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Keet, S.W.M.

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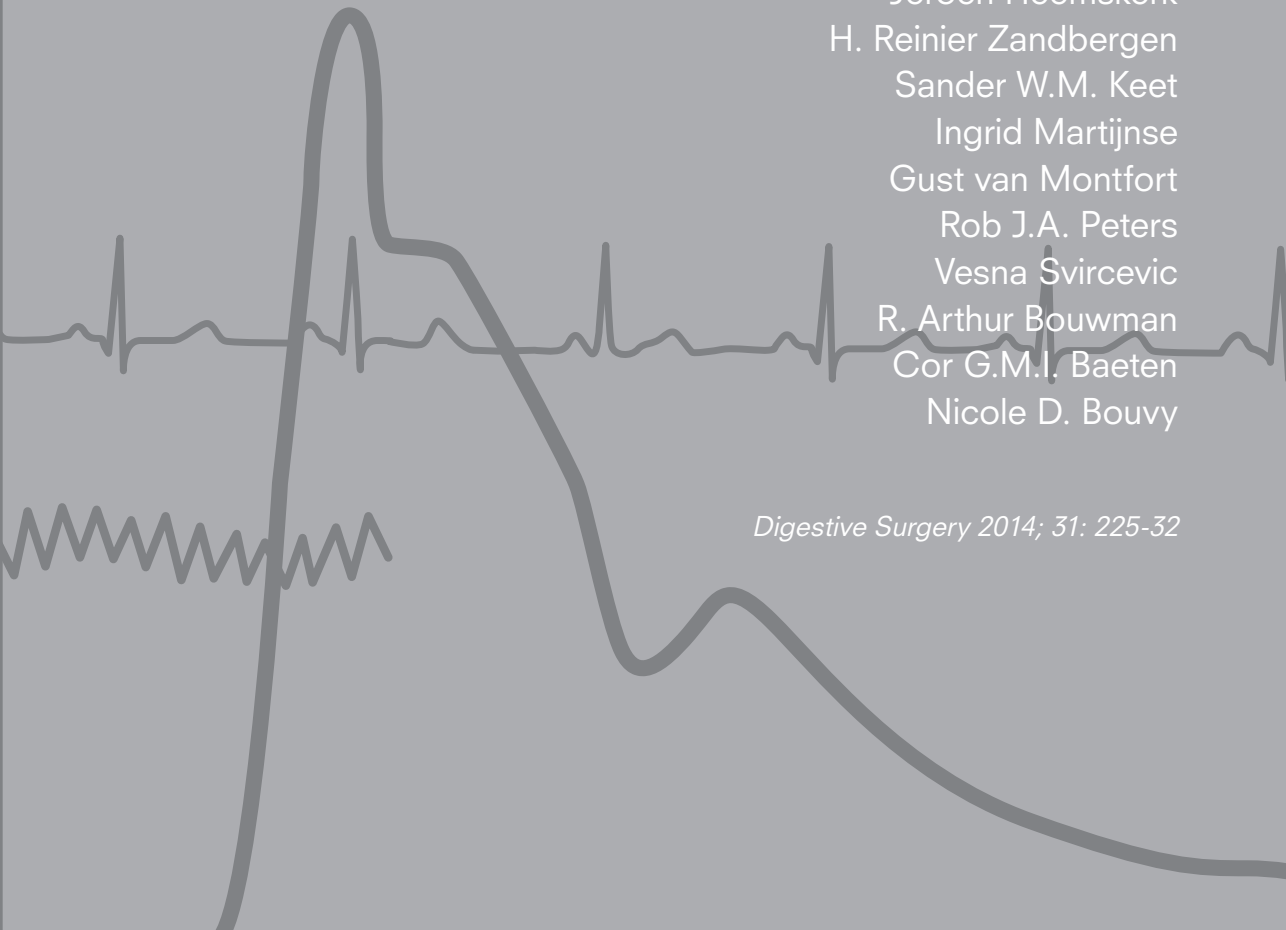
# Chapter 9

Relax, it's just laparoscopy!

A prospective randomised trial on heart rate variability of the surgeon in robot-assisted versus conventional laparoscopic cholecystectomy

Jeroen Heemskerk  
H. Reinier Zandbergen  
Sander W.M. Keet  
Ingrid Martijnse  
Gust van Montfort  
Rob J.A. Peters  
Vesna Svircevic  
R. Arthur Bouwman  
Cor G.M.J. Baeten  
Nicole D. Bouvy

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## ABSTRACT

**Introduction:** Laparoscopic surgery might be beneficial for the patient, but it imposes increased physical and mental strain on the surgeon. Robot-assisted laparoscopic surgery addresses some of the laparoscopic drawbacks and may potentially reduce mental strain. This could reduce the risk of surgeon's fatigue, mishaps and strain-induced illnesses, which may eventually improve the safety of laparoscopic surgical procedures.

**Methods:** To test this hypothesis, a randomised study was performed, comparing both heart rate and heart rate variability (HRV) of the surgeon as a measure of total and mental strain respectively during conventional and robot-assisted laparoscopic cholecystectomy.

