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Impact of miniport laparoscopic cholecystectomy versus standard port laparoscopic cholecystectomy on recovery of physical activity: a randomized trial

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Abstract

Introduction We conducted a randomized trial comparing minilaparoscopic cholecystectomy (MLC) to conventional laparoscopic cholecystectomy (CLC) to determine whether MLC accelerated recovery of physical activity after elective surgery (NCT01397565).

Methods A total of 115 patients scheduled for elective cholecystectomy were randomized to either CLC or MLC. Both procedures used a 10-mm umbilical port, but the three upper abdominal ports were 5 mm in CLC and 3 mm in MLC. Primary outcome was self-reported physical activity 1 month after surgery as estimated by Community Health Activities Model Program for Seniors questionnaire (kcal/kg/week). Secondary outcomes were umbilical pain, abdominal pain, nausea and fatigue (VAS, 1–10), and cosmetic result at one and 3 months. Patients received identical surgical dressings for 1 week, and assessors were blinded to group allocation.

Results Forty-two patients randomized to CLC group and 33 patients randomized to MLC remained in the trial and were analyzed. Both groups were similar at baseline characteristics. In the MLC group, at least one 5-mm port was used in 17 (51.5 %) mainly due to unavailability of ML equipment. Median (IQR) physical activity for the CLC and MLC groups was similar at baseline (23.4 [13.1, 44.6] vs 23.6 [14.2, 66.9] kcal/kg/week, $p = 0.35$) and at 1 month (20 [7.9, 52.5] vs 16.8 [11.8, 28.6] kcal/kg/week, $p = 0.90$). One month post-op, umbilical pain and abdominal pain were similar, but the CLC group reported higher fatigue (4 [1–5] vs 1 [0–4], $p = 0.05$) and worse scar appearance scores (4 [3, 4] vs 4.5 [4, 5], $p = 0.009$). At 3 months, the CLC group had worse scar appearance (4

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[3–5] vs 5 [4–5], $p = 0.02$) and lower scar satisfaction scores (4 [3, 4] vs 4 [3.5–4], $p = 0.04$).
Conclusion Recovery of physical activity was similar after MLC and CLC. MLC resulted in less fatigue and better scar appearance and satisfaction. These benefits were seen despite the need to upsize one or more ports in more than half of patients related to availability of the miniature instruments.

Keywords Minilaparoscopic · Needlescopic · Cholecystectomy · Randomized trial · Laparoscopy · Miniport

Since its introduction in 1987 [1], laparoscopic cholecystectomy replaced open cholecystectomy because of improved perioperative morbidity and faster recovery [2, 3]. Standard laparoscopic cholecystectomy uses four ports, a 10-mm port at the umbilicus and three 5- 10-mm size upper abdominal ports [4, 5].

Efforts to further improve patient-reported outcomes such as pain, recovery and cosmesis have focused on reducing port-related trauma to the abdominal wall. Examples include Natural-Orifice Transluminal Endoscopic Surgery (NOTES), Laparo-Endoscopic Single Site Surgery (LESS) and minilaparoscopic surgery [6]. Minilaparoscopic surgery, also known as "needlescopic" or "miniport" surgery, refers to the practice of replacing one or more standard (5–10 mm) ports with smaller ports and instruments (2–3 mm) [5]. This provides an attractive option compared to NOTES or LESS which represent significant changes from the standard operative approach and have an unclear safety profile [7]. While compelling, the miniport technique requires additional equipment and evidence for its benefits, particularly for outcomes of importance to patients like functional recovery [8], is required prior to widespread adoption.

Multiple previous studies compare outcomes after 4-trocar standard and miniport cholecystectomy, with a recent Cochrane meta-analysis including 12 randomized trials. Standard cholecystectomy included two 10-mm ports and two 5-mm ports, while miniport required at least two ports 3 mm or smaller. The review found no advantage of miniport cholecystectomy to decrease morbidity or decrease time to return to activity, return to work, improve quality of life or long-term cosmesis. However, relatively few studies included patient-reported outcomes, and there was also a high risk of bias in most studies including the fact that some studies excluded patients who were converted from miniport to standard laparoscopic or open cholecystectomy from further analysis (lack of intention to treat). Further studies with low risk of bias were recommended to address this knowledge gap, with adequate blinding (of patients and assessors) and improved outcome reporting. In addition, our current standard laparoscopic cholecystectomy uses three 5-mm ports, potentially decreasing the advantages of smaller ports compared to when at least one upper abdominal 10-mm port is used as the control.

The objective of this study was to compare patient-reported outcomes after miniport or standard port laparoscopic cholecystectomy, including recovery of physical activity, pain and cosmesis.

