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ORIGINAL SCIENTIFIC REPORT

Bradycardia During Laparoscopic Surgeries: A Retrospective Cohort Study

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Abstract

Background A recent analysis found bradycardia during laparoscopy as a potential early warning sign of cardiac arrest. Knowledge regarding bradycardia frequency and its consequences during laparoscopy is limited.

Methods Using the computerized record database, files of 9915 patients undergoing laparoscopic surgery, between June 2008 and August 2013 at a tertiary, academic medical center, were screened for intraoperative bradycardia (heart rate <50 beats/min for at least three consecutive measures).

Results Intraoperative bradycardia occurred in 1540 (15.5%) patients, in the majority (945, 61.3%) heart rate decreased to <45 beats/min. Mean (SD) duration of bradycardia was 14.8 (16.8) min. Bradycardia was more prevalent in males, older patients, smokers, patients with comorbidities and those treated with β, α and calcium channel blockers. The majority of events were related to CO_2 insufflation and bolus opioid administration. In 1343 (87%), noteworthy decreases in blood pressure were recorded; the average (SD) drop in systolic blood pressure was 35 (21) mmHg. Pharmacological intervention to alleviate bradycardia was used in up to 23% of episodes. Bradycardia did not result in intraoperative cardiac arrest, neither did it increase the frequency of intensive care unit admission or mortality rate.

Conclusion Bradycardia is common during laparoscopy. Despite being more prevalent in older and sicker patients, bradycardia did not significantly affect outcome, suggesting that routine preventive measures do not need to be implemented. Rather, intraoperative bradycardia events should be wisely followed with prompt response, when hemodynamic perturbations occur, the threshold of which is yet to be defined.

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Abbreviations

AIMS	Anesthesia Information Management System
ASA	American Society of Anesthesiologists physical status classification system
BP	Blood pressure
ICU	Intensive care unit

Introduction

Laparoscopic surgery is a well-established technique with proven postoperative benefits. Serious morbidity, however, is reported and includes major vascular injury, gas embolism and significant cardiac arrhythmias and cardiac arrest. Using the Australian Incident Monitoring Study, a recent analysis found bradycardia during routine laparoscopy as a potential early warning sign of cardiac arrest events [1]. The majority of events were directly associated with pneumoperitoneum and happened in relatively "fit" healthy patients. The effect of intraoperative bradycardia on patient outcome in healthy/unhealthy patients undergoing laparoscopic procedure has not been addressed in additional studies.

Bradycardia is common during laparoscopy [1–11]. With bradycardia defined as heart rate <50 or 60 beats/min, without remark regarding the duration of the event, the reported incidence during laparoscopy was 15–56% [2, 3, 9]. Information regarding this potentially harmful event, however, is deficient due to the limited number of patients included in previous studies, the flawed definition of bradycardia (no mention of event duration) and the inclusion of only relatively healthy patients who lack cardiac risk. Additionally, the surgical heterogeneity is poor, as most reports included patients undergoing gynecology procedures or cholecystectomy [3, 4, 6, 7, 9–11]. Vagally mediated reflexes can cause profound acute bradycardia and even asystole. During laparoscopic surgery, this may happen during peritoneal stretching with gas insufflation, in particular during light anesthesia which can also induce bradycardia during laryngoscopy [4, 9]. Except for the effect of muscle relaxant on the occurrence of bradycardia [6, 7], other events triggering bradycardia were not investigated and risk factors were reported only in a paucity of studies [8]. Thus, using the computerized medical and anesthesia record database in the Tel Aviv Medical Center, we undertook this study to identify in a large cohort of patients undergoing laparoscopic surgery, the frequency of bradycardia in a variety of surgical procedures, possible underlying triggers, patient's characteristics predisposing to bradycardia, the frequency and type of intervention taken to treat this happening and perioperative outcome.

Methods

This is a retrospective cohort study of 9915 patients, age > 18, who underwent laparoscopic surgery between 1.6.2008 and 31.8.2013 at the Tel Aviv Medical Center, a university-affiliated tertiary medical center. The reporting of the results from this cohort is according to the Strengthening the Reporting of Observational Studies in Epidemiology (STOBE) guidelines.

All patients that met inclusion criteria were screened for the occurrence of bradycardia. Intraoperative heart rate and blood pressure measurements were acquired from the Anesthesia Information Management System (AIMS) used at our operating rooms (MetaVision by iMDsoft).

