Chapter 9
Perioperative Care

Introduction

For anesthesiologists preparing patients for operations, perioperative care involves inducing a reversible state of loss of responsiveness, amnesia, analgesia, decreased stress response, and possibly unconsciousness (depending on the kind of operation), maintaining homeostasis under operations, and any treatment after operations to support the initial phase in the patient's recovery. Most anesthesiologic and surgical procedures can have profound effects on homeostasis, including fluid balance, the cardiovascular system, and the autonomic nervous system. The fact that one-third of all postoperative complications and 50 % of postoperative mortality are due to cardiac events underlines the importance of risk estimation (Laitio et al. 2007). But not only cardiac events are of interest. Simple methods like score or bedside investigations, which do not depend on advanced qualifications and experience (e.g., echocardiography) to detect fluid imbalances, beginning SIRS or other circumstances that can have consequences for the planning and execution of anesthesia are needed. In this context, anesthetists have been well aware for decades now of the association of pathological changes in ANS and worse outcome, for instance, in diabetic patients with advanced autonomous neuropathy (Burgos et al. 1989).

Not surprisingly, heart rate variability has been used to predict instability, to monitor anesthesia, and to guide perioperative treatments. It is, however, far from being an established tool for anesthetists. HRV has been recently proposed as "helpful, non-invasive, bedside, low-cost monitoring tool to evaluate the perioperative risk in patients with suspected autonomic dysfunction, to select individuals who need further cardiac testing and to optimize preoperative status" (Mazzeo et al. 2011).

Perioperative problems have been associated with ANS dysfunction (e.g., Mazzeo et al. 2011), but there is no clear evidence for this, as discussed in Chap. 4. This is not an issue in this chapter. The question itself is a very interesting research question for anesthetists, but our main focus here is on the associations between alterations of HRV and perioperative morbidity and mortality.

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Induction and Maintenance of General Anesthesia

General anesthesia is a pharmacologically induced and reversible state of amnesia, analgesia, loss of responsiveness, loss of skeletal muscle reflexes, and decreased stress response. Anesthetic agents are intravenous drugs or inhalation agents. All anesthetic agents have more or less profound effects on the cardiac and circulatory system. Most volatile agents are potent vasodilators and reduce systemic vascular resistance. They can increase heart rate due to reduced blood pressure but also independently of blood pressure. At least some volatile agents have a direct influence on SNS and PNS. They depress baroreceptor function and cause a decrease in stroke volume, which results in reduced cardiac output. All volatile agents sensitize the myocardium to adrenaline. In addition, anesthetic agents depress CNS function. All these elements are also part of the system that causes HRV; thus, one should expect any form of anesthesia to affect HRV.

Prediction of Hypotension

Nearly all forms of anesthesia cause hypotension, but some patients develop higher falls in blood pressure than others. Preoperative low blood volume is a frequent cause for low blood pressure after induction of anesthesia. In healthy patients, compensatory mechanisms blunt the effect of blood loss or dehydration. At the moment when anesthetic agents diminish cardiocirculatory reflex responses, blood pressure goes down. One issue in HRV research is therefore to identify patients at risk for a more pronounced blood pressure fall. Another issue is rhythm disturbances like brady- or tachycardia during or after the induction phase.

In an early study, low HF (then described as RF) predicted bradycardia in 80 % of included patients (Estafanous et al. 1992). Huang studied 46 patients with and 87 patients without diabetes, all of them ASA II or III undergoing elective surgery. They obtained 5 min HRV measurements under paced breathing immediately before anesthesia. TP, LF, and HF were lower in participants with hypotension (defined as decrease of greater than 30 % or a systolic BP under 85). Interestingly enough, in contradiction to results in association of spinal anesthesia presented later in this chapter, LF/HF showed no association. Unfortunately, Huang does not present mean and standard deviation of the HRV measures (Huang et al. 2006). In diabetic patients, HRV has been recommended as standard test, meant to give additional crucial information in preventing hypotensive episodes in diabetic patients with diabetic autonomic neuropathy (Oakley and Emond 2011).

