Introduction and outline of the thesis
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The introduction of new medical technology and surgical procedures promises improved surgical outcome and better treatment options in many clinical conditions. However, the application of these novel techniques, often results in important disturbances of the patients cerebral physiology. Since the brain is the most vulnerable organ, of which relatively modest injury often has major and irreversible consequences, this is of vital anaesthesiological concern. Therefore, as our surgical colleagues are dedicated to move the boundaries of the therapeutical limitations, it is essential that we maintain a full understanding and control of the impact of these interventions on the cerebral homeostasis. Reversely, many surgical approaches have only become possible as a consequence of a thorough understanding of the human physiopathology and resulting anaesthesiological anticipation. Protection and support of the human body in these highly unphysiological conditions is essential to allow further progress of the therapeutical options. A meticulous study of the consequences of surgical actions on the cerebral physiology and a determination of the essential diagnostic and therapeutic actions that must be taken in these cases is the only approach to deliver optimal anaesthesia care during these interventions.

As much, we aimed to:

- Elucidate the physiological changes during endoscopic neurosurgery.
- Describe the diagnostic value of the hemodynamical changes during these interventions.
- Describe in an animal model the physiopathology of isolated hyperacute intracranial hypertension.
- Define the optimal method for perioperative monitoring of the intracranial pressure.
- Investigate the limitations of non-invasive continuous pressure monitoring in neurosurgical procedures.
- Elucidate the physiological changes during combined steep Trendelenburg position and pneumoperitoneum.
- Determine the accuracy of different transcranial Doppler methods to examine the cerebral perfusion in this clinical setting.

Endoscopic Neurosurgery

During endoscopic neurosurgery, a continuous rinsing of the ventricular cavities is performed. This may have negative effects on the cerebral circulation. In fact, in clinical practice, we often noticed during neuro-endoscopical interventions, characteristic hemodynamical reflexes which resembled phenomena described by Cushing\(^1\) and Heymans\(^2\), and were suggestive for acute intracranial hypertension (ICP).
In a first article, we demonstrate that the initial hemodynamical reflexes following a hyperacute increase of the intracranial pressure consists of a combination of hypertension and tachycardia. The classical understanding of the Cushing reflex describes a combination of hypertension and bradycardia. In this particular clinical situation of endoscopic neurosurgery, the hyperacute nature of severe intracranial hypertension, produces a short lasting tachycardia that precedes the bradycardia which is classically associated with the Cushing reflex. This knowledge is essential to prevent severe complications during these procedures. Additionally, we show what combination of monitoring strategy should be taken and how to comprehend it to optimize and safeguard the cerebral perfusion.

In a second article, we illustrate using Transcranial Doppler what is the exact sequence of events after a complete stop of the cerebral blood flow. We confirm objectively that during these ‘minimal invasive procedures’ a complete brain ischemia can develop very swiftly without any clinical sign. Only after several seconds, the first clinical signs arise and it is only with the right diagnostic approaches this can be detected timely if the signs are interpreted correctly.

In both articles we demonstrate the extreme speed by which an excessively high intracranial pressure can be reached, and the importance of its fast detection.

**Animal model of endoscopic neurosurgery**

During neurosurgical procedures, an increased ICP often coincides with difficult intracranial manipulations. Moreover, The illustration shows that in several neuro-endoscopic procedures - like third ventriculostomy and pituitary surgery - there is a coincidental occasion of high rinsing activity and direct pressure on the brain stem. Therefore, it is difficult in these observational studies to differentiate the cause of the haemodynamical reflexes. Moreover, it is impossible to intentionally increase the ICP in order to study the hydrodynamical and haemodynamical consequences of excessive rinsing.

Therefore, in a third article, we present a rat model of endoscopic neurosurgery, where these effects of hyperacute isolated intracranial hypertension are demonstrated.
**Optimizing monitoring in endoscopic neurosurgery**

During our clinical and research work, we were confronted with a controversial problem that the optimal methodology for measuring the ICP during endoscopic neurosurgery was not yet decisively determined. Different views existed in literature, but no solid argumentation was ever made to conclude the best policy. Therefore, in a fourth article, we present an in-vitro study where different measuring methods and locations are evaluated and a decisive strategy is revealed to guarantee an accurate measurement.

**Minimal invasive anaesthesia in minimal invasive neurosurgery**

A key finding of our research is that the clinical conditions during endoscopic neurosurgery necessitate invasive arterial blood pressure measurement. A non-invasive method of obtaining continuous blood pressure information would allow for a safer means of providing optimal monitoring. Therefore, in a fifth article, we present the possibilities and limitations of this technique in neurosurgical procedures.

**Cerebral effects of steep Trendelenburg position and CO₂ pneumoperitoneum.**

Another recent anaesthesiological challenge for preserving the cerebral homeostasis is the introduction of robotic endoscopic surgery. This new technology offers superior surgical treatment options for multiple pathologies, but often necessitates a combination of steep Trendelenburg position and pneumoperitoneum. The influence of this condition on the cerebral homeostasis was never thoroughly investigated. Therefore in a sixth article, we examined the influence of this highly unphysiological condition on the human body and its clinical consequences. Apart from direct measurement of clinical parameters and its clinical interpretation, the influence if this combined Trendelenburg position and CO₂-pneumoperitoneum on more fundamental changes in the cerebral microvasculature has never been investigated either. On the other hand, our clinical experience with patients in the direct postoperative period hints for important disturbances of the cerebral microvasculature. A combination of high-resolution hemodynamic recordings and Transcranial Doppler measurement permits the analysis of this impact in our human patient population. Several important clinical and fundamental questions still needed to be answered. Many of these questions were elucidated in a seventh article.
References

2 Heymans C. The control of heart rate consequent to changes in the cephalic blood pressure and in the intracranial pressure. Am J Physiol. 1928;85:498-505.