Methods

Trial design

This was a prospective, parallel group, randomized controlled trial, conducted at the Montreal General Hospital (MGH). The study took place from February 2012 to September 2014. There were no changes in the trial design during the study period. The study was approved by the McGill University Heath Centre Research Ethics Board (11-053-SDR) and was registered at clinicaltrials.gov (NCT01397565). Reporting followed the CONSORT Statement [9].

Participants

Eligible participants were adults aged 18 years or older and referred to participating general surgeons for elective cholecystectomy. The exclusion criteria were current or previous acute cholecystitis, previous upper gastrointestinal surgery, planned cholangiography, American Society of Anesthesiologists (ASA) class $\geq$4, pregnancy and morbid obesity (BMI $\geq$ 35 kg/m^2). As the study required patients to fill out questionnaires, comprehension of either English or French was required for participation. Patients with psychiatric conditions that preclude cooperation were also excluded.

Sequence generation, allocation concealment mechanism, implementation and blinding

Patients were randomly assigned to MLC or CLC using computer-generated random numbers placed in sequentially numbered sealed opaque envelopes. The randomization sequence and the envelopes were prepared by a research assistant not involved with the interventions, postoperative assessments or data analysis. Once the day of surgery was confirmed for a patient, the corresponding envelope was opened and the surgeon's office was informed of the group allocation in order for the operating room to prepare the proper instruments.

The patients were asked to keep the applied dressing on port sites for 1 week to conceal their allocation. The research assistant carrying out the assessment questionnaire at pre-op, 1 and 3 months after visits was also blinded to the group allocation of patients.

Interventions

Patients were informed of the trial by one of three participating attending surgeons during their first clinic visit. Medical records were screened by the study coordinator for eligibility. The patients were approached, and consent was obtained during the visit to pre-op clinic.

Patients were randomly allocated into one of two groups. The control group received a conventional laparoscopic cholecystectomy (CLC), while the intervention group received minilaparoscopic cholecystectomy (MLC).

All surgeries were performed by one of three surgeons who had previously performed between 700 and 2000 laparoscopic cholecystectomies or by trainees under their direct supervision, as per their standard practice. Bupivacaine was injected at incision sites prior to trocar insertion in both groups, and abdominal access was obtained with a blunt-tipped trocar inserted at the umbilicus using an open (Hasson) technique (Versaseal Plus 5- to 12-mm trocar seal system with reusable titanium cannula, Medtronic). A CO_2 pneumoperitoneum to 12 mmHg was instilled, and a 5-mm 30° laparoscope inserted. In the CLC group, three reusable (Storz®) working 5-mm ports were inserted in the upper abdomen and standard laparoscopic instruments were used, including a 5-mm clip applier (Hem-o-lok, Weck). For patients in the MLC group, the working ports were replaced by three 3-mm ports and minilaparoscopic instruments were used (Storz®). For clipping and for removal of the specimen, the 5-mm laparoscope was replaced with a 3-mm scope inserted through the epigastric port, to allow for clip application through the umbilicus. At any time during the procedure, the surgeon had the option to upsize the ports in case of difficulty/issues with small instruments or the need to use a larger instrument, or to convert to open cholecystectomy as necessary.

The fascia of the umbilical trocar site was closed using 2–0 polydioxanone (PDS, Ethicon) in all patients. The skin of the umbilical site and 5-mm trocar sites was closed with 4–0 poliglecaprone 25 (Moncryl, Ethicon) subcuticular suture and steristrips. The 3-mm trocar sites were closed using steristrips. All patients had the same sized waterproof dressings applied to blind patients to their group allocation, and the patients were asked to keep the dressing for a week following the surgery.

All patients were cared for using a standard perioperative care plan, including an educational booklet [10] and standard orders for multimodal analgesia medication after discharge, including regular naproxen (375 mg po twice daily) and acetaminophen (650 mg po every 6 h) for 3 days and oxycodone 5 mg po q3 h for breakthrough. Patients in both groups were planned for same-day discharge, but were admitted if additional monitoring, testing or intervention was needed, as per standard practice.

The equipment for MLC including 3-mm ports, instruments and cameras was provided to the MGH on a trial basis, without cost, by Storz®, who were not involved in study design, analysis or funding. Participating surgeons had each completed a minimum of two cholecystectomies with the new equipment prior to the beginning of the trial.

