Functional walking capacity as an outcome measure of laparoscopic prostatectomy: the effect of lidocaine infusion

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Background. Intravenous lidocaine infusion has been shown to affect postoperative pain intensity. This present study was performed to assess the effect of intra- and postoperative lidocaine infusion on postoperative functional walking capacity, as a measure of surgical recovery.

Methods. Forty patients undergoing laparoscopic prostatectomy were randomized to receive an i.v. infusion of either lidocaine 2 mg kg⁻¹ h⁻¹ during surgery and 1 mg kg⁻¹ min⁻¹ for the first 24 postoperative hours (lidocaine group) or an equivalent volume of saline 0.9% (control group). All patients received postoperative patient-controlled analgesia with i.v. morphine. Primary outcome was functional walking capacity, as assessed by distance attained during the 2 min walking test (2MWT), recorded daily for the first 3 postoperative days. Morphine consumption and pain intensity were recorded.

Results. 2MWT distance decreased by an average of 60% (P<0.01) in both groups on postoperative day 1 (from 150 m before surgery to 53 m), but the decrease was 26 m less in the lidocaine group (P=0.009). During postoperative days 2 and 3, the 2MWT distance increased to an average of 96 m, still 30% less than the preoperative values. There was a significant negative correlation on postoperative days 1 and 2 between the 2MWT distance, pain intensity and fatigue, and morphine consumption. Lidocaine infusion was an independent predictor of the degree of postoperative decrease in 2MWT distance. More patients in the lidocaine group were free from PCA on the second postoperative day (P=0.011).

Conclusions. Infusion of lidocaine during surgery and for the first postoperative day attenuated the deterioration in functional walking capacity, and had an opioid sparing effect.

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Intravenous lidocaine infusion has been used as an adjuvant during and after surgery in patients undergoing retropubic prostatectomy, laparoscopic cholecystectomy, and laparoscopic colon resection; it is associated with a significant postoperative opioid-sparing effect, earlier return of bowel function or shorter hospital stay.¹–³ Animal and human studies have shown analgesic, anti-hyperalgesic, and anti-inflammatory properties of i.v. lidocaine,⁴⁻⁵ which could explain its effect in attenuating visceral pain associated with dissection of pelvic structures.

Surgical outcome has traditionally been reported in terms of mortality and complication rate. However, with major advances in surgical technology and anaesthesia, mortality and morbidity have become rare events. Similarly, the length of hospital stay has been used as a measure of outcome, but is influenced by the health-care system and the administrative culture. Recently, there has been some interest in assessing the influence of therapeutic interventions on the process of surgical recovery or return to baseline, with a particular emphasis on patient-reported outcomes of well-being.⁶⁻⁷
Physical activity is an important aspect of day-to-day life, and tests of functional exercise capacity like walking tests reflect every day activity. These can be influenced by health status, pain, fatigue, and can help to quantify the recovery process. Although different walking tests (12, 6, and 2 min walking tests: 12MWT, 6MWT, 2MWT) indicate aspects of functional exercise capacity, the 2MWT has been found more suitable for patients in compromised health states in the early postoperative period. Walking test is a measure that could be administered as part of an assessment to determine functional performance, to evaluate treatment effectiveness, or to assess readiness for discharge.

This prospective, randomized, controlled trial was designed to analyse the effect of intraoperative and postoperative lidocaine infusion on the immediate postoperative functional walking capacity and other measures of recovery such as consumption of opioids and return of bowel function. It was hypothesized that by attenuating the inflammatory response and reducing analgesic requirements, lidocaine infusion would improve the capacity to mobilize, thus promoting earlier recovery.

Methods

Patients

The study was approved by the McGill University Health Centre Ethics Board (Gen#06–023) and was conducted between May 2007 and February 2008. Patients undergoing laparoscopic prostatectomy for prostate cancer aged 18–85 yr were eligible. Exclusion criteria were: ASA physical status ≥4, history of hepatic, renal, or cardiac failure, organ transplant, insulin-dependent diabetes mellitus, morbid obesity (BMI >40 kg m⁻²), chronic use of opioids, allergy to local anaesthetics, or inability to comprehend pain assessments. Patients were instructed before surgery in the use of the visual analogue scale (VAS) to assess pain and fatigue. Before induction of anaesthesia, patients were randomly assigned (using a computer-generated randomization schedule and sealed brown envelopes) to two groups of 20 patients each: lidocaine group receiving an intraoperative and postoperative i.v. infusion of lidocaine, and control group receiving an equivalent i.v. infusion of saline 0.9%.