Bradycardia was defined as a heart rate <50 beats/min that persisted for at least three consecutive measures on AIMS—the resolution of which is 1 min with values stored in 1-min interval. Included in the study were also patients in whom bradycardia was treated by the anesthesiologist prior to that time frame (3 min). Excluded were patients with initial heart rate ≤55 beats/min and those who developed bradycardia only at the end of surgery following the administration of neostigmine to reverse muscle relaxant effects.

Files of patients that met inclusion criteria were manually screened to identify artifacts. Artifacts were found in patients with heart rate recorded from the arterial line in which blood sampling interfered with correct heart rate recording. Recorded parameters included length of bradycardia, occurrence of more than one event of bradycardia and identification of possible triggers for bradycardia. Bradycardia that developed following initiation or termination of CO_2 insufflation or immediately following the intravenous administration of a β-blocker, phenylephrine, neostigmine or opiates was attributed to that event. If none of these occurrences happened immediately prior to bradycardia, it was defined as "unknown cause."

Additionally, the anesthesiologist's response/no response to the bradycardia event and the type of intervention applied were documented. Blood pressure (BP) response to bradycardia and BP during peak of bradycardia event was recorded, and the delta BP (change in systolic pressure) was calculated.

Further data retrieved from the AIMS and other electronic medical record systems in use at our hospital included: (1) patient preoperative data—age, gender, American Society of Anesthesiologists physical status classification (ASA), comorbidities, chronic medical treatment and hemoglobin level before surgery; (2) surgical data—surgical procedure and length; (3) outcome parameters—admission to intensive care unit (ICU), re-operation rate and perioperative mortality (within 30 days of surgery).

Endpoints

The primary endpoint measure was the frequency of bradycardia among patients undergoing laparoscopic surgery.

Secondary outcomes were—patients demographics associated with bradycardia, possible triggers for bradycardia, use of pharmacological interventions to alleviate bradycardia, intraoperative cardiac arrest, re-operation rate, perioperative mortality, need for ICU admission.

Statistical analysis

Statistical analysis was performed—using the SPSS software, version 22.0.

Continuous variables were compared using the Student's *T* test or ANOVA for unpaired samples when normal distribution was assumed. When the data did not deviate normally, nonparametric tests were used. Continuous data are presented as mean (SD).

Categorical data were analyzed using the χ^2 test. The Fisher's exact test was used when more than 20% of the expected observations were less than five, or any expected observation was less than two. Categorical data are presented as a number of cases and percent. p values of 0.05 were considered statistically significant.

A multivariate analysis was conducted using logistic regression to predict the risk factors for bradycardia in the overall sample population. Covariates with $p < 0.1$ were included in the initial model.

Results

Of the 9915 laparoscopic surgeries performed in the study period, the majority was general surgery (7833, 79.0%). The rest were either gynecology or urology procedures. Urgent procedures comprised 2101 (21.2%) of the surgeries.

Of the 9915 patients, 2679 (27.0%) were identified by initial screening of having at least one potential documentation of bradycardia. Each of these files was retrieved and manually analyzed for meeting inclusion criteria as defined above. Overall, 1540 patients (15.5%) met inclusion criteria and thus made up the bradycardia group (Fig. 1). The majority (945, 61.3%) had heart rate <45 beats/min, 296 (19.2%) of whom had a heart rate <40 beats/min. In many of the patients (618, 40.1%), more than one event of bradycardia occurred. The mean (SD) duration from the start of bradycardic event to its peak was 7.6 (9.3) min. Mean (SD) duration of bradycardia was 14.8 (16.8) min. Anesthetic depth of the patients during bradycardia was evaluated from end-tidal anesthetic gas concentrations in minimal alveolar concentration equivalents which was [median (interquartile range)] 0.98 (0.93–1.06) and by recorded bispectral index which was 41 (37–45) (n = 231), suggesting that these patients were not lightly anesthetized during the event.

Demographics and surgery (Table 1)

Bradycardia was more prevalent in males, older patients and smokers, as well as patients with cardiovascular and renal comorbidities, but not diabetes mellitus and those who treated with β, α and calcium channel blockers. Likewise, there was a significantly higher ASA score in the bradycardia group patients. Demographics of patients with extreme bradycardia (heart rate <40 beats/min) were not significantly different from the overall population of patients with bradycardia (heart rate <50 beats/min) (data not shown). The strongest risk factor for bradycardia among drugs was treatment with β-blockers (OR 2.8, 2.3–3.3, $p < 0.0001$), and ischemic heart disease was the most prominent one among comorbidities (OR 2.4, 1.9–3.0, $p < 0.0001$).