Primary outcome

The primary outcome was recovery of self-reported physical activity at 1 month postoperatively, compared to preoperative levels, estimated using the Community Health Activities Model Program for Seniors (CHAMPS) questionnaire. CHAMPS is a 41-item questionnaire where subjects estimate the frequency and time spent in a range of physical and social activities in the previous week. Each activity is weighted according to metabolic value (one MET = 1 kcal/Kg/h). METS represent the ratio of calories expended during an activity to the metabolic rate when sitting quietly. For example, leisurely walking is assigned 2.5 METS, while jogging is assigned seven METS. The duration spent over the week in each activity is multiplied by METS, and total weekly caloric expenditure (kcal/kg/week) is estimated by summing all the values. Evidence is available for the validity of CHAMPS as a measure of recovery after laparoscopic cholecystectomy [11]. In our study, we used a modified, shorter version of the CHAMPS questionnaire that consisted on 19 questions that combined multiple categories of the original CHAMPS and including only activities of relevance to the general population.

Secondary outcomes

Pain, fatigue and nausea were measured using visual analogue scales (VAS, 0 = none 10 = severe). Self-rated health state was measured using the EQ-VAS scale (0 = worst imaginable health state; 100 = best imaginable health state).

Cosmetic results were measured using four items from the Patient Scar Assessment Questionnaire [12]: "Overall what do you think of the appearance of the scar" (5 = excellent, 1 = very poor); "Overall, how troublesome are the symptoms from your scar" (5 = not at all, 1 = unbearable); "Overall, how self-consciousness are you of your scar" (4 = not at all, 1 = very); and "Overall, how

satisfied are you with the appearance of your scar" (4 = very satisfied, 1 = very dissatisfied).

Data collection

The patients were seen initially at the preoperative clinic where demographic variables were collected. Patients completed the CHAMPS questionnaire and VAS scales for pain, nausea, fatigue and general health state. Patients were also given a questionnaire regarding their attitudes about the impact of incision size on recovery: "The size of the incision after surgery is an important determinant of the amount of pain I will have after surgery" (5 = strongly agree, 1 = strongly disagree); "The size of the incision is an important determinant of how long my recovery will take after surgery" (5 = strongly agree, 1 = strongly disagree); "I expect to have limitations to my usual physical activities during my recovery after surgery" (5 = strongly agree, 1 = strongly disagree); "The size of the incision is an important determinant of how I will feel about my body after surgery" (5 = strongly agree, 1 = strongly disagree). The patients were also asked to estimate how many days they thought it would take to recover completely.

Immediately following the operations, surgeons were asked to complete a questionnaire including type of surgery performed (CLC, MLC or open), port sizes and insertion points, estimated blood loss, amount of bupivacaine used, intraoperative complications, difficulty of the case and the resident's participation (percent dissection of Calot's triangle and liver bed) and duration of surgery.

Postoperatively, the patients were scheduled a clinic visits at 3–5 weeks and either a clinic visit or phone follow-up at 3 months after the surgery. In each visit, the patients were asked to complete CHAMPS questionnaire, VAS for pain, nausea and fatigue. The patients were also asked to rate their health state at each visit, fill out a scar assessment questionnaire and report whether they returned to work or studies, and at which date.

Incidence of postoperative complications was by review of the medical record (missing in four subjects).

Sample size

Sample size calculation was based on estimates of recovery from a previous study where patients reported 12 kcal/kg/week less activity 1 month postoperatively compared to baseline. A sample size of 115 patients was necessary to detect a 50 % improvement in recovery of physical activity at 1 month (from 12 to 6 kcal/kg/week below baseline), with a two-sided 5 % significance level and a power of 80 %.

Approximately 150 elective laparoscopic cholecystectomies are performed yearly in our center. We assumed that if an estimated 75 % of patients are eligible and agree to participate, with 15 % subsequent losses to follow-up, we estimated 115 patients could be feasibly enrolled in 12–15 months (approximately two patients per week). With an additional 3 months of follow-up required for the primary outcome, the proposed timeline for our study was approximately one and a half years.

Patients converted to alternate techniques, including upsizing of ports or open surgery, were analyzed according to the intention-to-treat principal.

Statistical methods

The data were analyzed according to "intention-to-treat" principle. Continuous data were compared with independent Student's t test (if normal distribution) or Wilcoxon rank-sum test (if non-normal distribution). Categorical variables were compared using Fisher's exact test. As the frequency of missing values for the primary outcome measure was low (12 %) and the values were not normally distributed, we opted to conduct a complete case analysis as opposed to imputing data [13]. A *(*post hoc*)* sensitivity analysis was conducted to compare patients' outcomes based on the treatment that they actually received (i.e., per-protocol analysis). A p value <0.05 was considered statistically significant. Data analysis was performed using Stata 12 (StataCorp, College Station, Tx).