**Results:** Heart rate was decreased and heart rate variability was significantly increased using robotic assistance.

**Conclusion:** These data suggest the use of the daVinci® Surgical System leads to less physical and less mental strain of the surgeon during surgery. However, assessing mental strain by means of heart rate variability is cumbersome since there is no clear cut-off point or scale for maximum tolerated strain levels and its related effects on surgeon's health.

## INTRODUCTION

The demanding nature of surgery poses significant physical and mental strain on surgeons. Increased sympathetic activity increases mean heart rate over 120 beats per minute (bpm) during surgery. Peak heart rates well over 150 bpm secondary to catecholamine release have been reported [1]. Although laparoscopic surgery is beneficial for patients in terms of postoperative pain, convalescence and duration of hospital admission, various drawbacks may contribute to increased mental and physical strain for the surgeon. Advanced laparoscopic procedures compared to conventional open surgery are more time consuming and exhausting, and may thus contribute to an increase in mental strain [2]. Mental strain has been identified as a risk factor for the development of myocardial infarction, hypertension, atherosclerosis, arrhythmia, heart failure and sudden death. This might account for the impaired health of physicians and other professionals suffering from high work-related mental strain [3-6].

Robotic assistance in laparoscopic surgery addresses some of the drawbacks such as inconvenient posture, non-intuitive manipulation suffering from limited degrees of freedom and a fulcrum effect, and two-dimensional vision. Therefore, the use of robots could potentially lead to faster, more accurate and less exhausting surgery. Despite numerous comparative studies, the benefits of robot-assisted laparoscopy over conventional laparoscopy previously shown in preclinical studies [7-8], could not be convincingly affirmed in clinical studies in terms of time consumption, complication rate or cost-effectiveness [9-11]. However, the improved ergonomics from robotic assistance may well reduce operative mental strain of the surgeon, leading to reduced fatigue, less complications and perhaps to a better outcome. In addition, it might reduce stress-induced illness of the surgeon.

In this study, we investigated the level of experienced mental strain of the surgeon performing robot-assisted laparoscopic surgery compared to conventional laparoscopic surgery. We decided to differentiate between stress and strain, according to the definition used by Böhm et al [2]. While stress comprises all objective environmental factors influencing an individual, strain is defined as the physical and mental effects of this stress on the individual. A variety of conditions or stressors (even under defined stress conditions) may give rise to different physical responses and different perceived levels of strain. This depends on coping mechanisms, previous experience, level of training and the emotional status of the surgeon at a specific time. For example, an experienced surgeon may be more relaxed intraoperatively than a less experienced surgeon

when an inadvertent bleeding occurs. Therefore, perceived mental strain seems to be more relevant than stress. Although total strain (defined as a combination of mental and physical strain) is probably best assessed by measuring heart rate and physical strain is best measured by physical activity, mental strain can be best assessed by measuring heart rate variability (HRV) of the surgeon [12]. HRV is the quantitative assessment of beat-to-beat variation in heart rate reflecting parasympathetic and sympathetic control of the sinoatrial node. The autonomic nervous system is a major determinant of the functional properties of the heart in that it alters spontaneous sinus node depolarisation and cardiac rhythm. Increased mental strain leads to a more regular heart rhythm and thus decreased HRV [13-15]. In particular, the low frequency component (LF) increases whilst the high frequency component (HF) decreases. Previously, intraoperative HRV measurements in surgeons performing general [16] or thoracic surgery [17] showed significant increased heart rate and a decreased HRV in surgeons.

We hypothesised that the use of robotic assisted laparoscopy might support the surgeon sufficiently to decrease mental strain compared to conventional laparoscopy, bringing heart rate variability levels back to lower levels while still offering the benefits of laparoscopic surgery to the patient.

## **METHODS**

### **Participants**

In order to minimise inter-individual variations, only two surgeons (one female and one male) participated in this study (I.M. and G.v.M.). Both of them were sufficiently experienced in conventional and robot-assisted laparoscopic cholecystectomy to perform the operation safely and with adequate comfort levels. In order to reduce external influences as much as possible, preoperative activities were standardised [18-19]. The procedures were performed after at least 7 hours of sleep the night before. Participants refrained from smoking, alcohol and caffeine-containing beverages from 24 hours before the surgical procedure. The participants were cardiovascular healthy and used no cardiac modifying medication.

### **ECG recording**

R-R intervals were obtained from standard bipolar ECG leads connected to a recorder. The electrocardiogram recorded continuously with a sam-

Table 1.  
The seven stages of laparoscopic cholecystectomy.