Triggers for bradycardia (Fig. 2)

The possible triggers for bradycardia were identified in 1390 (85%) patients. In 157, there was flawed documentation of CO_2 insufflation and in 91 no apparent cause was found. As stated previously, patients in whom bradycardia developed solely following the administration of neostigmine to reverse muscle relaxant effect (n = 98) were not included in the bradycardia group.

The majority of bradycardia events during laparoscopy were related to CO_2 insufflation and opioid administration (bolus administration or sudden increase in infusion rate), as well as deflation of pneumoperitoneum. Bolus intravenous administration of phenylephrine or β-blockers preceded the development of bradycardia in a small number of patients. It is, however, worthwhile to mention that whereas bradycardia following phenylephrine administration was indeed rare (15 of 316 cases) events, bradycardia following β-lockers use was quite frequent (44 of 98 cases).

Risk factors for bradycardia

A multivariate logistic regression analysis, to predict risk factors for bradycardia in the overall sample population, was performed. The best predictive model included age, β-blocker use, preoperative hemoglobin, gender, ASA and dyslipidemia. The only risk factor with a statistical significance was age (p = 0.0001, OR = 1.1).

Hemodynamic perturbations

BP changes during peak bradycardic events were analyzed. Decreases in BP were noticed in 1343 (87.2%) patients. The average (SD) drop in BP was 35 (21) mmHg. In about three-quarters of patients [986 (73%)] with bradycardia-

