLER, J. *(corresponding author)****, T. MRHALEK, M. VAVRECKA, S. OSTRY, M. BOMBIC, J. KUBALE, V. PRIBAN, M. PREISS a I. STUCHLIKOVA. Kognice a hemodynamika po karotické endarterektomii pro asymptomatickou stenózu [Cognition and Hemodynamics after Carotid Endarterectomy for Asymptomatic Stenosis]. *Ceska a Slovenska Neurologie a Neurochirurgie*. 2016, **79**(2), 201–206. ISSN 1210-7859.
Document Type: Article; IF = 0,368; Quartile by IF: SURGERY Q4; Quartile by AIS: SURGERY Q4

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
60%		70%	100%

[4] ***FIEDLER Jiří*(corresponding author)****, V. PRIBAN a M. BOMBIC. Peroperační kontrola funkce extra-intrakraniálního bypassu ultrazvukovými metodami. *Ceska a Slovenska Neurologie a Neurochirurgie*. 2011, **74**(1), 62–66. ISSN 1210-7859.
Document Type: Article; **IF = 0,279; Quartile by IF: SURGERY Q4; Quartile by AIS: SURGERY Q4**

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
60%		100%	100%

[5] FIEDLER J, OSTRY S, BOMBIC M, STERBA L, KOSTAL P. Urgent Middle Cerebral Artery Embolectomy of Calcified Embolus After Intravenous Thrombolysis: 2-Dimensional Operative Video. Oper Neurosurg (online) 2019 Aug 1;17 (2): E54-E55. ISSN 2332-4252. Dostupné z: doi:10.1093/ons/opy404

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
90%		90%	

[6] FIEDLER, **Jiri**, Martin ROUBEC, Marek GRUBHOFFER, Svatopluk OSTRY, Vaclav PROCHAZKA, Katerina LANGOVA a David SKOLOUDIK. Emergent microsurgical intervention for acute stroke after mechanical thrombectomy failure: A prospective study. Journal of Neurointerventional Surgery [online]; 2022; 0:1–8. ISSN 1759-8478. Dostupné z: doi:10.1136/neurintsurg-2022-018643
Document Type: Article; IF = 8,572; Quartile by IF: SURGERY Q1; Quartile by AIS: SURGERY Q1 (data from 2021)

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
40%	30%	20%	50%