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Comparison of postoperative pain at umbilical wound after conventional laparoscopic cholecystectomy between transumbilical and infraumbilical incisions: a randomized control trial

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Abstract

Background Transumbilical incision has been applied in single-incision laparoscopy. Evidence for the effect of transumbilical incision on postoperative pain compared with infraumbilical incision is still lacking.

Methods A randomized controlled trial (RCT) was conducted in a university hospital. Patients who underwent conventional laparoscopic cholecystectomy were randomized to have transumbilical or infraumbilical incision. Postoperative pain was measured using visual analog score at 6, 24 h, and 7 days post operation. Secondary outcomes were analgesic usage, length of stay, superficial surgical site infection (SSI), wound numbness, and hypersensitivity. Risk ratio and mean difference (MD) along with their 95% confidence intervals (CIs) were estimated. Adjusted analysis was done, if clinical unbalanced characteristics presented. The study was registered at http://ClinicalTrial.gov (ID NCT02738710).

Results A total of 102 patients were enrolled in which 51 patients were randomized to each interventional group. Postoperative pain was not significantly different between the groups with the MD of − 0.07 (95% CI − 0.47, 0.35). Paracetamol usage was significantly 1 tab (95% CI − 1.9, − 0.1) less after transumbilical incision, but this was not significant after adjusting for unbalanced characteristics. Superficial SSI rate was much higher in the transumbilical than the infraumbilical group, i.e., 16 versus 4%, but this was not significant ($p = 0.070$). Satisfaction scores at 3 months were not different between the groups, with the corresponding means of 8.9 [standard deviation (SD) 1.3] and 9.0 (SD 1.0).

Conclusions Transumbilical incision had non-significant different pain compared to infraumbilical incision. Most patients in both groups were satisfied with the operation at 3 months. A further large RCT is required for comparing SSI between the two incisions.

Keywords Transumbilical · Infraumbilical · Laparoscopic cholecystectomy · Postoperative pain · Randomized controlled trial

Gallbladder disease is a common surgical condition with the incidence rate of 120–160 per 100,000 individuals per year in general population [1]. Laparoscopic cholecystectomy

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(LC) is a standard treatment with its inherent minimally invasive benefits of shorter wound length, less postoperative pain, and rapid recovery when compared to open cholecystectomy. LC can be done via 3–4 ports with a camera port inserted periumbilically usually via infraumbilical incision. With effort toward less invasive surgery and cosmetic concern, many technical advancements have been developed including single-incision LC (SILC), natural orifice transluminal endoscopic surgery (NOTES), and transumbilical incision [2–4].

A survey of women's attitude for type of cholecystectomy in France found that 87% of women favored SILC performed through transumbilical incision than conventional LC because of better cosmesis. However, 19% of them expressed concern about more postoperative pain after transumbilical compared to infraumbilical incision [5]. A recent randomized controlled trial (RCT) found similar satisfaction scores between transumbilical and periumbilical incisions after conventional LC, but this study did not compare postoperative pain [6]. Previous evidence from meta-analyses demonstrated no difference [7] and less postoperative pain [8] after SILC than conventional LC. However, these results could not answer the question whether postoperative pain between transumbilical and infraumbilical incisions is different. A different number of incisions between SILC and conventional LC [9, 10] and larger sheath size necessary for multiple ports insertions in SILC [11, 12] might confound the effect of transumbilical incision on wound pain.

To the best of our knowledge, no RCT has directly compared postoperative pain after transumbilical versus infraumbilical incision in conventional LC. Therefore, we conducted a RCT which primarily aimed to compare postoperative pain between transumbilical and infraumbilical incisions in conventional LC. In addition, total analgesic usage, length of stay (LOS), superficial surgical site infection (SSI), patient's satisfaction scores, wound numbness, and wound hypersensitivity were also compared.

Materials and methods

A parallel RCT was conducted from September 2016 to November 2017 at Thammasat University Hospital in Thailand after approval by the Institutional Ethics Committee. The study was registered with http://ClinicalTrial.gov (ID NCT02738710). Adult patients, aged > 18 years, who underwent elective conventional LC were invited to participate with our study. Patients were excluded if they were pregnant, immunocompromised host (i.e., patients with human immunodeficiency virus, taking immunosuppressive drug, during chemotherapy, autoimmune disease), on peritoneal dialysis, were obese [body mass index (BMI) > 35 kg/m^2], with end-stage renal disease, and cirrhosis with ascites. Informed consent was taken before operations. Data were collected in standardized data form by a research assistant or attending physicians. In case of loss to follow-up, telephone contact was done to prevent missing data.