Results

The study CONSORT diagram is shown in Fig. 1. We assessed 194 patients for eligibility, and 115 patients were randomized to either CLC or MLC (58 and 57, respectively). The primary analysis was intention to treat and involved all patients who were randomly assigned, excluding patients who had surgery elsewhere, had emergency surgery, withdrew consent, were randomized in error, or were lost to follow-up. Forty-two patients were included in the analysis for CLC, and 33 patients were analyzed in the MLC group; of those patients, 36 and 30 patients from the CLC and MLC groups, respectively, have physical activity scores both at baseline and at first follow-up and were included in the analyses for the primary outcome. Recruitment and procedures took place between February 2012 and September 2014. During this time, a total of 178 elective laparoscopic cholecystectomies were performed by the three surgeons at the Montreal General Hospital.

The study proceeded slower than planned, in part due to having only one miniinstrument set which complicated case booking, and breakage of the single 3-mm hook dissector. As this altered the ability to provide the MLC intervention, we decided to stop the trial early.

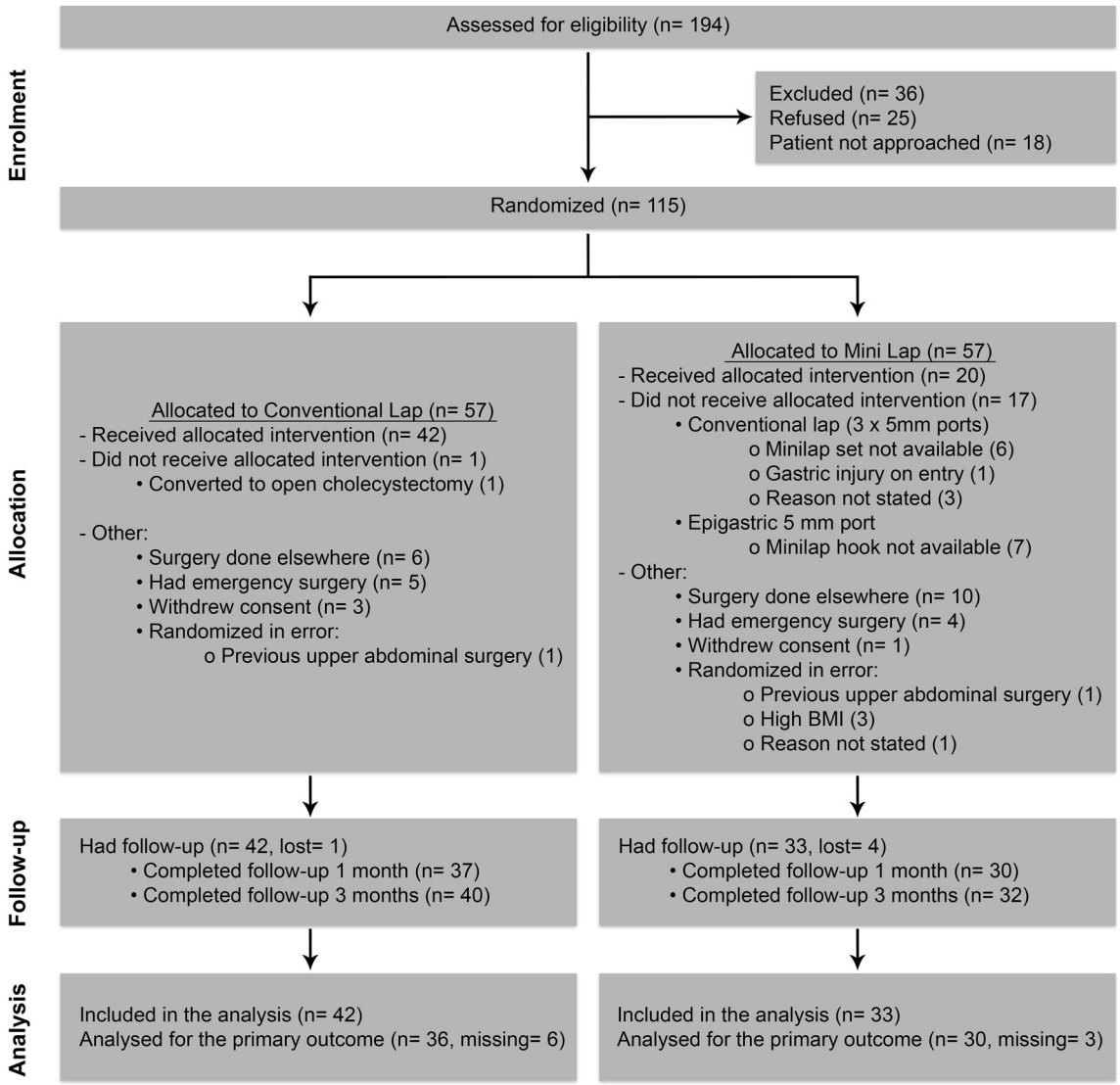

Fig. 1 Participants flow for the trial including screening, randomization and follow-up

Demographic and clinical characteristics were similar at baseline, including self-reported physical activity (CHAMPS; Table 1). The most common indication for surgery was biliary colic.