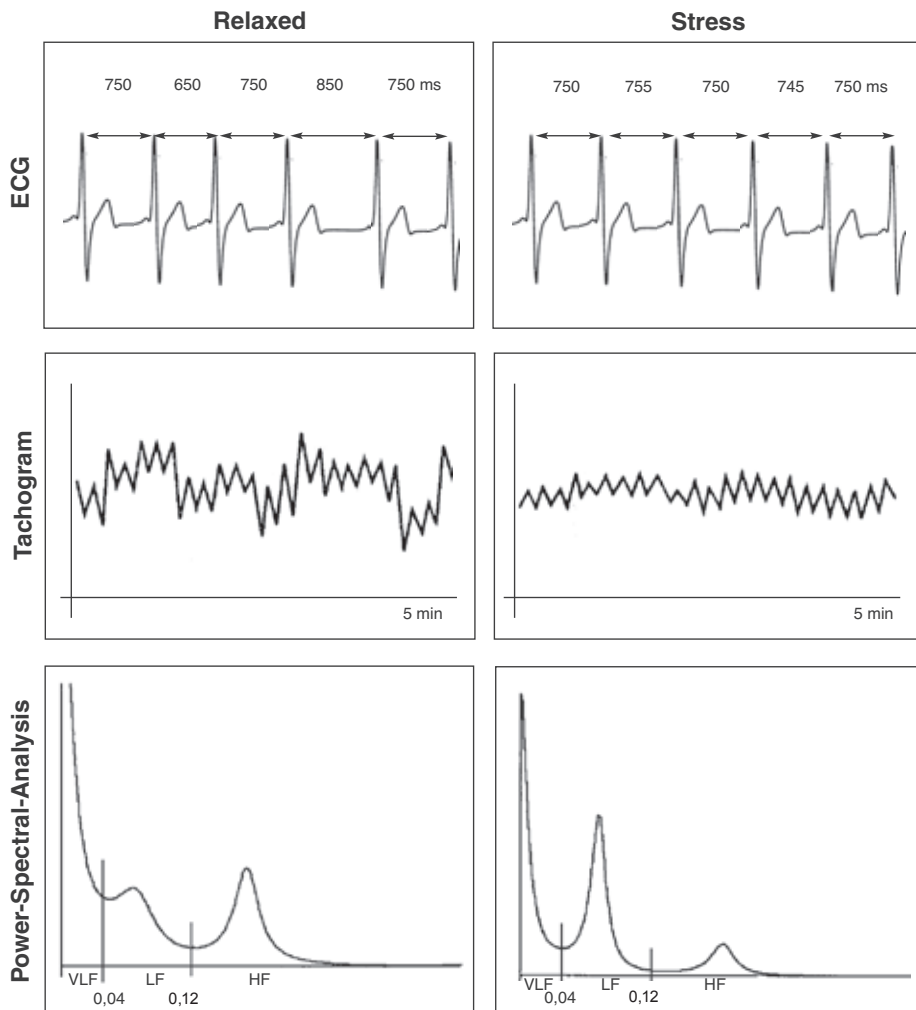
Stages	Procedure
1	Baseline
2	First incision and introduction of the trocars
3	Dissection of Calot's triangle
4	Clip and cut of the cystic duct and artery
5	Dissection of the gallbladder from the liver bed
6	Removal of the gallbladder
7	Closure of the incisions

ple rate of 400 Hz. All digital data were transferred to a personal computer after surgery for off-line analysis. Using one baseline and six well-defined stages in the surgical procedure as explained in Table 1, seven interval tachograms of five minutes beginning at the start of each stage were selected and analysed.

### HRV analysis

Since mental strain is difficult to measure, HRV was chosen as the primary end point. HRV analysis was performed according to the recommendations of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [20]. Signals were visually inspected for premature beats, arrhythmias and movement artefacts and further analysed using free available software (Kubios HRV version 2.0, University of Kuopio, Finland) [21]. Mean heart rate and R-R intervals were analysed. From the recorded R-R intervals, this software performs spectral analysis using fast Fourier transformation, and translates the overall variability into its composing frequencies. This provides insight into what extent a frequency contributes to the overall variability of the signal. The power spectrum of HRV has been shown to consist of three peaks: the very low frequency (VLF) band (<0.04 Hz), the low frequency (LF) band (0.04 – 0.12 Hz) and the high frequency (HF) band (0.12 – 0.40 Hz) [19-22]. Increased mental strain is closely associated with increased sympathetic and decreased parasympathetic (vagal) activity, leading to an increased LF component, a decreased HF component and an increased LF/HF Ratio [23] as explained in Figure 1.

Figure 1.  
Heart rate variability in a relaxed state and under severe mental strain.



ECG indicates electrocardiogram; VLF, very low frequency component; LF, low frequency component; and HF, high frequency component.

### Study protocol

In order to obtain reliable, well-comparable data, selection of a well-standardised procedure with limited variation in operation-induced mental strain to the surgeon was necessary. Therefore, only elective laparoscop-

ic cholecystectomy procedures were studied. Procedures in patients with (a history of) acute cholecystitis were excluded. The type of procedure (conventional vs robot-assisted laparoscopic cholecystectomy) was randomised on the day of the operation. Laparoscopic cholecystectomy was performed using a 4-trocar technique. In case of robot-assisted cholecystectomy, the daVinci® four-armed telemanipulator was used as described by Heemskerk et al. [9]. A professional dedicated scrubbed assistant participated throughout the entire operative procedure. Before surgery, the surgeon was connected to the Holter portable recording unit and a 5-minute baseline ECG was obtained during rest in a relaxed setting at least 15 minutes before surgery and continuously throughout the surgical procedure.