Randomization

A block-randomization with block size of 4–6 and a ratio of 1:1 was applied. Randomization sequence was generated by independent statistician using STATA version 12.0. Sealed opaque envelopes were applied for allocation concealment. The envelopes were opened in the operative room by scrub nurses just before skin incision.

Blinding

Neither physicians nor patients were blinded because of the nature of operative procedure. However, the umbilical wound was dressed with occlusive dressing; therefore, outcome assessors, i.e., research assistants were blinded when assessing postoperative pain at 6 and 24 h postoperatively.

Interventions

LC was routinely performed as inpatient procedure under general anesthesia. The techniques of LC were similar to all patients except the type of umbilical incision. Operations were done via 3–4 ports which depended on surgeon's preference. A 10-mm port was used for umbilical incision, whereas 5–10-mm ports were used for other abdominal incisions. For transumbilical intervention, incision was done in the umbilicus either transverse or vertical direction which depended on the characteristics of the umbilicus. Then, linear alba was grasped and incised longitudinally to expose peritoneal cavity. In the infraumbilical group, transverse incision was done 1–2 cm below the umbilicus. Linear alba was incised similar to that in the transumbilical group. Surgery was done by surgeons (BS, PL, AT, ES, and CM) with more than a hundred cases' experience of conventional LC. Only closed suction drains were used.

Cointerventions

Pre- and post-surgery treatments and/or interventions were standardized including prophylaxis antibiotics, preoperative scrub, type of anesthesia, wound closure, postoperative analgesia, and wound care. Only cefoxitin 1 gram (g) intravenous (iv) was prescribed for preoperative prophylaxis. Ciprofloxacin 400 milligram (mg) iv was used instead if patients were allergic to penicillin. General anesthesia and umbilical scrub were performed for all patients. Subcutaneous fat was closed with Vicryl 4#0 interruptedly and the skin was closed by a subcuticular suture using

Vicryl 5-0 continuously. Then, sterile strip was applied. Occlusive dressing to cover and seal the umbilical wound was applied. Dressing was changed before discharge. Liquid diet was resumed immediately after operation. Patients were prescribed parecoxib 40 mg iv every 12 h or ketorolac 30 mg iv every 8 h and morphine 0.05 mg/kg iv per request every 4 h for 24 h. Naproxen (250 mg) 1 tab was given twice a day with paracetamol (500 mg) 1 tab oral per request every 4 h. Patient was discharged when they could tolerate soft diet and take good care of themselves.

Outcomes

Postoperative pain at and around the umbilicus was measured by research assistants at 6, 24 h, and 7 days postoperatively using visual analog scale (VAS) 0–10, in which 0 represented no pain and 10 represented worst pain. Accumulative dosages of requested morphine and paracetamol during the first 24 h were collected. LOS was counted from the day of surgery to discharge date. Satisfaction score using VAS score of 0–10, umbilical wound numbness, and hypersensitivity was measured at 3 months by telephone contact. If patient complained of wound numbness or hypersensitivity, severity of symptoms would be asked using VAS scale of 0–10.

Superficial SSI at umbilical wound was assessed by attending surgeons before discharge, and 7–10 days at outpatient department. Diagnosis of SSI was done following the Center for Disease Control (CDC) criteria [13], i.e., occurring within 30 days, only skin/subcutaneous tissue involvement, and one of the following: purulent drainage, organism isolated from fluid or tissue, or at least 1 of the following signs/symptoms: pain or tenderness, localized swelling, redness, or heat, and the superficial incision was deliberately opened by surgeon without a positive culture.

Sample size

Mean VAS at 8 h postoperatively after three-port LC with infraumbilical incision was 3.5 with a standard deviation (SD) of 1.6 in a study by Pan et al. [9] Type I error, power, and ratio were set as 0.05 (2-sided test), 0.80, and 1:1, respectively. Size of difference of 0.9 which was considered as a minimum clinically significant difference in VAS pain score was used for calculation [14]. Sample size calculation was done by STATA version 12.0 using Post method with correlation between follow-up value of 0.5 within three follow-ups, which yielded 45 samples per group. Accounting for 10% loss to follow-up rate, this resulted in a total of 100 participants.