Intraoperative and postoperative variables

There was a significant difference in failure of the planned technique between the two groups, with 17 patients (51.5 %) in the MLC groups requiring upsizing at least one port to 5-mm, compared to only one patient in the CLC group (2.4 %) who required a conversion to an open procedure for inability to obtain a critical view of safety (Table 2). In ten MLC cases, conversion was to a standard procedure, using three 5-mm ports, most commonly because the miniinstrument set was not available. In another seven cases, only the epigastric port was upsized, due to insulation breakage on the minihook that was sent for repair. The operative time was similar between the two procedures [mean (SD) 67 (15) and 73 (22) min for CLC and MLC, respectively]. Other intraoperative variables were also similar, including trainee involvement, case difficulty, incidence of gallbladder perforation, amount of bupivacaine used and estimated blood loss. Five patients were admitted postoperatively. In the CLC, three patients were admitted for conversion to open, nausea and vomiting post-op, and observation of a liver laceration. In the MLC group, two patients were admitted, one for ERCP for a stone on cholangiogram and one for observation after repair of gastric laceration. There were three other postoperative complications: melena (likely secondary to the use of non-steroidal anti-inflammatory drugs), umbilical surgical site infection and postoperative pain requiring admission.

Table 1 Baseline demographic and clinical characteristics

	CLC $n = 42$	MLC $n = 33$	p value
Age (years)	55.3 (13.3)	53.8 (15.9)	0.67
Gender			0.47
F	29 (69 %)	20 (60 %)	
M	13 (31 %)	13 (40 %)	
Diagnosis			0.62
Biliary colic	33 (78.6 %)	23 (69.7 %)	
CBD stones	4 (9.5 %)	4 (12.1 %)	
GB polyps	4 (9.5 %)	3 (9.1 %)	
Pancreatitis/cholangitis	1 (2.4 %)	3 (9.1 %)	
ASA			0.55
I	6 (14.3 %)	8 (24.2 %)	
II	32 (76.2 %)	22 (66.7 %)	
III	4 (9.5 %)	3 (9.1 %)	
BMI (kg/m^2)	26.5 (3.7)	26.2 (4.7)	0.75
Missing	0	1	
Employed			0.81
Yes	26 (61.9 %)	22 (68.7 %)	
No	16 (38.1 %)	10 (31.3 %)	
Missing	0	1	
CHAMPS (kcal/kg/week)	23.4 [13.1, 44.6]	23.6 [14.2, 66.9]	0.35
Light activity	10.5 [2.6, 26.2]	10.5 [3.9, 18.4]	0.77
Mod activity	4.7 [0, 12.9]	14.2 [4.7, 32.6]	0.03
Missing	1	0	
Symptoms (0–10)			
Abdominal pain	0 [0, 1]	0 [0, 1]	0.86
Umbilical pain	0 [0, 0]	0 [0, 0]	0.61
Nausea	0 [0, 0]	0 [0, 0]	0.19
Fatigue	2 [0, 5]	3 [0, 5]	0.55
Overall health state (0–100)	87.5 [80, 92]	80 [75, 90]	0.12
Believes incision size affects pain (1–5)	4 [2, 4]	3 [3, 4]	0.82
Missing	1	0	
Believes incision size affects physical activities (1–5)	4 [3, 4]	4 [4, 4]	0.95
Missing	1	0	
Believes incision size affects recovery (1–5)	4 [2, 4]	4 [3, 4]	0.32
Missing	1	0	
Believes incision size affects Image (1–5)	2 [1, 3]	3 [1, 4]	0.17
Missing	2	0	
Expected days for recovery	6 [3, 10]	7 [3.5, 14]	0.39
Missing	5	1	

Data expressed as mean (SD), median [IQR], or n (%)

ASA American Society of Anesthesiologists class

Outcomes

Recovery of physical activity

There was no statistical difference in the primary outcome (physical activity 1 month post-op compared to pre-op) between the two groups (Table 3). Patients from the CLC reported 5 kcal/kg/week more physical activity at 1 month compared to baseline, while the MLC group remained 5.6 kcal/kg/week below their baseline (Fig. 2), but the difference was not enough to detect a statistical difference. There was also no difference in the number of patients