### Statistical Analysis

Statistical analysis was carried out using SPSS 19 (SPSS Inc., Chicago, IL, USA). Univariate differences between two groups were analysed using the Student T-test for the parametric and the Mann-Whitney U test for the non-parametric data. Primary outcome of interest was defined as LF/HF ratio of the surgeon. We tested the null hypothesis that robot-assisted laparoscopic cholecystectomy (RC) does not lead to an altered HRV with the surgeon, compared to conventional laparoscopic cholecystectomy (CC). The alternative hypothesis was that RC does change HRV compared to CC. Secondary outcome parameters were Heart Rate and VLF, LF and HF components during the surgical procedure, and duration of the operative procedure.

## RESULTS

Procedures were not totally evenly distributed between the two surgeons. G.v.M. performed 5 RC and 2 CC procedures, whereas I.M. performed 6 RC and 9 CC procedures. Operating time was measured, starting from first skin incision until the final suture. Robot-assisted laparoscopic cholecystectomy (RC) did take significantly longer to perform than conventional laparoscopic cholecystectomy (CC) (86 vs 48 minutes,  $p=0.003$ ). Intraoperative complications did not occur and there were no conversions in either group. The postoperative course of all patients was uneventful. Heart rate registration and heart rate variability analysis were performed, comparing the RC and the CC group. Results are shown in Table 2.



Table 2.  
Mean heart Rate and VLF, LF, HF and LF/HF ratio during the seven stages of the operation in robot-assisted and conventional procedures.

Heart Rate mean (SD)			
	RC	CC	p
1 Baseline	84.6 (10.4)	84.9 (5.6)	0.93
2 Trocar placement	82.7 (5.9)	89.2 (7.3)	0.01
3 Dissection Calot	78.7 (7.9)	92.8 (6.9)	<0.001
4 Clip and cut	75.7 (9.4)	97.2 (6.7)	<0.001
5 Dissection gallbladder	75.3 (8.9)	96.2 (6.7)	<0.001
6 Start removal	76.6 (11.1)	95.6 (7.4)	<0.001
7 Closure	79.3 (5.6)	91.3 (4.9)	<0.001
VLF median (range)			
	RC	CC	p
1 Baseline	1987 (605-39739)	1354 (633-3737)	0.28
2 Trocar placement	609 (271-6006)	1268 (166-4117)	0.87
3 Dissection Calot	1746 (501-3546)	526 (159-930)	0.01
4 Clip and cut	1180 (792-11631)	581 (209-934)	<0.001
5 Dissection gallbladder	1486 (394-11177)	704 (107-1370)	0.03
6 Start removal	1303 (769-2560)	864 (372-1938)	0.02
7 Closure	2350 (1268-18422)	845 (351-1194)	<0.001
LF median (range)			
	RC	CC	p
1 Baseline	741 (204-2344)	941 (370-2755)	0.34
2 Trocar placement	965 (572-1916)	730 (285-2630)	0.31
3 Dissection Calot	956 (309-3682)	436 (233-832)	0.01
4 Clip and cut	506 (255-4846)	592 (198-1057)	0.47
5 Dissection gallbladder	513 (321-3861)	436 (194-1136)	0.36
6 Start removal	902 (270-2.220)	487 (148-1076)	0.05
7 Closure	1829 (821-5494)	522 (227-1218)	<0.001
HF median (range)			
	RC	CC	p
1 Baseline	266 (45-2868)	277 (145-1102)	0.77
2 Trocar placement	447 (168-3073)	176 (83-1381)	0.01
3 Dissection Calot	308 (153-1623)	218 (75-404)	0.05
4 Clip and cut	418 (184-6037)	170 (51-374)	0.01
5 Dissection gallbladder	569 (157-3062)	171 (53-491)	0.01
6 Start removal	600 (164-5000)	158 (59-444)	0.01
7 Closure	500 (179-3399)	152 (76-248)	<0.001

		LF/HF Ratio median (range)		
		RC	CC	p
<b>1</b>	<b>Baseline</b>	2.67 (0.38-8.82)	2.70 (1.54-7.51)	0.62
<b>2</b>	<b>Trocar placement</b>	2.23 (0.31-5.75)	3.30 (1.48-9.45)	0.18
<b>3</b>	<b>Dissection Calot</b>	2.26 (0.65-4.67)	2.26 (1.08-6.08)	0.67
<b>4</b>	<b>Clip and cut</b>	1.21 (0.31-2.21)	2.98 (1.66-5.60)	<0.001
<b>5</b>	<b>Dissection gallbladder</b>	1.60 (0.25-3.28)	3.12 (0.77-4.16)	0.01
<b>6</b>	<b>Start removal</b>	1.48 (0.39-2.62)	2.71 (1.34-8.50)	0.01
<b>7</b>	<b>Closure</b>	2.99 (1.41-5.93)	3.48 (1.55-7.43)	0.38

VLF, very low frequency component; LF, low frequency component; HF, high frequency component; and LF/HF ratio, ratio between low frequency and high frequency components. RC means robot-assisted laparoscopic cholecystectomy and CC means conventional laparoscopic cholecystectomy.