Anaesthesia and intraoperative care

Upon arrival in the operating theatre, baseline values of heart rate (HR), arterial pressure, oxygen saturation, and bispectral index (BIS) were recorded. The anaesthesiologists (S.L. and F.C.) who executed the study protocol were blinded to the group allocation and were not involved in preoperative or postoperative data collection. After premedication with i.v. midazolam 0.03 mg kg⁻¹, general anaesthesia was induced with fentanyl 3.0 μg kg⁻¹, propofol 2.5 mg kg⁻¹, and rocuronium 0.8 mg kg⁻¹. At induction of anaesthesia, the lidocaine group received an i.v. bolus injection of lidocaine 1.5 mg kg⁻¹ up to a maximum of 100 mg, followed by a continuous infusion of lidocaine 2 mg kg⁻¹ h⁻¹ until the end of surgery. The control group received an equivalent volume of saline 0.9%. Anaesthesia was maintained with desflurane at an end-tidal concentration adjusted to maintain BIS values between 40 and 50, and HR and systolic pressure within 20% of baseline values. No supplemental fentanyl was given during surgery. 0.9% saline was administered i.v. at a rate of 6 ml kg⁻¹ h⁻¹ and intraoperative normothermia (nasopharyngeal temperature between 35.8 and 36.5°C) was maintained with forced air warming over blankets. All patients received dexamethasone 8 mg and droperidol 0.625 mg as prophylactic anti-emetics. Episodes of intraoperative hypotension (MAP <60 mm Hg), and bradycardia (HR <40 beats min⁻¹) were recorded, and treated with i.v. boluses of phenylephrine 40 μg or atropine 0.4 mg, respectively. All patients received ketorolac 15 mg i.v. Desflurane was discontinued after the last skin suture, and intermittent doses up to 0.08 mg kg⁻¹ of morphine were given i.v. at return of spontaneous respiration. Lidocaine and the saline infusions were discontinued before patients left the operating theatre.

All operations were performed using a standard laparoscopic technique with infiltration of bupivacaine 0.25% with adrenaline 1:200 000 at the trocar entry ports.

Postoperative analgesia and surgical care

Lidocaine infusion 1 ml kg⁻¹ h⁻¹ (or equivalent volume of saline 0.9%) was recommended in the PACU and continued for 24 h. PCA morphine (1 mg bolus, 7 min lockout) was started in PACU and continued for 48 h. Patients also received acetaminophen 1.0 g 6 hourly and naproxen 500 mg 12 hourly for the first 72 h. Once PCA morphine was discontinued, patients were offered oxycodone 5–10 mg 4 hourly if the VAS (0=no pain and 10=excruciating pain) was >3 at rest. Ondansetron 2 mg i.v. was prescribed for persistent nausea (lasting >5 min) or vomiting. An i.v. infusion of dextrose 5% and saline 0.45% was started after surgery and continued for up to 48 h until the patients were tolerating oral fluids. Clear fluids were allowed during the first 24 h, and if tolerated, liquid diet and full diet were then offered. Starting on the first postoperative day, patients in both groups were encouraged by the nurses to mobilize twice a day, whether sitting or walking.

Readiness for hospital discharge was determined according to the following criteria: tolerance of solid food, passage of stool, absence of infection, VAS pain score <3, and ambulation without assistance. Patients were seen 4 weeks after surgery, at which time any complications were
Effect of lidocaine infusion on functional walking capacity

Outcome measures

The 2MWT

This was measured before surgery and in the early afternoon (between 1:00 and 5:00 pm) of the first, second, and third postoperative day. Patients were asked to walk back and forth along a 15 m stretch of hallway as much as they could over a period of 2 min. Standardized encouragement (‘you are doing well’ or ‘good, keep going’) was given every 30 s. To ensure safety, the evaluator walked behind the patient. Patients were told that they could rest if necessary, and they were allowed to use their regular walking aids. Any i.v. lines, tubes, or PCA pumps were attached to an i.v. pole and pushed by the patient. The distance covered was then recorded in metres. If the patient was unwilling or unable to walk, 0 was recorded for that day. Baseline predicted 2MWT distance was calculated using gender-specific reference equations for the 6MWT, which were then divided by 3 to estimate the 2MWT distance.