Table 2 Intraoperative and postoperative characteristics

	CLC ($n = 42$)	MLC ($n = 33$)	p value
Failure of technique (%)[a]	1 (2.4 %)	17 (51.5 %)	<0.001
Operating time (min)	67 (15)	73 (22)	0.20
Range (min)	36–126	45–95	
Case difficulty (0–10)			
Liver bed	2 [1, 4]	1 [0, 4]	0.42
Missing	3	1	
Calot's triangle	3 [2, 5]	3 [1, 5]	0.55
Missing	5	6	
Bupivacaine used (ml)	17.9 (5.6)	15.3 (4.7)	0.07
Missing	12	9	
EBL (%)			0.9
Minimal (<50 ml)	34 (82.9 %)	26 (81.3 %)	
51–100 ml	4 (9.8 %)	4 (12.5 %)	
100–150 ml	3 (7.3 %)	2 (6.3 %)	
Missing	1	1	
Gallbladder perforation	17 (44 %)	8 (29 %)	0.55
Missing	4	5	
Intraoperative complication[b]	1 (2.6)	1 (3.1)	1.0
Missing	3	1	
Proportion (%) performed by resident			
Calot's triangle	100 [80, 100]	95 [0, 100]	0.06
Liver bed	100 [100, 100]	100 [100, 100]	0.12
Missing	6	6	
Day surgery	39 (93 %)	31 (94 %)	0.61
Postoperative complications[c]	1 (2.6 %)	2 (6.3 %)	0.59
Missing	3	1	

Data expressed as mean (SD), median [IQR], or n (%)

EBL estimated blood loss

[a] This included one conversion to open in the CLC group and upsizing of one or more of the 3-mm ports in the MLC group

[b] This includes one case of liver laceration in CLC and one case of gastric laceration in MLC

[c] Includes one case of surgical site infection after CLC and one case each of melena and postoperative pain requiring admission after MLC

considered to have recovered postoperatively, defined as CHAMPS score 10 % above or below the patient's baseline CHAMPS score.

The median estimated weekly physical activity was similar between the two groups at 1 and 3 months. The days to return to work or studies were similar between the two groups.

Pain, fatigue, nausea and health state

Abdominal pain scores at 3 months were lower in the MLC group compared to the CLC group ($p = 0.006$), but the median score in both groups was 0. Patients in the MLC group reported less fatigue at 1 month ($p = 0.05$) and better overall health state at 3 months ($p = 0.013$). Other symptom scores were similar between the two groups (Table 4).

Cosmetic result

There was a statistically significant benefit for MLC in patients' assessment of their scar appearance at 1 and 3 months, and with satisfaction with the scar at 3 months. The other reported variables in the scar assessment questionnaire were similar between the two groups (Table 5).

Per-protocol analysis

Our "per-protocol" analysis compared 17 patients with completed MLC to 57 patients who received CLC. There

Table 3 Recovery of self-reported physical activity

	CLC ($n = 42$)	MLC ($n = 33$)	p value	n CLC/MLC
Physical activity (kcal/kg/week)				
Pre-op	23.4 [13.1, 44.6]	23.6 [14.2, 66.9]	0.35	41/33
1 month	20 [7.9, 52.5]	16.8 [11.8, 28.6]	0.90	37/30
3 months	24.3 [13.1, 42.7]	25.1 [15.1, 34.1]	0.95	39/32
Physical activity versus pre-op (kcal/kg/week)				
1 month	+5 [−11.8, 16.7]	−5.6 [-25.6, 5.8]	0.06	36/30
3 months	+1.4 [−19.8, 16.2]	−2.4 [−29.4, 8.7]	0.23	37/32
Number of patients recovered*				
1 month	22 (61 %)	13 (43.3 %)	0.21	36/30
3 months	23 (60.5 %)	15 (46.9 %)	0.33	38/32
Return to work (days)	15 [7, 27]	14 [7, 19]	0.16	23/22

Median [IQR]

* Defined as ±10 % of CHAMPS score compared to baseline score

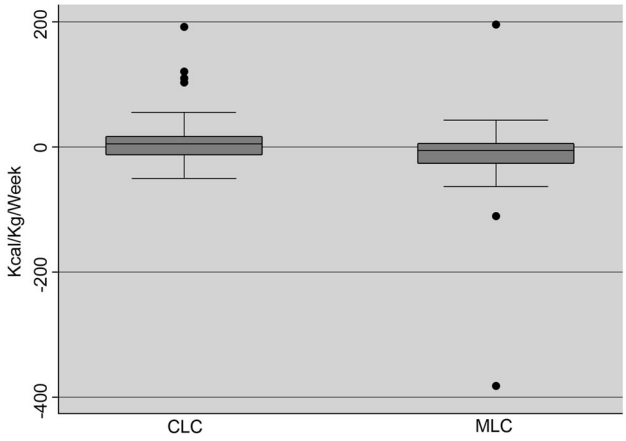

Fig. 2 Difference in weekly total physical activity from baseline to 1 month after surgery