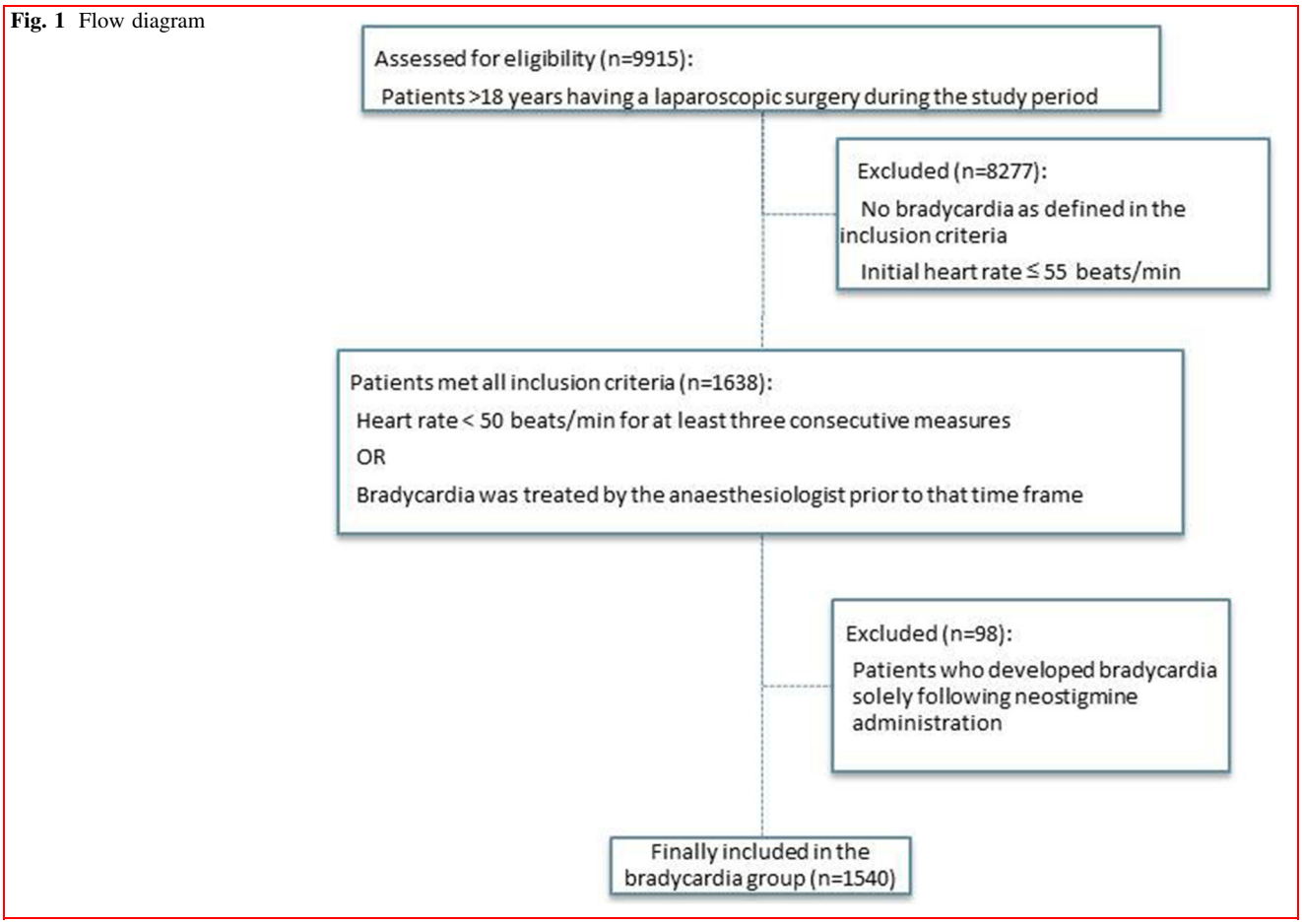

Fig. 1 Flow diagram

induced decrease in BP, systolic BP did not decrease below 100 mmHg. Overall, lowest documented systolic BP < 70 mmHg was recorded in only 23 patients.

Intervention by anesthesiologist

Anesthesiologists intervened pharmacologically (ephedrine or atropine administration) in 11.6% to 23.0% of the episodes, depending on the precipitating factor, with the highest response following CO_2 insufflation or the use of opioids (20.6% and 23.0%, respectively) and the least following termination of CO_2 insufflation (11.6%). Non-pharmacological interventions such as the release of pneumoperitoneum for a short period were not recorded and thus cannot be reported.

Outcome

None of the patients with bradycardia suffered from intraoperative cardiac arrest. When comparing patients experiencing bradycardia vs. those who did not, we found similar re-operation rate [10 (0.6%) vs. 72 (0.9%), respectively = 0.38], ICU admission rate [32 (2.1%) vs. 218 (2.6%), respectively, $p = 0.24$] and 30-day mortality [6 (0.4%) vs. 39 (0.5%), respectively, $p = 0.40$].

Discussion

Laparoscopy surgeries come with their own unique challenges. Systematic knowledge regarding the occurrence of intraoperative bradycardia and its significance is lacking. This is the first study to evaluate in a large cohort of patients this common clinical event and its effect on patient outcome. The present study, which included 9915 patients undergoing a variety of laparoscopic procedures, shows that intraoperative bradycardia is common and might be long-lasting. More than one event is frequently encountered. It is more prevalent in males, smokers, sicker patients and those on chronic cardiac and antihypertensive medications. There is no association with diabetes mellitus. The bradycardia events are mostly related to CO_2 insufflation and opioid (bolus) administration. Other possible triggering events are termination of CO_2 insufflation and bolus administration of β-blocker or phenylephrine. As patients in the present study were adequately anesthetized,

Table 1 Patients demographics

	Bradycardia group $n = 1540$	No bradycardia group[a] $n = 8375$	OR	95% CI	p value
Age; years	57.8 (17.5)	47.2 (18.0)			< 0.001
Gender: male	836 (54.3%)	3253 (38.8%)			< 0.001
ASA ≥ 3	348 (22.6%)	1357 (16.2%)	1.5	1.3–1.7	< 0.001
Comorbidities					
Smoking	137 (8.9%)	579 (6.9%)	1.3	1.1–1.6	0.01
Diabetes mellitus	112 (7.3%)	505 (6.0%)	1.2	1.0–1.5	> 0.05
Ischemic heart disease	102 (6.6%)	232 (2.8%)	2.4	1.9–3.1	< 0.001
Hypertension	302 (19.6%)	902 (10.8%)	2.0	1.7–2.3	< 0.001
Dyslipidemia	180 (11.7%)	588 (7.0%)	1.7	1.5–2.1	< 0.001
Chronic renal failure	32 (2.1%)	83 (1.0%)	2.0	1.4–3.1	< 0.001
Drugs					
β-blocker	183 (11.9%)	364 (4.3%)	2.9	2.4–3.5	< 0.001
α-blocker	119 (7.7%)	257 (3.1%)	2.6	2.0–3.2	< 0.001
CCB	95 (6.2%)	215 (2.6%)	2.5	2.0–3.2	< 0.001
Preoperative hemoglobin; mg dl^{-1}	13.1 (1.6)	13.0 (1.7)			> 0.05

