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Evaluation of the Dissertation of **MUDr. Michal Mihalovič** on the topic
**"Acute stroke and cardiovascular system. Assessment of myocardial injury
with impact on patients outcome"**.

To the Board of the Doctoral Program in cardiovascular science,
it is my pleasure to submit herewith the evaluation report on the above doctoral thesis.

Assessment of the scientific topic and clinical significance

The heart-stroke interaction is a major factor in the epidemiology, pathophysiology and clinical course of stroke. Cardiac complications contribute to the outcome after stroke. Accordingly, the term heart-stroke syndrome has been coined some time ago to define this important clinical field and to promote further research and improved interdisciplinary clinical treatment of stroke patients. Therefore, understanding cardiovascular complications in acute stroke and develop predictive tools to identify patients at high risk is of very high clinical value. The clinical topic of this thesis is therefore highly timely and clearly of wider clinical and academic interest.

Description and assessment of scientific work

Dr. Mihalovič describes in this thesis his studies on the interaction of cardiovascular pathologies and cerebral stroke. These studies were conducted at the Cardiocenter of the University Hospital Kralovske Vinohrady and the 3rd Faculty of Medicine of the Charles University.

The heart-brain interaction are investigated as a crucial aspect in the complex pathophysiologic inter-organ interaction in the setting of acute stroke. The focus of the studies is on

- the dynamic changes of biochemical biomarkers of myocardia injury are studied and their significance for prediction of outcome.
- the potential role of subclinical electrocardiographic and echocardiographic changes in the setting of acute stroke are investigated.

The introduction provides a comprehensive overview on the key aspects of the topic. A short historical review, epidemiologic key data and general clinical facts are presented in a concise and informative way. Major pathophysiologic mechanisms of myocardial injury in acute stroke are described on a clear and systematic overview.

Beside widely accepted mechanisms such as calcium overload or inflammation, the author also addressed gut dysmicrobiosis, which is a novel and less well acknowledged factor on this context. Localisation aspects of focussed brain injury resulting in cardiac injury are reviewed as well. Finally an overview is presented on state of the art diagnostic tools to clinically investigate cardiac injury in the setting of acute stroke with emphasis on blood born biomarkers, electrocardiac and echocardiatic assessments.

Following this well-structured introduction, a hypothesis is formulated that is rather minimalistic and reflects not more than the currently established pathophysiologic understanding, i.e. 'myocardial injury is associated with worse outcome after stroke. The aims of the study are given in a similarly abbreviated way. Some detail and elaboration of the aims (and potentially the scope) of the studies could have benefited this section.

Methods are described in a short overview outlining general aspects of the study design, study population, main methods (lab assessments, ECG assessment). This section is, again, very condensed and omits relevant aspects of methodical description (e.g., echo assessments are described not more than as 'standard echo examination'). The results section reports in detail and in systematic order the findings from multiple investigations related to biomarkers, ECG and echo assessments. In some figures legends are incomplete or seemingly wrong (Figure 3A vs. text p.37). Outcome data are somewhat limited by low event numbers.

The findings are adequately discussed in relation to current literature and conclusions for the clinical application of the findings for improved patient monitoring post stroke are drawn.

The thesis utilised well current publications that are relevant to his studies as shown by a sufficiently large and up to date reference list. However, a key publication defining the stroke-heart syndrome as clinical entity is unfortunately missing (Scheitz et al., Lancet Neurology 2018).

The clinical studies presented in this thesis were successfully published in peer-reviewed medical journals: 2x Journal of Clinical Medicine (MDPI, IF 3.0), European Heart Journal Supplements (Oxford University press, IF 1.7). The Publisher MDPI has previously been controversially discussed as a predatory publisher and had been listed in predatory publishers lists; the discussion in the academic community on this characteristic of the publisher is, however, ongoing.

Assessment of the quality of thesis (structure, language level, quality of tables and figures)

The thesis is very well written, clearly structured and well referenced. Figures and tables are of acceptable quality. Some figure legends seem incomplete or incorrect.

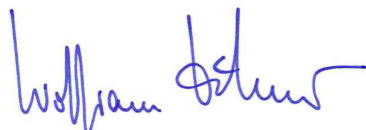
Preclusion:

This report does not include a systematic assessment of the references and does not include search for plagiarism.

Conclusion

Dr. Mihalovič provided with this thesis convincing proof of his clear and in-depth medical and scientific insight of the topic, his systematic and skilful work as clinical scientist and his substantial academic capability of scientific publishing. He can be fully recommended for the successful completion of this scientific project and this thesis.

Sincerely,



Wolfram Doehner