Prediction of Cardiac Events

In a study, Mamode included 297 patients undergoing elective peripheral arterial surgery and used a plethora of blood samples, myocardial perfusion scanning, and heart rate variability (Holter monitoring) preoperatively. Patients were screened for myocardial infarction the first three postoperative days with ECG and cardiac isoenzymes (CK-MB). Primary end point of the study was the occurrence of myocardial infarction or cardiac death within 30 days postoperatively. Twenty-one patients reached this end point (14 death, 7 myocardial infarction). Clinical risk factors were poor predictors. High predictive value had increased age, ECG evidence for previous myocardial infarction, prior aortic surgery, positive thallium scan, and impaired HRV (triangular index). For the interpretation of the study, it is of major significance that several different HRV measures had no predictive value, so SDNN, SDANN, pNN50. They did not apply frequency-domain algorithms, neither nonlinear measures. Their combined model showed a sensitivity and specificity of 84 and 80 %, respectively, for perioperative cardiac events (Mamode et al. 2001).

For measuring preoperative HRV on 32 patients >60 years of age undergoing operations for traumatic hip fractures, Holter ECG recordings were made using short-term fractal scaling exponent. In stepwise multivariate logistic regression, this variable was the only independent predictor of postoperative prolonged ischemia, showing an odds ratio of 7.7 (Laitio et al. 2004).

One hundred patients ASA 3–4 scheduled for major vascular or abdominal surgery were examined with a 24-h Holter monitoring, and the revised cardiac risk index was calculated; patients were only included with a score of three or more. Intraoperative hypotension was defined as a fall of MAP to 60 % of preoperative MAP, bradycardia as a decrease of heart rate to 60 % of baseline or lower than 50 beats per minute. The first 50 patients were analyzed retrospectively, the second 50 prospectively. A cutoff for TP of 500 ms^2 was chosen after the retrospective part to distinguish low-risk and high-risk patients, lower TP indicating possibly unstable patients. $TP < 500$ did predict bradycardia, hypotension, and use of vasopressors but not atropine (Hanss et al. 2008).

Mazzeo proposes HRV to guide premedication with beta-blockers. According to this idea, HRV with low variability should give a relative indication for perioperative use of beta-blockers. This has not been studied yet, but Mazzeo quotes an intervention study for myocardial infarction (Lampert 2003). This patient population consists of postmyocardial infarction patients. HF was a predictor for outcome. HF was more increased in patients treated with propranolol than in patients with placebo. The conclusion that beta-blockers should be considered for patients with low HF (or generally low HRV) is not backed by this evidence, but it is a good indication for a well-controlled study.

Effects of Anesthesia on HRV

Inducing anesthesia with propofol and maintaining it with isoflurane/nitrous oxide led initially to reduction of HF and increase of LF, but HF returned subsequently under isoflurane/nitrous oxide, while LF remained depressed (Galletly et al. 1992).

Thiopental has a bigger effect on HRV frequency domain than etomidate (Latson et al. 1992; Scheffer et al. 1993). Inhalation of 30 % N_2O in healthy subjects led to reduction in HF and to a rise in LF/HF ratio. The authors discussed the effect as consistent with an enhanced sympathetic balance of sinoatrial control through reduced parasympathetic tone (Galletly et al. 1993). No difference has been observed between isoflurane 1.5 % and halothane 0.75 % (Galletly et al. 1994a).

Induction of anesthesia with propofol in ten women undergoing laparoscopy led to reduction of TP, LF, and HF, maintenance with propofol in further reductions of TP and LF but not HF. Placement of the laparoscopic trocar led to an increase in HF. This was interpreted to mean that propofol had less of an effect on the parasympathetic tone than on the sympathetic tone, which makes the patients more sensitive to bradycardia-inducing events (Deutschman et al. 1994). In another study, LF, MF, and HF was decreased, but LF reduction was less than MF and HF reduction (Galletly et al. 1994b).