were no significant differences in baseline demographic and clinical characteristics, physical activity, or intraoperative and postoperative course. There we no differences in reported physical activity between the groups at 1 or 3 months. However, while the CLC group reported similar levels of physical activity at 3 months compared to their baseline, the MLC group remained below their baseline (+2.1 [−14.7, 15.2] vs −13.3 [−45.5, 5.1], $p = 0.04$, respectively). Patients who received MLC reported better scar appearance scores at 1 month in the per-protocol analysis ($p = 0.03$). Other outcomes were similar between the two groups ("Appendix" in ESM).

Discussion

In this randomized trial, there was no benefit of minilaparoscopic cholecystectomy (MLC) using three 3-mm upper abdominal ports on recovery of physical activity compared to CLC using three 5-mm upper abdominal ports. However, patients in the MLC group had better cosmesis, less fatigue, less pain and better overall health state up to 3 months postoperatively, although the differences were quite small.

These results are consistent with some previous published trials demonstrating less early pain and better early cosmetic outcomes [14–16], while other trials have not shown these differences [17, 18]. Unlike other studies, we used three 5-mm ports in the control, while previous studies included one 10-mm upper abdominal port in their controls [7]. Moreover, these benefits on pain, fatigue and cosmesis were seen in the context of a high rate of upsizing at least one port to 5-mm in the MLC group (51.5 %). There were no differences in operative time or complications despite the involvement of trainees to the same degree in both techniques.

In the "per-protocol" analysis of the subset of patients receiving full MLC ($n = 17$) versus those receiving CLC, there were no differences in self-reported physical activity between the groups at baseline, 1 or 3 months. However, in this subset of patients, the MLC group remained below baseline physical activity at 3 months, while the CLC group was back to baseline. This may in part reflect a trend toward higher baseline physical activity in the MLC group, as patients with higher levels of physical activity require longer time to recover [19].

Patients often seek information about the time it will take to recover from surgery. The metabolic impact of surgery is proportional to the degree of surgical trauma [20]. Abdominal surgery involves two separate wounds, one in the abdominal wall and one to the viscera and peritoneum. A key strategy of laparoscopic surgery is to improve recovery by minimizing abdominal wall trauma. In this regard, the use of smaller ports and instruments is a natural evolution of minimally invasive surgery. However,

Table 4 Symptoms at 1 and 3 months postoperatively

	CLC ($n = 42$)	MLC ($n = 33$)	p value	n CLC/MLC
Pain (0–10)				
Abdominal				
1 month	0 [0, 2]	0 [0, 2]	0.71	37/30
3 months	0 [0, 1]	0 [0, 0]	0.006	40/32
Umbilical				
1 month	1 [0, 1]	0 [0, 1]	0.14	37/30
3 months	0 [0, 0]	0 [0, 0]	0.91	40/32
Nausea (0–10)				
1 month	0 [0, 0]	0 [0, 0]	0.55	37/30
3 months	0 [0, 0]	0 [0, 0]	0.47	40/32
Fatigue (0–10)				
1 month	4 [1, 5]	1 [0, 4]	0.05	36/30
3 months	2 [0, 4]	0 [0, 2.5]	0.24	40/32
Overall health state (0–100)				
1 month	80 [70, 90]	85 [80, 95]	0.25	36/29
3 months	85 [80, 90]	90 [89, 95]	0.013	39/32

Median [IQR]

Table 5 Cosmetic results at 1 and 3 months postoperatively

	CLC ($n = 42$)	MLC ($n = 33$)	p value	n CLC/MLC
Scar appearance (1–5)				
1 month	4 [3, 4]	4.5 [4, 5]	0.009	37/30
3 months	4 [3, 5]	5 [4, 5]	0.02	40/32
Scar symptoms (1–5)				
1 month	4 [4, 5]	4.5 [4, 5]	0.23	37/30
3 months	5 [4, 5]	5 [5]	0.38	40/32
Scar consciousness (1–4)				
1 month	4 [4]	4 [4]	0.86	37/30
3 months	4 [4]	4 [3.5, 4]	0.81	40/32
Scar satisfaction (1–4)				
1 month	4 [3, 4]	4 [3, 4]	0.87	37/30
3 months	4 [3, 4]	4 [3.5, 4]	0.04	40/32

Median [IQR]

recovery from surgery is multidimensional, and post-discharge functional outcomes, like return to physical activity, should be included [21]. Only two previous studies [15, 16] in a Cochrane meta-analysis of randomized trials comparing miniport and standard laparoscopic cholecystectomy included return to activities as an outcome, with no differences found between the groups. These were secondary outcomes for these studies and were assessed by asking patients when they returned to normal, without measuring "normal" at baseline. In contrast, we chose physical activity as the primary outcome for our study and measured recovery by comparing 1-month activities to preoperative activities [21]. Physical activity levels were measured using the validated CHAMPS questionnaire [11], and the minimal clinically important difference (MCID) in the context of surgical recovery has been estimated to be 8 kcal/kg/week [22].