Figure 2 shows the mean heart rate for both groups during the seven stages of the operation. We did not study whether there was inter-observer variability in defining when a new stage started. The baseline was the same for both groups, but in the course of the operation, CC led to a significantly higher mean heart rate compared to baseline level, whereas RC led to a lower HR compared to baseline level. As an example, during stage four (clipping and cutting of cystic artery and duct), mean heart rate increased from 84.9 at baseline to 97.2 when performing CC. However, when using robotic assistance, mean heart rate decreased from 84.9 at baseline to 75.7.

Figure 3 shows the LF/HF ratio for both groups over the seven stages of the surgical procedure. Again, the baseline was similar for both groups, but during the operation, CC led to a significant higher LF/HF ratio than RC. Figure 3 exemplifies the significant differences in LF/HF ratio during the different stages.

Interestingly, the LF/HF ratios performing RC are significantly lower than those performing CC during stage four, five and six of the operation, even despite the rather small numbers of operations (Figure 4).

Figure 2.  
Heart rate during the seven stages of the operation.

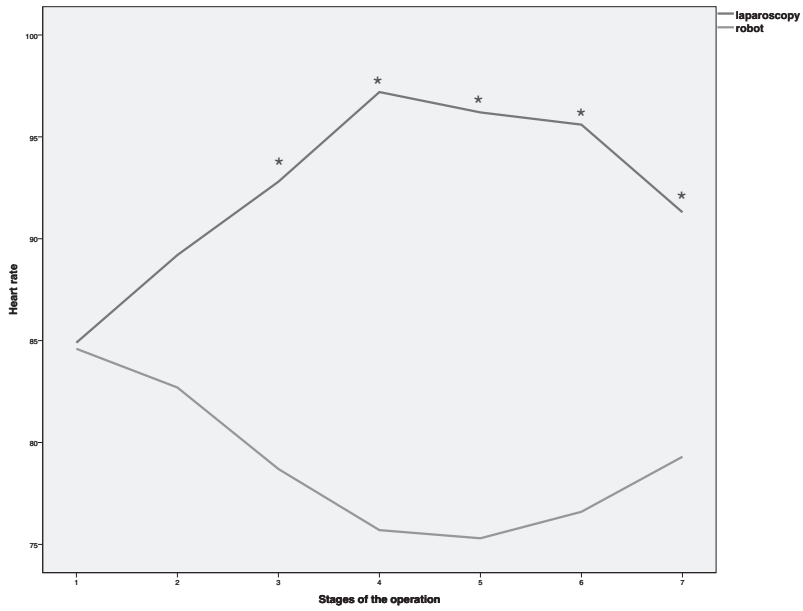


Figure 3.  
LF/HF ratio during the seven stages of the operation.

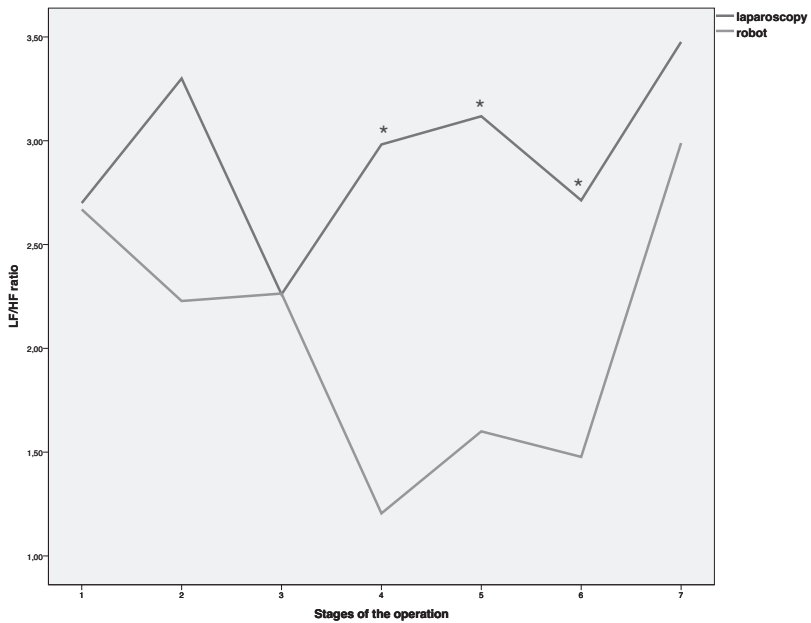
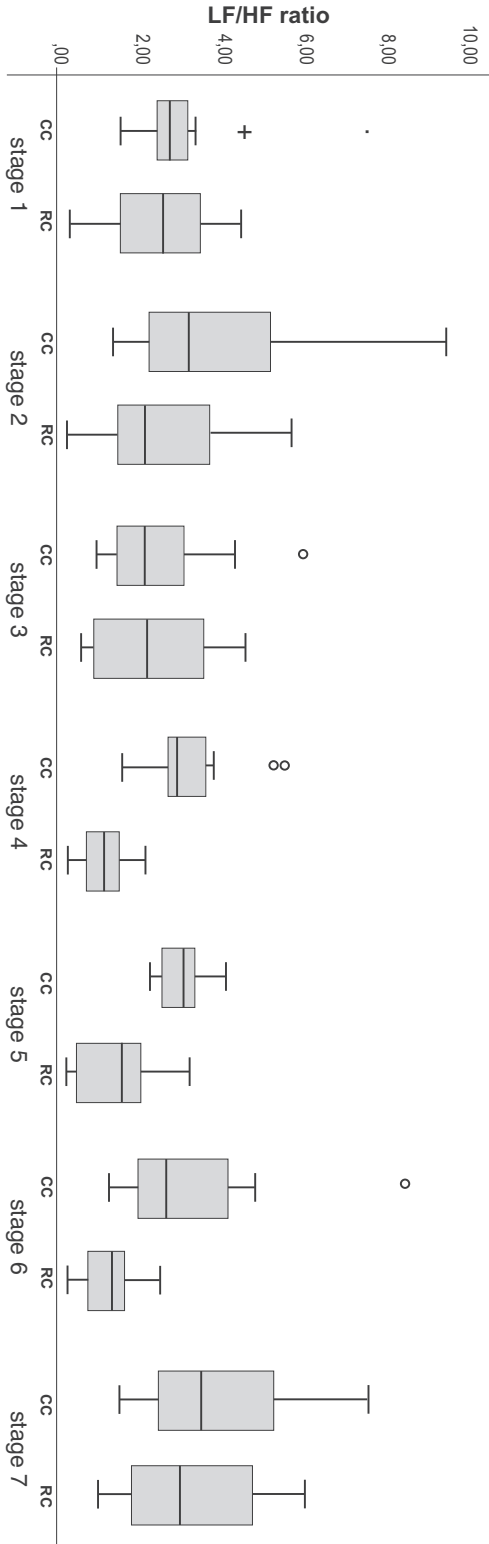