Induction with thiopental alone caused a higher blood pressure increase than a thiopental/midazolam induction. After induction with thiopental alone, HF increased under intubation conditions, whereas in the thiopental/midazolam group, HF continued to decrease (Nishiyama et al. 2002).

In a study comparing propofol and sevoflurane anesthesia, propofol had no effects on LF but induced a decrease in HF. Sevoflurane decreased LF but had no effect on HF. LF/HF ratio was not changed in either group (Kanaya et al. 2003).

Premedication with temazepam before induction with propofol or thiopental led to a higher HF, LF, and TP as without premedication but not in the LF/HF ratio. The induction itself induced reductions in TP and HF and an increase in LF/HF ratio (Howell et al. 1995).

Thirty-eight patients undergoing lung resection for cancer were randomized to thoracic-epidural treatment or general anesthesia followed by patient-controlled analgesia (PCA) as postoperative pain treatment. After operation there were no differences in regard to pain but lower incidence of hypertensive or tachycardia periods in patients with epidural. HRV data were collected four times, preoperatively, 4 h after the operation and at the first and second postoperative day. Frequency-domain measures were used. HRV values decreased generally after operation and remained low in both groups until the second postoperative day. However, in the epidural group, HRV increased day one and two. LF/HF remained unchanged in the PCA group all the time, whereas it was reduced during the whole observation period after use of epidurals. This was discussed as a shift in sympathovagal balance toward vagal predominance (Licker et al. 2003).

In a randomized study, propofol or propofol/midazolam inductions were compared and their effects on short-term HRV post-induction. Propofol was administered at 2.5 mg/kg in the propofol group and midazolam at 0.1 mg/kg followed by propofol at 1.5 mg/kg in the midazolam–propofol group. The midazolam–propofol combination had an increased LF/HF ratio the first minutes after induction, which was interpreted as compensated modulatory effects on the cardiovascular system (Win et al. 2007).

In summary, there is good evidence that anesthesia changes HRV parameters. In most studies LF increases and/or HF decreases, leading to a changed LF/HF ratio. No nonlinear factors have been tested, probably due to the necessary use of short-term HRV of less than 10 min.

Spinal Anesthesia

In spinal anesthesia, a small amount of local anesthetics is injected intrathecally on the level of L3 or L4, where damage to the spinal cord is unlikely. Depending on the amount, spinal anesthesia can anesthetize the legs or bigger parts of the body up to the Th4 level. The physiological effects of spinal anesthesia depend on the level. The effects depend also on the concentration of the agent, the speed of injection, the specific gravity of the solution, the position of the patient, the presence of increased intra-abdominal pressure, and other factors. The SNS is blocked in proportion to the height of the anesthesia level obtained. Total sympathetic block can be expected from high spinal anesthesia exceeding Th2. This produces a 15–20 % decrease in mean arterial pressure, central venous pressure, and total peripheral resistance. Cardiac output, stroke volume, and heart rate are not substantially affected but can change due the decreased resistance. Hypotension is a well-known side effect of spinal anesthesia and can be profound. In some departments, either infusion of 1 l saline or use of catecholamines is used as preventive measure. Here too, it is of interest to identify patients with possible major blood pressure drop after induction.

In a retrospective study, short-term HRV was analyzed in 41 patients scheduled for elective cesarean delivery. They were grouped in three categories: mild decrease of systolic blood pressure (>100 mmHg); moderate decrease (80–100); and severe decrease (<80). LF/HF was increased in patients with moderate to severe BP decrease (2.8; 2.7 and 1.2, respectively). In a prospective study with 19 patients, this result was confirmed (Hanss et al. 2005). These results led to an intervention study in the same patient group: patients received vasopressors or preoperative colloid infusion if LF/HF was greater than 2.5. Hypotension did not occur in 17 of 20 patients with LF/HF > 2.5; in the control group, 20 of 23 patients with LF/HF > 2.5 developed hypotension (Hanss et al. 2006).