Statistical analysis

Baseline characteristics of the patients were described by the interventional groups using mean (SD) or frequency (proportion) for continuous and categorical data, respectively. All analyses were done using intention-to-treat approach. Primary outcome (i.e., VAS for pain) was repeatedly measured, so it was compared between the interventional groups using a mixed effects regression model. Other continuous outcomes without repeated measures were compared between the interventional groups using linear or quantile linear regression analysis depending on distribution of the data. Binary regression analysis was applied for binary outcomes. Unbalanced baseline characteristics between the incisional groups were also included in these regression models for adjusting possible confounding effects. Mean difference (MD) and risk ratio (RR) along with their 95% confidence interval (CI) were estimated and described.

Results

One hundred and two patients were successfully enrolled and randomly allocated to the infraumbilical ($n=51$) and transumbilical ($n=51$) groups, see Fig. 1. Mean age was 52 (SD = 13) years, and 60% of the patients were females. About 20% of the patients had diabetes. Most of the indications for surgery were symptomatic gallstone and chronic cholecystitis which accounted for about 61% followed by common bile duct stone (33%), gallbladder polyp (4%), and history of acute cholecystitis (2%). No patient required blood transfusion. Six patients required open conversion because of severe adhesion ($n=5$) and right hepatic artery tear ($n=1$). No incisional hernia occurred during follow-up period.

Baseline characteristics were described by the interventional groups (see Table 1), and none of them was clinically different between the interventional groups, except conversion rate (10 vs. 2%), intraoperative bile leak (22 vs. 10%), and drain (20 vs. 8%). These three unbalanced characteristics were further included in the multivariable analysis of the outcomes for adjusting purpose.

Postoperative pain and use of analgesia

Postoperative pain was not different between the interventional groups with overall VAS means of 3.18 (95% CI 2.89, 3.47) and 3.25 (95% CI 2.96, 3.54) in the transumbilical and infraumbilical groups, respectively, with the MD of −0.07 (95% CI −0.47, 0.35, $p=0.756$), see Table 2. Unbalanced baseline characteristics (i.e., conversion, intraoperative bile

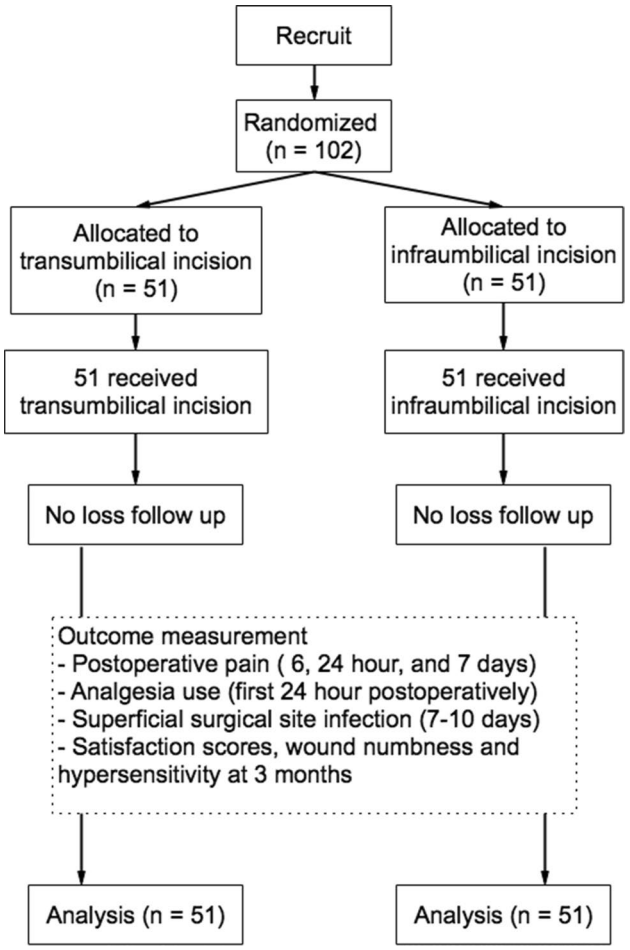

Fig. 1 CONSORT flow diagram

leak, use of drain) and use of paracetamol were included in the multivariable analysis and yielded the adjusted MD of −0.02 (95% CI −0.42, 0.38), see Supplement Table 1.

Median dosages of morphine usage within 24 h post operation were 3.4 mg [interquartile range (IQR): 0, 5.3] and 2.7 mg (IQR: 0, 4) for the transumbilical and infraumbilical groups, respectively, with the median difference of −0.6 (95% CI −2.7, 1.4; $p=0.525$). Paracetamol dosage was significantly lower in the transumbilical than in the infraumbilical group with a median difference of −1 tab (95% CI −1.9, −0.1; $p=0.038$). After adjusting for unbalanced characteristics, results were not changed except use of paracetamol, which became a non-significant difference between the groups, see Supplement Table 1.