Data presented as mean (SD) or number (proportion)

ASA American Society of Anesthesiologists physical status classification system, *CCB* calcium channel blocker

[a]Included in this group were all patients who did not meet inclusion criteria for the bradycardia group as defined in Methods section

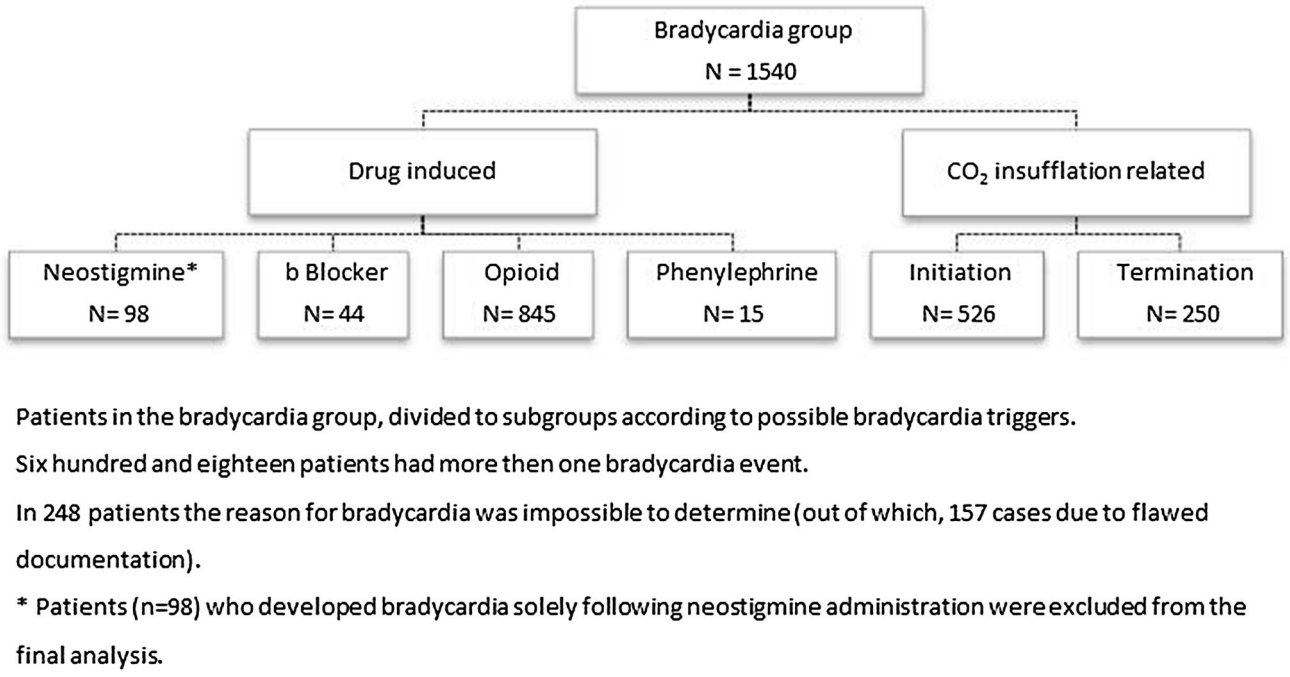

Fig. 2 Possible triggers for bradycardia during laparoscopic surgery

light anesthesia cannot be accounted for triggering bradycardia, emphasizing the point that bradycardia might also be expected to occur in well-anesthetized patients. Bradycardia significantly affects BP in the majority of patients. Nevertheless, it did not result in intraoperative cardiac arrest, neither did it adversely affect other outcome measures. It is noteworthy to mention that pharmacological intervention took place in up to one-quarter of the episodes.

