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Assessment of cardiovascular autonomic function in the anaesthesia population

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ENGLISH SUMMARY

Autonomic dysfunction is commonly observed among patients undergoing anaesthesia and surgery, and may be of influence on perioperative outcome. At present, autonomic function measurements are not yet incorporated in the routine preoperative risk evaluation of surgical patients. In this thesis we provide more insight into the prevalence of health risk factors and autonomic dysfunction in relation to cardiometabolic disease in the anaesthesia population. Moreover, we describe the implementation of autonomic function measurements in an ambulatory setting under non-standardised conditions in healthy volunteers and patients at risk of autonomic dysfunction, in order to evaluate whether they may replace standardised autonomic function testing as prescribed in the literature (i.e. executed in the morning and fasted from midnight). Finally, we studied the ability to predict intraoperative haemodynamic instability based on preoperative heart/pulse rate variability measurements in order to elucidate whether simplified autonomic function testing may be of added value during preoperative health risk profiling.

Elderly patients and those suffering from obesity, hypertension and diabetes mellitus increasingly dominate the anaesthesia population. These conditions are frequently complicated by impaired cardiovascular autonomic innervation, which leads to cardiovascular autonomic neuropathy. Cardiovascular autonomic neuropathy is associated with increased perioperative morbidity and mortality. Therefore, preoperative risk assessment to gain insight into the level of autonomic dysfunction and therapeutic optimisation may prevent perioperative complications.

Chapter 1 is the general introduction of this dissertation.

Chapter 2 provides an overview of the scientific literature with a focus on the association of cardiovascular autonomic neuropathy with perioperative cardiovascular complications. Cardiac complications in patients undergoing non-cardiac surgery account for 40% of perioperative mortality. The most important cardiac complications of surgery are cardiac death, myocardial ischemia or infarction, cardiac arrest and pulmonary oedema. General anaesthesia results in increased activation of the sympathetic nervous system, which may increase the risk of (postoperative) tachycardia and hypertension. These haemodynamic alterations increase myocardial oxygen demand and may lead to unstable angina, myocardial infarction or arrhythmias, especially in patients with autonomic neuropathy. Since anaesthesia has a marked effect on perioperative autonomic

function, the interplay between diabetic neuropathy and anaesthesia may result in unexpected haemodynamic instability during surgery. Inclusion of autonomic function testing in the preoperative period may contribute to improved intraoperative safety, and may result in the development of tailor-made anaesthesia for patients with autonomic dysfunction.

Chapter 3 investigates the prevalence of lifestyle risk factors in patients undergoing non-cardiac surgery who are admitted to the preoperative assessment outpatient clinic for health risk profiling. Patient self-reports and anaesthetist reports of health risk factors were compared to evaluate the patient self-image of preoperative health. The study shows a high prevalence of lifestyle risk factors among perioperative patients, with overweight, obesity, smoking and hypertension the most frequently reported. Patients with two or more lifestyle risk factors were older and had a higher body mass index and ASA classification. We showed that lifestyle risk factors such as overweight and hypertension are frequently under-reported in self-reports by patients; this suggests that patients are unaware of their unhealthy state, or that they ignore the risks. The use of patient self-reports in the preoperative assessment outpatient clinic need critical appraisal in order to prevent underreporting of health risks before surgery.

Chapter 4 presents the level of agreement between heart rate variability and pulse rate variability in healthy individuals. Evaluation of autonomic function is commonly performed by quantitative assessment of beat-to-beat heart rate variability reflecting parasympathetic and sympathetic control of the sinoatrial node. The characteristic oscillations in heart rate are reduced where autonomic innervation is impaired. Since heart rate variability is difficult to assess in some situations, pulse rate variability may be used as an alternative for heart rate variability. However, the level of agreement between these different types of measurement is unclear. We showed that pulse rate variability derived from interbeat intervals from non-invasive arterial blood pressure measurement, corresponds well with heart rate variability derived from an electrocardiogram, with less sensitivity to perioperative environmental disturbances such as artefacts caused by patient movement or diathermy. We concluded that pulse rate variability may be used to evaluate perioperative cardiovascular autonomic function.

Chapter 5 defines the reference values for short-term (5-minute) heart rate variability, and investigates the influence of gender and age in the

young and middle-aged population, since the lack of reference values for autonomic function in young and middle-aged subjects limits the implementation of heart and pulse rate variability analysis in the perioperative setting. The majority of heart rate variability parameters were significantly higher in men than in woman. Age had no influence on heart rate variability parameters. The publication of these reference values may support further implementation of heart rate variability in preoperative patient risk stratification.

Chapter 6 presents the comparability of autonomic function tests under both non-standardised and standardised test conditions in healthy subjects. Cardiovascular autonomic function is classically evaluated using Ewing tests and quantitative assessment of beat-to-beat heart rate variability. Current guidelines recommend that patients should refrain from smoking, eating and drinking, and that the tests be performed in a quiet ambiance at room temperature in order to eliminate the influence of cyclic physiological variations and environmental factors. However, the standardised test conditions hamper clinical implementation during routine preoperative assessment as diagnostic and prognostic tools for cardiovascular disease. We showed that reproducibility of autonomic function tests under non-standardised conditions was comparable to standardised test conditions. Furthermore, we demonstrated that reproducibility for most autonomic tests under non-standardised conditions is acceptable. Our findings suggest that implementation of these tests during preoperative assessment may be feasible.

Chapter 7 investigates the reproducibility of autonomic function testing (classical Ewing cardiovascular autonomic function tests, heart and pulse rate variability) under non-standardised and standardised conditions in patients with type II diabetes mellitus and cardiovascular disease. Secondly, we studied the level of agreement between traditional heart rate variability derived from an electrocardiogram, and pulse rate variability derived from blood pressure waveforms in this particular patient population.

We found that most classical Ewing cardiovascular autonomic function tests, heart and pulse rate variability in type II diabetic patients provided similar results under standardised and non-standardised test conditions. Additionally, we demonstrated an acceptable reproducibility for most autonomic function tests, heart and pulse rate variability under non-standardised as well as standardised test conditions. Secondly, our data also show that in this patient population, pulse rate variability corre-

sponds well with traditional heart rate variability under resting conditions. In agreement with previous findings in healthy volunteers, this study supports the performance of cardiovascular autonomic function tests under non-standardised test conditions as an alternative to standardised test conditions in type II diabetic patients, which may facilitate implementation of autonomic function testing during preoperative assessment. Moreover, pulse rate variability may be used in clinical or research settings where an ECG signal is absent or disturbed.

Chapter 8 describes the relationship between preoperative pulse rate variability and intraoperative haemodynamic stability in patients undergoing surgery during local or general anaesthesia. We showed that an impaired pulse rate variability in the preoperative phase is associated with more intraoperative hypotension compared to subjects with a normal pulse rate variability. Therefore, the implementation of simple preoperative autonomic test may be feasible to detect patients at risk for complications due to intraoperative hypotension.

Chapter 9 describes a randomised trial where the level of mental strain experienced by the surgeon performing robot-assisted laparoscopic surgery was compared to the strain during conventional laparoscopic surgery. Increased mental strain leads to a more regular heart rhythm and thus decreased heart rate variability. Laparoscopic surgery might be beneficial for the patient, but it imposes increased physical and mental strain on the surgeon. Our data suggest that the use of robot-assisted laparoscopic surgery is associated with less physical and mental strain for the surgeon than conventional surgical procedures.

Chapter 10 discusses the main results and conclusions of this dissertation and deliberates on methodological limitations and future directions for research.