Secondary outcomes

Superficial SSI rate was much higher in the transumbilical group than in the infraumbilical group (16 vs. 4%) with the estimated RR of 4.0 (95% CI 0.9, 17.9; $p=0.070$). However, this risk was not statistically significant. Characteristics of patients with SSI were further explored and demonstrated, see Supplement Table 2. Ten out of 51 patients in the transumbilical group developed SSI, in which 2/10 (10%) had diabetes. Two out of 51(4%) in the infraumbilical group developed SSI, in which 1/2 patient had conversion from severe adhesion. LOS showed very small difference between the two groups with the mean of 2.5 (SD = 1.27) and 2.2 days (SD = 0.57) in the infraumbilical and transumbilical groups, respectively. Only 1 patient (2%) complained about umbilical wound numbness at 3 months after infraumbilical incision. Hypersensitivity rate was a bit lower after transumbilical incision than after infraumbilical incision (10 vs. 16%) with the RR of 0.6 (95% CI 0.2, 1.8; $p=0.379$), although this did not reach statistical significance. Despite that, severity of symptoms was mild with corresponding VAS of 2 (SD = 0.7) and 3 (SD = 1.8), respectively. Most patients were satisfied with the operation after 3 months which was not significantly different between the groups. After adjusting for unbalanced characteristics, results were not much changed, see Supplement Table 1.

Discussion

We conducted a RCT primarily which compared clinical outcomes after transumbilical and infraumbilical incisions in conventional LC. Based on intention-to-treat analysis approach, postoperative pain was not different between the groups. In addition, none of the secondary outcomes was significantly different including 24-h morphine usage, LOS, superficial SSI, satisfaction scores, wound numbness, and hypersensitivity except paracetamol usage which was significantly different.

Our results were similar to previous aforementioned meta-analyses with similar and less postoperative pain after SILC than conventional LC [7, 8]. However, we compared pain at and around the umbilicus after conventional LC with similar number of incisions and sheath size between the groups of interventions, and so had less confounders. Paracetamol usage was only 1 tab significantly lower after transumbilical than after infraumbilical incision, but this difference was neither clinically significant nor statistically significant after adjusting for unbalanced covariables.

Our findings indicated that superficial SSI was surprisingly high after transumbilical incision (16%) despite preoperative prophylaxis antibiotics and umbilical-scrub protocol before operation in every case. Although the difference was not statistically significant compared to infraumbilical incision, it was clinically significant because the RR was as high as 4 (95% CI 0.9, 17.9). Sample size calculation of this RCT was initially planned to detect postoperative pain difference, not for superficial SSI. Therefore, with a total of 102 patients it only had power of test to detect SSI

Table 1 Baseline characteristics of the patients between interventions

Characteristics	Infraumbilical incision ($n=51$)	Transumbilical incision ($n=51$)
Age, year, mean (SD)	53 (13)	50 (13)
Gender, *n* (%)		
Male	18 (35)	24 (47)
Female	33 (65)	27 (53)
BMI, kg/m^2, mean (SD)	24.3 (3.5)	24.5 (3.9)
Diabetes, *n* (%)	10 (20)	9 (18)
Indication for cholecystectomy, number (%)		
Symptomatic gallstone	15 (29)	22 (43)
Chronic cholecystitis	13 (25)	12 (24)
Gallbladder polyp	2 (4)	2 (4)
Previous CBD stone	19 (37)	15 (29)
History of acute cholecystitis	2 (4)	–
ASA classification, *n* (%)		
Class I	20 (39)	19 (37)
Class II	28 (55)	29 (57)
Class III	3 (6)	3 (6)
Number of ports, *n* (%)		
3 Ports	40 (78)	42 (82)
4 Ports	11 (22)	9 (18)
Operative time, min, mean (SD)	91 (32)	82 (33)
Conversion to open cholecystectomy, *n* (%)	5 (10)	1 (2)
Intraoperative bile leak, *n* (%)	11 (22)	5 (10)
Use of drain, *n* (%)	10 (20)	4 (8)

ASA American Society of Anesthesiologists, *CBD* common bile duct, *SD* standard deviation

Table 2 Comparisons of outcomes between infraumbilical and transumbilical incisions: an intention-to-treat analysis approach