Secondary outcomes were morphine consumption during the first two postoperative days and recovery of gastrointestinal function. Pain intensity was assessed using the VAS every afternoon after 1:00 pm for the first 3 postoperative days, sitting on the bed at rest, on coughing and walking. PCA morphine consumption was recorded every 24 h for the first 2 postoperative days. The number of hours until first passage of gas and first bowel movement, and hours to first full diet from surgery were recorded daily at bedside.

Statistical analysis

All data are presented in the tables as means (SD), median [interquartile range], absolute values (percentage), or relative number of patients. Comparisons for each characteristic and clinical variable among the two groups were performed by Student’s t-test, Wilcoxon rank-sum test, or Pearson χ² test depending on the type of the variable under study and the sample distribution. Non-parametric correlations were performed with Spearman test. Univariate linear regressions were used for normally distributed, continuous variables to estimate the extent to which key explanatory variables predicted change in functional walking capacity over the perioperative period. The level of significance was set at $P<0.05$. All analyses were performed with the Intercooled Stata 9.2 statistical package (Stata Corporation, College Station, TX, USA).

The primary outcome was functional walking capacity as measured by the 2MWT. Calculations for sample size were based on a previous study12 in which a change in 20 m in 6MWT was considered to be clinically meaningful. Twenty subjects in each group were sufficient to detect a 15% less decrease in 2MWT in the lidocaine group compared with the control group, with a type-1 error of 0.05 and a power of 80%.

Results

Patient characteristics

The study groups had similar characteristics (Table 1). Co-morbidities included hypertension, non-insulin-dependent diabetes, hypercholesterolemia, coronary artery disease, and asthma. There were three patients with intra-operative bleeding (two in the lidocaine group and one in the control group) and only one needed blood transfusion. There were no conversions to open surgery. There was no significant difference in the consumption of PCA on the first postoperative day. On the second day, 70% of the patients in the lidocaine group and 30% in the control group did not use PCA morphine ($P=0.011$). Total morphine consumption over the 2 postoperative days was less in the lidocaine group though this difference was not statistically significant. Postoperative complications included bleeding, infection, and bladder leak. There was one re-admission in the lidocaine group for bleeding, which was resolved within 15 h. Return of bowel function, readiness for discharge, and length of hospital stay were similar in both groups. BIS values were 48 (SD 8) in the lidocaine group and 46 (9) in the control group, respectively, and end-tidal concentrations of desflurane 5.6 (1.1)% in the lidocaine group and 6.3 (1.6)% in the control group, respectively.

Preoperative values of 2MWT were similar in both groups and accounted for approximately 60% of the predicted values based on Canadian norms (Table 2). On the first day after surgery, the average 2MWT in both groups decreased significantly when compared with the preoperative value ($P<0.01$) (Fig. 1). However, the decrease in the control group was significantly greater, with an average difference of 26 m between the two groups. There was no difference between the two groups on the second and third postoperative days.

Median VAS scores were <3 in both groups at rest, <4 on coughing, and <2 on walking in both groups on all postoperative days; median VAS fatigue scores were <3 in both groups throughout the study. Both pain and fatigue scores were very similar with no significant differences between groups at any time point. Higher pain intensity and greater fatigue scores correlated with lower 2MWT distances (Table 3). Morphine consumption was also negatively correlated with 2MWT on Day 2. Those patients who walked less on Day 2 stayed in hospital longer. Analysis by univariate linear regression (Table 4) indicated that group (lidocaine or control), ASA, preoperative 2MWT, and difference between predicted and preoperative 2MWT were predictors of change in 2MWT (preoperative—first postoperative day).
Discussion

There are few published data about the course of recovery in the immediate period after surgery and the possible impact of interventions in modifying the outcome. We used the 2MWT to determine whether lidocaine infusion would influence in-hospital recovery of functional walking capacity. Although there was a significant decrease in the postoperative values of the 2MWT in both groups, the deterioration was significantly less in the lidocaine group during the first postoperative day. The average difference in distance covered was 26 m that can be considered to be clinically meaningful in a population at risk such as the early postoperative period. There was an overall negative correlation between the distance covered over 2 min and the pain intensity, fatigue score, and morphine consumption. Both groups recuperated by the third postoperative day, but were still well below preoperative levels.