Figure 4.  
Boxplot diagram of the LF/HF ratio during the seven stages of the operation.



RC means robot-assisted laparoscopic cholecystectomy and CC means conventional laparoscopic cholecystectomy.

## DISCUSSION

In this study we measured heart rate and its variability in surgeons performing a conventional or robot-assisted laparoscopic cholecystectomy. Our results show that the mean heart rate during robotic assisted laparoscopic cholecystectomy is lower compared to conventional laparoscopic cholecystectomy. This suggests that the use of robotic assistance for this procedure reduces total strain, which is combined physical and mental strain. However, mean heart rate differences alone cannot differentiate between physical and mental strain. We therefore performed HRV analysis.

The relatively high baseline heart rate of the surgeons in both groups, might suggest that wearing a Holter device in participating in this study might in itself be stressful. Interestingly, the LF/HF ratio was lower when the surgeon used robot-assistance for the cholecystectomy. This suggests that a commonly performed and generally considered hardly stressful laparoscopic procedure leads to significant mental strain and that the use of robotic assistance seems to be able to significantly reduce this mental strain. The more ergonomic position of the surgeon and the motorised manipulation offered by robotic-assistance may reduce physical strain on the surgeon, and may explain our findings. This line of reasoning is supported by evidence of Klein et al. [16], who suggest that optimal ergonomics in the operating room are able to reduce mental strain in the operating surgeon. They clearly show a decrease in postoperative physical strain and pain measurements in the surgeon working in a modern, ergonomically optimised operating room compared to the surgeon working in a standard operating room. However, other parameters undermined their conclusions, as differences in HRV parameters were not detected because of high inter- and intra-individual variation. In our study, we therefore limited our surgeons to two individuals performing well-standardised operations, leading to a lower inter- and intra-individual variation. Preoperative power analysis showed that a sample size of 11 patients per group should be sufficient to compensate for such variation and for other surgeon related factors (compliance with adequate sleep, no alcohol and no caffeine, mental strain from other factors unrelated to surgery) as well as for patient related factors (BMI, medical co-morbidities, prior surgery).

Surgeons generally evaluate a procedure based on the advantages and disadvantages for their patients. It is rather unconventional to assess the drawbacks imposed on the surgeon, such as increased physical or mental strain and fatigue. Our present results were quite comparable

with previous publications [1, 24-25], which demonstrate that increased mental and physical strain during surgery can significantly increase the surgeon's heart rate till well up to 150 bpm. Importantly, these excessive tachycardia rhythms were not limited to generally considered "high risk operations". They also included generally considered "low risk and low strain" operations such as cholecystectomy and hernia surgery. Whether experienced surgeons really are as well adapted to this kind of stress as stated above remains debatable [26]. The fact that the vast majority of surgeons reach these extreme fast heart rhythms during their daily occupational activities, and that they are at a significantly increased risk of death from ischaemic heart disease compared to general practitioners, might suggest that even experienced surgeons might overestimate their own capability of coping with occupational strain [27].

Looking at the different stages of the operation, it is interesting to notice that the significant difference in LF/HF ratio between CC and RC is present in stage four (clip and cut of the cystic artery and duct), stage five (dissection of the gallbladder from the liver bed) and stage six (removal of the gallbladder). During stage three (dissection of Calot's triangle) there was no significant difference. This is quite remarkable, since stage three could generally be considered one of the most stressful stages of the operation. An explanation could be, that the measurable physical effects of decreased heart rate variability due to increased sympathetic activity caused by increased mental strain, do only occur after a delay of a few minutes. In that case, the interval tachograms should probably have been selected only after a delay of three to five minutes. We did not perform such an analysis in this study.