Fifty two Patients undergoing elective transurethral surgery were tested before and after onset of spinal anesthesia with HRV, using traditional indices and ultra short-term entropy (UsEn) as a nonlinear index. The patients were then assigned to two groups (Group LO and HI) according to preoperative UsEn. Spinal anesthesia decreased LF/HF but did not affect UsEn. The number of patients who developed hypotension was significantly higher in the group with lower UsEn (Fujiwara et al. 2007).

Short-term HRV of 80 ASA I–II patients scheduled for spinal anesthesia was obtained, and the predictive value for severe bradycardia after onstart (defined as <45 bpm) was analyzed. Nineteen of 80 patients developed bradycardia. HF in the bradycardia group was significantly higher (1,061 ± 1,301 vs. 696 ± 1,378). With the help of ROC analysis, a sensitivity and specificity of 65 % was detected; however, low baseline HF had a sensitivity and specificity of 74 % (Chatzimichali et al. 2011).

The studies by Hanss are one of the few examples that used HRV (successfully) to guide interventions.

Maintenance of Anesthesia

In 20 spontaneously breathing patients undergoing minor surgical procedures with a propofol/fentanyl anesthesia, the relationship between heartbeats and respiration was examined. There was evidence for phase coupling in whole number ratios. Phase coupling seemed to be unidirectional from the respiratory system to the sinus rhythm. Six different coupling patterns were observed (Galletly and Larsen 1997). Apnea during stable anesthesia leads to reduction of HF but not LF (Nakatsuka et al. 2002).

Using point correlation dimension (PD2), it was possible to predict hypotension accompanying spinal anesthesia for cesarean delivery in all 11 patients with a systolic blood pressure <75 % of baseline compared to 11 patients without hypotension (Chamchad et al. 2004). Short-term HRV was used to monitor the stress response during awake craniotomy. Specially LF/HF ratio yielded a stress/response pattern and could probably be used to monitor stress responses during anesthesia (Conte et al. 2009).

Postoperative Course

One hundred and six patients admitted in the ICU after abdominal aortic surgery were analyzed with the help of 24-h Holter ECGs. VLF was a rather strong predictor for length of stay at the ICU. Other predictors were increased age and insulin-dependent diabetes (Stein et al. 2001).

Eighty patients with a history of PAF were evaluated by Holter monitoring and blood samples measuring neuropeptides and catecholamines pre- and postoperatively. 36.3 % of patients developed AF postoperatively and showed a significant lower HF and LF/HF ratio. HF decreased in both groups postoperatively. Neither neuropeptides nor catecholamines differed between the groups (Jideus et al. 2001).

Between 1994 and 1996, Mamode examined 297 patients in terms of different risk factors for perioperative mortality undergoing peripheral arterial surgery (92 aortic, 47 carotid, 37 infrainguinal, 13 major amputation, and 108 miscellaneous procedures) and used Holter monitoring to obtain HRV (SDNN, SDANN5, triangular index, and pNN50). The primary end point of the study was the occurrence of myocardial infarction or cardiac death within 30 days of surgery. Twenty-one patients had myocardial infarction or died within 30 days. Independent end point predictors determined through a logistic regression analysis were increased age, ECG evidence of previous myocardial infarction, aortic surgery, impaired heart rate variability (triangular index), and positive thallium scan. The mean triangular index for patients with fatal events was 21.5 (±1.7), for patients without 26.6 (±0.6). The authors propose a cutoff value of <25 to identify high-risk patients. Interestingly, SDNN seemed not to be a significant factor in the statistical model, neither in univariate analysis; it is not mentioned in the results of the article (Mamode et al. 2001).