Outcomes	Infraumbilical incision ($n=51$)	Transumbilical incision ($n=51$)	Effect size[a] (95% CI)	*p* values
Postoperative pain, VAS, mean (SD)				
6 h	6.5 (1.7)	6.4 (1.7)	−0.07 (−0.47, 0.35)	0.756
24 h	2.9 (1.6)	2.6 (1.8)		
7 days	0.3 (0.7)	0.5 (1.0)		
Morphine use, mg, median (IQR)	3.4 (0, 5.3)	2.7 (0, 4)	−0.6 (−2.7, 1.4)	0.525
Paracetamol use, tab, median (IQR)	2 (0, 2)	1 (0, 2)	−1 (−1.9, −0.1)	0.038
Length of stay, day, mean (SD)	2.5 (1.27)	2.2 (0.57)	−0.4 (−0.7, −0.03)	0.073
Superficial SSI, *n* (%)	2 (4)	8 (16)	4 (0.9, 17.9)	0.070
Satisfaction score, VAS, mean (SD)	9.0 (1.0)	8.9 (1.3)	−0.1 (−0.6, 0.4)	0.670
Wound numbness, *n* (%)	1 (2)	0 (0)	–	1.000
Wound hypersensitivity, *n* (%)	8 (16)	5 (10)	0.6 (0.2, 1.8)	0.379
Hypersensitivity score, VAS, mean (SD)	3 (1.8)	2 (0.7)	−1 (−2.8, 0.9)	0.260

IQR interquartile range, *MD* mean difference or median difference, *RR* risk ratio, *SD* standard deviation, *SSI* superficial surgical site infection, *VAS* visual analog scores

[a]Effect size = mean difference for continuous outcome, risk ratio for dichotomous outcome

difference approximately 52.4%. As a result, we were faced with a false-negative rate of no difference of SSI of 48%. This corresponded with uncertainty of estimation given the 95% CI width was very wide. A larger sample size of at least 97 patients per group is required to detect RR of 4 and narrow down the CI width.

Incisional wound can be contaminated by bacteria from skin microflora or organisms from intraabdominal contamination such as bile. Nearly a quarter of umbilical microflora could still be cultured after skin preparation with antiseptic which might have contaminated the wound during transumbilical incision [15]. In addition, wound care was difficult in some patients with a deep umbilicus and who had much sweat from hot climate in Thailand. Further controlled or well-performed systematic review and meta-analysis study to increase power of detection should be done.

Satisfaction scores at 3 months post operation were high and not much different between the two groups. This finding was consistent to another RCT comparing cosmetic satisfaction scores between transumbilical and infraumbilical incisions in conventional LC with the scores of 9 (IQR 8–10) in both groups [6]. Only 28% of patients in this RCT valued their umbilical appearance. Most patients in our study were old (mean age 52 years) who might not pay attention to umbilical appearance. Recent meta-analysis found better cosmesis and body image after SILC than conventional LC [8]. Interviewing enrolled patients after completion of the study demonstrated that 31 (61%) of the infraumbilical groups stated that if they could choose, they would choose transumbilical incision, whereas 11 (22%) of the transumbilical group would choose infraumbilical incision.

To the best of our knowledge, our study is the first RCT which compared the effect of transumbilical versus infraumbilical incision on postoperative pain. The sample size was calculated and reported with adequate power to detect clinically different VAS pain scores but not for superficial SSI, resulting in low power to detect SSI difference, or in other words high false-negative rate of detection of SSI. Three baseline clinical characteristics were unbalanced between the intervention groups. The randomized sequence was checked and found that actual received interventions were all matched with sequence generations, indicating that the unbalance should be due to chance, which more likely occurred because of small number of subjects. However, we performed multivariable analyses to adjust effects of these unbalanced characteristics. The study was conducted according to CONSORT guidelines. Furthermore, the outcome assessors of primary outcome which was postoperative pain were blinded to the randomization. However, other outcomes were not assessed blindedly. Some missing data were filled by telephone contact that might cause recall bias.

In conclusion, postoperative pain was not significantly different between transumbilical and infraumbilical incisions. Most the patients were satisfied at 3 months after both types of incision. However, transumbilical incision might have higher risk to develop superficial SSI than infraumbilical incision. A further large-scale RCT or a systematic review and meta-analysis should be conducted to detect difference of SSI between these two types of incision. Preoperative discussion with the patients to select type of incision might improve patient satisfaction.

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Compliance with ethical standards

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