Studies comparing HRV in conventional open surgery versus laparoscopic surgery have previously been published. However, to our knowledge there have been no previous publications comparing conventional laparoscopic surgery and robot-assisted surgery. Therefore, we are the first to show that the use of high-tech surgical solutions such as the da-Vinci® Surgical System seems to be able to reduce the increased mental strain that is being put on the surgeon during the performance of minimal invasive surgical procedure. This suggests the use of robotics in minimal invasive surgery might well lead to improved ergonomics, less fatigue, and better health of the surgeon.

### Limitations

Several limitations need to be taken into account with the interpretation of the present results. Assessing mental strain by means of heart rate variability is cumbersome. This is partly due to the fact that interpreta-

tion of HRV is challenging and subject to bias. As we measured only a limited number of participants and focused on HRV changes in time, we circumvented several of the potential sources of bias of HRV analysis. Secondly, previous studies have shown that laparoscopic surgery is more demanding than conventional open surgery and puts a higher mental strain on surgeons [2]. Our study suggests that the use of robotic assistance in laparoscopic surgery might (partially) compensate for this increase in mental strain imposed on the surgeon. Although reference values for short-term heart rate variability in healthy adults have been determined [28], there is no clear cut-off point or scale for critical mental strain during surgery. Furthermore, as the effects of daily recurrent increased mental strain and the potentially associated health risk for the surgeon are unclear, the exact relevance of the observation on the difference in LF/HF ratio for clinical practice remains speculative. Thirdly, from our present results we cannot accurately differentiate between the relative contributions of mental strain and physical activity on our findings regarding HRV. However previous studies comparing laparoscopic versus open procedures have been using the HRV parameter similarly [2].

During both procedures we found remarkably high heart rates at baseline. It might be questioned whether this is a normal physiological phenomenon, or whether the measurements were biased by the extra mental strain caused by the study circumstances. Surgeons may not recognise this anticipative strain themselves, and also we may be underestimating the effects of surgery on the surgeon's body and mind. This is nicely illustrated by the previous publication by Foster et al. [1]. In this study it was demonstrated that all surgeons who participated in their study did have significant tachycardia during surgery, even while performing quite routinely low-stress operations such as hernia repair and cholecystectomy. Interestingly, a significant rise in heart rate well over 100 bpm began as soon as scrubbing for an operation was commenced. The mean heart rate for the whole group was over 120 bpm, with peak heart rates of over 150 bpm. These data suggest that significant preoperative anticipative mental strain and intraoperative mental strain do occur on a regular basis in general surgery. Considering these observations, the surgeons in our present study were not more stressed compared to other surgeons studied before [16].

### **Future studies**

Our study was limited to surgeons performing laparoscopic cholecystectomy, generally considered a relatively low stress well-standardised operation. It would be very interesting to see if the differences in HRV

increase if a more stressful operation is selected such as laparoscopic total mesorectal resection or surgery for aortic aneurysm.

At this moment, the exact impact of decreased HRV on the health status of the surgeon is difficult to measure, although previous studies have shown a significant increase in potentially lethal health issues after prolonged exposure to decreased HRV [29]. More research should be performed in order to clarify whether a decrease in HRV does impose an unacceptable health risk on the surgeon which would therefore warrant stress-reducing measures such as the acquisition of high-tech, costly, ergonomically improving tools such as the daVinci® Surgical System.

### **Conclusion**

We conclude that the use of robotic assistance in laparoscopic surgery leads to a significant decrease in mean heart rate and an increase in heart rate variability of the surgeon during surgery, strongly suggesting a reduction in intraoperative mental strain.

A decrease in mental strain of the surgeon could potentially lead to less fatigue, less surgical mistakes and less stress-induced illnesses to the surgeon. The continuous drive to introduce new, less invasive techniques for our patients is leading to exposure of our surgeons to more stress inducing techniques. In an era where mean life expectancy increases and the length of the medical career elongates accordingly with it, prevention of work-related stress induced illnesses is likely to increase in importance. The use of robotics could therefore potentially prove to be beneficial to the health of both patients and surgeons. Preventing work related illnesses and associated work incapacity, the acquisition and use of a robotic surgical system might prove to be a cost effective strategy to enable surgeons to perform minimally invasive surgery until their retirement at old age.

The associated disadvantages such as increased operative time and increased costs have to be taken into account before a decision can be made to use or abandon robotic surgery. Until then, surgeons should be aware that if they try to accomplish multiple, prolonged and demanding procedures per day, they will probably risk the health of their patients through exhaustion-induced surgical mishaps, as well as risking their own health.