Laitio studied 32 patients over 60 who had been admitted to hospital for surgical repair of a traumatic hip fracture. He used preoperative Holter monitoring. Twelve patients experienced in all 384 ischemic episodes. Preoperative α1 was significantly lower (i.e., increased randomness in HRV) during nighttime compared with daytime in patients with postoperative myocardial ischemia. In stepwise multivariate logistic regression analysis, increased preoperative night/day difference of α1 was the only independent predictor of postoperative prolonged ischemia. LF in patients with no ischemia was 179 ± 63 compared with 278 ± 131 in patients with ischemic episodes, HF 127 ± 34 compared to 325 ± 176. SDNN was 28.9 ± 3.3 compared to 30.1 ± 4.8. Thus, although only α1 remained significant in this small study, it is not improbable that LF and HF can be relevant predictive factors if analyzed in a higher number of patients (Laitio et al. 2004).

With a prospective study, Filipovic showed that LF/HF ratio <2 analyzed only 6 min before induction of anesthesia was the best predictor for 2 year all-cause mortality in 167 patients (odds ratio 6.4, CI 1.9–21). This study included risk score established by Eagle et al. (2002) and Detsky et al. (1986) and the Revised Cardiac Risk Index (Lee et al. 1999). The only other main independent predictors were a history of congestive heart failure and age over 70 (Filipovic et al. 2005).

Our own preliminary results in hip fracture patients support the studies above. In a pilot study, we enrolled 22 consecutive patients with hip fracture scheduled for operation. Within 24 h after the event, we took a 10-min ECG analyzed for time and frequency domain, in addition ApEN. Perioperative complications were recorded, including pneumonia and cardiac events. Thirty percent of patients had some perioperative problems, such as stroke, MI, or pneumonia. We found significant univariate associations between perioperative problem and several HRV parameters. Heart rate, TP, normalized LF and HF, LF/HF, and VLF were significantly lower in patients developing postoperative problems. In multivariate analysis, LF/HF and VLF had the highest predictive value (Ernst G, 2011, unpublished results) (Fig. 9.1).

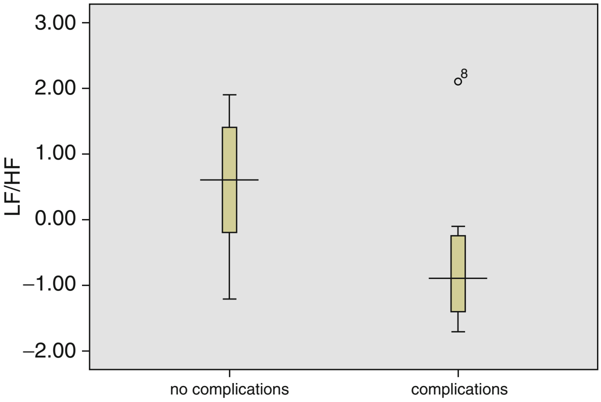

Fig. 9.1 LF/HF and perioperative complications

Conclusion

There is evidence that preoperative HRV measurement offers a feasible technique for stratifying perioperative risks and for estimating the need for further preoperative evaluation and optimization. Mazzeo concludes: "In an ideal setting, a preoperative HRV measurement should be performed to evaluate perioperative risk in patients with known ANS dysfunction or in patients with suspected dysautonomia undergoing high risk procedures." Mazzeo suggests that such an evaluation be performed at least 2 weeks before scheduled operation (Mazzeo et al. 2011). Different linear and nonlinear HRV measures have been used to identify patients at risk before surgical procedures and to predict successful outcome in therapeutic procedures. There have been some promising results, but HRV analysis in anesthesiology has not been used often. Thus, it is not possible to draw conclusions regarding clinical usefulness. Mazzeo et al. (2011) proposes to investigate patients with cardiac history or an existing risk for ANS imbalances at least 2 weeks before elective surgery and to use HRV beyond others to select patients who need further examination (e.g., by cardiologists) preoperatively. Existing studies offer strong evidence in this regard, but this conclusion seems premature. We need more efficacy studies that not only describe HRV abnormalities but also use the results within a preoperative algorithm.

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