Despite the small incision size, there was no statistical difference in recovery of physical activity after MLC and CLC. At 1 month, the differences in physical activity compared to baseline were lower than the MCID, suggesting that both groups had recovered by that time. In addition, there were no differences in physical activity demonstrated between the two groups at 1 or 3 months postoperatively. However, there was a wide range of reported activity, and more than half of the patients were not recovered to within 10 % of baseline by 1 month. The sample size calculation was based on a previous validation

study of CHAMPS as a measure of recovery after laparoscopic cholecystectomy. In that study, patients without complications had recovered to baseline by 1 month, and there were very few patients with complications in the present study. In addition, while lower-intensity activities were recovered by 1 month, moderate- to high-intensity activities were not; in the present study, patients in the MLC group performed higher-intensity activities at baseline and these may require longer time to recover (10). It is also possible that the timing of the assessment was too late to detect differences in recovery between the groups, which may be more evident early in the postoperative period [11].

A strength of the study is the attempt to standardize perioperative care for all subjects using an established care pathway. All subjects received the same written and oral education in the pre-op clinic by nurses unaware of group allocation. Multimodal analgesia was used including infiltration of long-acting local anesthetic preemptively into the incisions, and multimodal opioid-sparing analgesia was prescribed. We attempted to blind patients to their group allocation by using the same wound dressings for all subjects. However, these remained for only 1 week, and outcomes were determined at 1 and 3 months. There was also a difference in skin closure technique for the 3-mm and 5-mm ports. Subcuticular 4–0 poliglecaprone (Monocryl) suture and adhesive strips (Steristrips) were used to close the 5-mm ports, while adhesive strips alone were sufficient to close the 3-mm ports. Previous studies do not suggest improved cosmesis with adhesive strips compared to suture, although there may be a lower incidence of wound redness [23].

This study has several limitations. The study enrolled patients with uncomplicated gallbladder diseases requiring laparoscopic cholecystectomy. Patient with previous acute cholecystitis, morbid obesity or previous upper abdominal surgeries were excluded, eliminating a subgroup of cases that are more technically challenging. Due to small numbers, we were unable to account for potential confounders in recovery such as need for hospital admission, final pathology or complications. While there was an attempt to "blind" patients to group allocation using equivalent dressings for 1 week, we did not query patients to determine whether they in fact were aware of their group allocation. There was a high "conversion" rate in the MLC group mostly due to only having a single miniinstrument set, with re-sterilization usually not enabling more than one case per day, or to insulation breakage of the minihook instrument, which required repair. This required upsizing of the epigastric port to 5 mm to use a conventional hook cautery for the dissection and reducing the differences between the groups. However, this is representative of a real-world situation where lack of availability for specialized instruments may limit applicability of the technique. In this regard, this trial could be considered as a "pragmatic" rather than "explanatory" trial. Issues with instrument availability also delayed completion of the trial. The slow progress led to early termination of the trial, and while the planned number of subjects was randomized, losses after randomization resulted in fewer patients remaining for analysis for the primary outcome. Although our intended target sample was 115 patients, the patients included in the final analysis were 75 in total. This was mainly due to the number of enrolled patients having their surgeries at other institutions or requiring emergency surgery. However, with the primary outcome not consistent with the hypothesis in the sample size calculations (i.e., that MLC would be associated with faster recovery of physical activity), increasing the number of patients would not be likely to change the conclusions of the study.

In summary, we found that in selected patients with uncomplicated biliary disease, MLC with 3-mm ports provides small benefits compared to CLC with 5-mm ports, in terms of pain, fatigue, overall health status and cosmesis up to 3 months postoperatively. These benefits were seen despite the need to upsize one or more ports in more than half of the patients related to durability and availability of miniature instruments and support the use of the MLC approach in appropriate patients.

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Compliance with ethical standards

Disclosures Drs. Mohsen Alhashemi, Mohammed Almahroos, Julio F. Fiore Jr., Juan Mata Gutierrez, Amy Neville, Melina Vassiliou, Gerald M. Fried, Liane S. Feldman and Ms. Pepa Kaneva have no conflict of interest or financial ties to disclose.

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