## REFERENCES

1. Foster, GE, Evans DF, Hardcastle JD. Heart-rates of surgeons during operations and other clinical activities and their modification by oxprenolol. *The Lancet* 1978; 1: 1323-5.
2. Böhm B, Rötting N, Schwenk W, et al. A prospective randomized trial on heart rate variability of the surgical team during laparoscopic and conventional sigmoid resection. *Archives of Surgery* 2001; 136: 305-10.
3. Vrijkotte TG, vanDoornen LJ, de Geus EJ. Effects of work stress on ambulatory blood pressure, heart rate, and heart rate variability. *Hypertension* 2000; 35: 880-6.
4. Lynch J, Krause N, Kaplan GA, et al. Workplace demands, economic reward, and progression of carotid atherosclerosis. *Circulation* 1997; 96: 302-7.
5. Siegrist J, Peter R, Junge A, et al. Low status control, high effort work and ischemic heart disease: prospective evidence from blue-collar men. *Social Science & Medicine* 1990; 31: 1127-34.
6. Bosma H, Peter R, Siegrist J, et al. Two alternative job stress models and the risk of coronary heart disease. *American Journal of Public Health* 1998; 88: 68-74.
7. Garcia-Ruiz A, Gagner M, Miller JH, et al. Manual vs robotically assisted laparoscopic surgery in the performance of basic manipulation and suturing tasks. *Archives of Surgery* 1998; 133: 957-61.
8. Sarle R, Tewari A, Shrivastava A, et al. Surgical robotics and laparoscopic training drills. *Journal of Endourology* 2004; 18: 63-9.
9. Heemskerk J, van Dam R, van Gemert WG, et al. First results after introduction of the four-armed daVinci Surgical System in fully robotic laparoscopic cholecystectomy. *Digestive Surgery* 2005; 22: 426-31.
10. Heemskerk J, van Gemert WG, Greve JW, et al. Robot assisted versus conventional laparoscopic Nissen fundoplication. *Surgery Laparoscopy Endoscopy & Percutaneous Techniques* 2007; 17: 1-4.
11. Heemskerk J, de Hoog DE, van Gemert WG, et al. Robot-assisted versus conventional laparoscopic rectopexy for rectal prolapse: a comparative study on costs and time. *Diseases of the Colon & Rectum* 2007; 50: 1825-30.
12. Pagani M, Furlan R, Pizzinelli P, et al. Spectral analysis of R-R and arterial pressure variabilities to assess sympatho-vagal interaction during mental stress in humans. *Journal of Hypertension* 1989; 7: S14-5.
13. Hjortskov N, Rissen D, Blangsted AK, et al. The effect on mental stress on heart rate variability and blood pressure during computer work. *European Journal of Applied Physiology* 2004; 92: 84-9.
14. Nieminen T, Kähönen M, Kööbi T, et al. Heart rate variability is dependent on the level of heart rate. *American Heart Journal* 2007; 154: e13.
15. Nunan D, Sandercock GR, Brodie DA. A quantitative systematic review of normal values for short-term heart rate variability in healthy adults. *Pacing and Clinical Electrophysiology* 2010; 33: 1407-17.
16. Klein M, Andersen LP, Alamili M, et al. Psychological and physical stress in surgeons operating in a standard or modern operating room. *Surgery Laparoscopy Endoscopy & Percutaneous Techniques* 2010; 20: 237-42.
17. Song MH, Tokuda Y, Nakayama T, et al. Intraoperative heart rate variability of a cardiac surgeon himself in coronary artery bypass grafting surgery. *Interactive Cardiovascular and Thoracic Surgery* 2009; 8: 639-41.
18. Gerritsen J, TenVoorde BJ, Dekker JM, et al. Measures of cardiovascular autonomic nervous function: agreement, reproducibility, and reference values in middle age and elderly subjects. *Diabetologia* 2003; 46: 330-8.

19. Keet SW, Bulte CS, Boer C, Bouwman RA. Reproducibility of non-standardised autonomic function testing in the pre-operative assessment screening clinic. *Anaesthesia* 2011; 66: 10-4.
20. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation* 1996; 93: 1043-65.
21. Niskanen JP, Tarvainen MP, Ranta-Aho PO, Karjalainen PA. Software for advanced HRV analysis. *Computer Methods and Programs Biomedicine* 2004; 76: 73-81.
22. Vinik AI, Ziegler D. Diabetic cardiovascular autonomic neuropathy. *Circulation* 2007; 115: 387-97.
23. Akselrod S, Gordon D, Ubel FA, Shannon DC, Berger AC, Cohen RJ. Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. *Science* 1981; 213: 220-2.
24. Payne RL, Rick JT. Heart rate as an indicator of stress in surgeons and anaesthetists. *Journal of Psychosomatic Research* 1986; 30: 411-20.
25. Czyzewska E, Kicka K, Czarnacki A, et al. The surgeon's mental load during decision making at various stages of operations. *European Journal of Applied Physiology* 1983; 51: 441-6.
26. Becker WG, Ellis H, Goldsmith R, et al. Heart rates of surgeons in theatre. *Ergonomics* 1983; 26: 803-7.
27. Arnetz BB, Andreasson S, Strandberg M et al. Comparison between surgeons and general practitioners with respect to cardiovascular and psychosocial risk factors among physicians. *Scandinavian Journal of Work Environment & Health* 1988; 14: 118-24.
28. Keet SW, Bulte CS, Garnier RP, Boer C, Bouwman RA. Short-term heart rate variability in healthy subjects. *Anaesthesia* 2013; 68: 775-7.
29. Hillebrand S, Gast KB, de Mutsert R, et al. Heart rate variability and first cardiovascular event in populations without known cardiovascular disease: meta-analysis and dose-response meta-regression. *Eurospace* 2013; 15: 742-9.