The pattern of acute deterioration in functional walking capacity followed by recovery is what is expected from an index quantifying the impact of surgical stress. Several factors affect the ability to ambulate in the very early postoperative period, the commonest being severe blood loss, dizziness, and pain. None of our patients refused to walk, and except for one patient who bled during surgery, none of them were anaemic or felt dizzy during the walking test. The deterioration in 2MWT distance on the first postoperative day was greater than 50%, and overall negatively correlated with the intensity of pain, fatigue score, and morphine consumption. The decrease in 2MWT was greater on Day 1 in the control group; they required more morphine indicating a strong causative association between the walking distance covered (functional outcome) and pain (impairment as directly related to surgical stress). This would fit with the surgical outcome model previously proposed by our group, whereby short-term changes like pain intensity might impact on short-term outcome (here functional mobility).

Baseline performance of the 2MWT was an independent predictor of deterioration, thus confirming other studies that demonstrated a relationship between preoperative health status and functional reserve, and the course of recovery. It was rather surprising to observe a 60% decrease in 2MWT in both groups on the first postoperative day as these patients were clinically fit (most ASA I
or II) and undergoing laparoscopic surgery. Several studies on the metabolic effects of laparoscopic surgery have shown a reduction in the inflammatory response to surgery, less pain, and shorter duration of hospital stay compared with laparotomy.

One would have therefore expected less deterioration in functional walking capacity and an earlier return to baseline in both groups. However, it is not known whether the observed decrease in 2MWT was because of the surgical stress itself or to the changes that are associated with the laparoscopy. On the third day after surgery, the distance covered increased significantly from Day 1 but remained significantly below baseline.

There is some difficulty in identifying suitable indicators to assess surgical recovery. Exercise tolerance is a good indicator of the impact of surgery, and the most accepted measure of exercise tolerance is the amount of oxygen consumed at maximal effort (VO2 max). Unfortunately, specialized equipment is required for this measure and the test may be too demanding for a surgical patient. Very little published data exist on the use of

**Table 3** Correlations between VAS scores and postoperative 2MWT. All 40 patients of the lidocaine study were evaluated together. ρ, Spearman correlation coefficient

<table>
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<th>P-value</th>
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<td>POD 1 2MWT vs VAS rest</td>
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<td></td>
<td>VAS on coughing</td>
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<td></td>
<td>VAS on walking</td>
<td>0.0441</td>
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<tr>
<td></td>
<td>Fatigue</td>
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<td>POD 2 2MWT vs VAS rest</td>
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Fig 1 2MWT data presented as box plots showing median and interquartile range. Bars represent 95% confidence intervals; circles are outlier values. *P<0.01. 2MWT, 2 min walking test; POD, postoperative day. (a) 2MWT before and after surgery. POD1 differs from all others values. POD2 and POD3 are similar, and both different from postoperative values. There are no differences between study groups at any time. (b) Significant difference of 26 m between the two groups in ‘preoperative minus POD1’.
walking tests to estimate in-hospital surgical recovery. Brooks and colleagues\textsuperscript{15} measured the 2MWT in 122 patients undergoing cardiac surgery at baseline, immediately before discharge from hospital and 6–8 weeks after discharge. The mean distance declined from baseline to hospital discharge by an average of 40\%, and this returned to baseline at 6–8 weeks follow-up. The authors found the test easy to administer, accepted by the patients, sensitive to baseline at 6–8 weeks follow-up. The authors found the relationship with self-reported outcome measures was only one type of physical activity. The 2MWT was collected only for the first 3 postoperative days and no relationship with self-reported outcome measures was studied. Nevertheless, this study is an attempt to address issues related to meaningful patient outcomes and how to accelerate the recovery process.

In summary, lidocaine infusion had a significant impact on the 2MWT with patients in this group able to walk a longer distance over a short period of time. It is possible that lidocaine, with its anti-inflammatory action,\textsuperscript{5} had an opioid-sparing effect as shown by a trend towards less PCA morphine consumption in the lidocaine group.\textsuperscript{3, 4}

This study has some limitations. One disadvantage is that a 2MWT measures walking capacity at only one point and not throughout the day. In addition, walking represents only one type of physical activity. The 2MWT was collected only for the first 3 postoperative days and no relationship with self-reported outcome measures was studied. Nevertheless, this study is an attempt to address issues related to meaningful patient outcomes and how to accelerate the recovery process.

In summary, lidocaine infusion throughout surgery and for the first 24 postoperative hours attenuated the deterioration in postoperative 2MWT. Preoperative 2MWT performance and use of lidocaine were important predictors of change in functional walking capacity. Development and testing of measures of surgical recovery are needed in order to understand how to improve the recovery process.

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**References**