Bradyarrhythmias and asystole have been recognized as a complication of laparoscopic surgery for over 35 years [1–4, 6–11]. Early reports involved patients undergoing cholecystectomy with gynecology procedures to follow. The majority of bradycardia events were related to CO_2 insufflation and traction on pelvic structures and spontaneously resolve without the need for pharmacological treatment [9]. Following studies found similar results in limited number of healthy (ASA I–II) patients [2, 3, 6, 7, 10, 11]. The frequency of bradycardia in the present study was 15.5%, much lower than previously described (20–30%) [2, 3, 9]. Unlike previous reports, our study involved a much larger cohort of healthy (ASA I–II) and unhealthy (ASA III–IV) patients, undergoing a variety of surgical procedures, of varying duration, urgent included. The reasoning for our finding of lower prevalence might be attributed, in part, to the smaller number of patients included in previous studies. Also, bradycardia was not clearly defined in earlier studies—the definition included only a heart rate threshold (<50 beats/min) with no definition of duration. In the present study, bradycardia (<50 beats/min) had to persist for at least three consecutive measures on the IMD Soft file, and patients with initial heart rate ≤55 beats/min were excluded.

Some predisposing factors for bradycardia during laparoscopic surgery were previously noted, such as CO_2 insufflation, traction on pelvic structures, certain drugs and more. The present study demonstrates, in agreement with earlier reports, that one of the two main triggers for bradycardia was CO_2 insufflation. Termination of CO_2 insufflation, however, was not previously recognized as a trigger, and this occurrence needs further evaluation. Several agents, in particular opioids [12, 13], have been implicated as potentiating factors for intraoperative bradycardia, especially fentanyl and remifentanil, both having vagotonic effects, and known for their potential to induce bradycardia [12–14]. Indeed, in the present study, opioid bolus administration was found as one of the main triggers for bradycardia.

Remarkable reductions in BP occur in the majority of patients during the bradycardic event and their significance needs evaluation. In 64 ASA I–II patients undergoing elective urology laparoscopic procedure [2], both systolic and diastolic BP decreased during bradycardia by 23.5 (9.8) mmHg and 12.1 (6.2) mmHg, respectively. The study, though, did not follow the patients postoperatively. In the present study, significant decreases in BP during the bradycardic event were observed in most patients and bradycardia resolved spontaneously, or with pharmacological treatment in up to one-fifth of the patients. As many of the intraoperative bradycardic episodes are attributed to increased vagal output during laparoscopy, it was suggested that preventive administration of an anticholinergic agent just prior to surgery is justified. Indeed, two randomized controlled trials [2, 3] reported the beneficial effect of atropine on the frequency of bradycardia. In our cohort, despite the fact that bradycardia was more prevalent in older and sicker patients and those on cardiac medications, bradycardia did not result in intraoperative cardiac arrest, neither did it adversely affect other outcome measures such as rate of ICU admission, need for re-operation or mortality. Thus, we believe that no preventive pharmacological measures need to be implemented. Intraoperative bradycardia events should be wisely followed with careful observation and prompt response when hemodynamic perturbations occur the threshold of which is yet to be defined.

This study has several limitations. First, the data were collected based on the standard clinical care delivered and documented. As a result, we were unable to address the intra-abdominal pressure during pneumoperitoneum and the frequency of its release in response to bradycardia, as these events are not marked by the anesthesiologists. An earlier study, though, found that it has no significant effect on the rate of bradycardia [4]. Second, as in every retrospective study, physicians were not mandated to adhere to a clinical protocol or describe reasoning for their intraoperative management—implementing/not implementing an intervention to alleviate bradycardia cannot be evaluated. Finally, the data are from a single tertiary care center, which may not serve as a representative sample of laparoscopic surgery patients throughout the world.

Despite the aforementioned limitations, the study offers insight into previously not adequately studied area. By identifying the frequency, possible triggers and risk factors, we are now able to provide patients and clinicians with an estimation of the risk for developing bradycardia during laparoscopic surgery and the resultant outcome consequences. Furthermore, although a recent study found bradycardia during laparoscopy as a potential early warning sign of cardiac arrest [1], we have not been able to demonstrate that bradycardia is associated with either increased severe morbidity or in mortality. Further studies should evaluate the hemodynamic threshold, in which intervention should be undertaken, to alleviate bradycardia during laparoscopy.

Compliance with ethical standards

Ethical approval Ethical approval for this study (Ethical Committee No. 0173-13-TLV) was provided by the Ethical Committee of the Tel Aviv Sourasky Medical Center, Tel Aviv, Israel (Chairperson Prof. Marcel Topilsky) on May 23, 2013.

Informed consent Informed consent was waived by the ethical committee.

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