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ORIGINAL SCIENTIFIC REPORT

Subcuticular Sutures Versus Staples for Wound Closure in Open Liver Resection: A Randomised Clinical Trial

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Abstract

Background Subcuticular sutures reduce wound complication rates only in clean surgeries. Repeat resection is frequently required in liver surgery, due to the high recurrence rate (30–50%) of liver cancers. The aim of this study is to assess that subcuticular sutures is superior to staples in liver surgery.

Methods This single-centre, single-blinded, randomised controlled trial was conducted at a university hospital between January 2015 and October 2018. Patients were randomly assigned (1:1) to receive either subcuticular sutures or staples for skin closure. Three risk factors (repeat resection, diabetes mellitus and liver function) were matched preoperatively for equal allocation. The primary endpoint was the wound complication rate, while secondary endpoints were surgical site infection (SSI), duration of postoperative hospitalisation and total medical cost. Subset analyses were performed only for the 3 factors allocated as secondary endpoints.

Results Of the 581 enrolled patients, 281 patients with subcuticular sutures and 283 patients with staples were analysed. As the primary outcome, the wound complication rate with subcuticular sutures (12.5%) did not differ from that with staples [15.9%; odds ratio (OR), 1.33; 95% confidence interval (CI), 0.83–2.15; p = 0.241]. As secondary outcomes, no significant differences were identified between the two procedures in the overall cohort while overall wound complications [7 patients (8.5%) vs. 17 patients (20.0%); OR, 2.68; 95% CI, 1.08–7.29; p = 0.035] with repeat incision were significantly less frequent with subcuticular sutures.

Conclusion Subcuticular sutures were not shown to reduce wound complications compared to staples in open liver resection, but appear beneficial for repeat incisions.

Introduction

Abdominal skin closure is frequently achieved using either subcuticular sutures or approximation by metallic staples. Subcuticular sutures for skin closure are known to offer effective approximation for skin closure in most types of surgery, whereas approximation by metallic staples contributes to faster wound closure and easier handling. Several clinical trials of clean surgery have demonstrated that subcuticular sutures are associated with a significantly lower incidence of wound complications. [1–3] However, regarding clean-contaminated surgeries such as digestive tract surgery, subcuticular sutures have shown superiority only in sub-group analyses. [4, 5]

The incidence of wound complications is higher in hepatobiliary surgery than in other fields. [6–11] Compared to other surgeries, hepatobiliary surgeries require complex procedures, show a background of chronic liver disease, associated with longer operation times and greater length of surgical incision with thoracotomy, which often

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escalates to wound complications. To reduce wound complications, methods that have been performed include intraoperative administration of antimicrobial prophylaxis, irrigation of wounds before closure, use of absorbable sutures at the subcutaneous level and application of wound-protective dressing materials. [12–15] However, wound complications still arise in more than 10% of hepatobiliary surgeries. Furthermore, liver cancers such as hepatocellular carcinoma and colorectal metastasis have a high frequency of recurrence and around 30–50% of patients undergo repeat surgery. [16, 17] The same incision is frequently used for repeat resections. However, no studies appear to have focused on the reduction of wound complication rates for repeat incisions according to unique factors in liver surgery. We therefore planned a large randomised controlled trial (RCT) to analyse differences in prevention of wound complications between subcuticular sutures and staples after elective open liver resection (OLR). To further analyse whether type of closure contributes to reduced wound complication rates, three risk factors linked to wound complications (diabetes mellitus, liver function and repeat resection) were matched for prior to randomisation.

Patients and methods

Study design

Between January 2015 and October 2018, this single-centre, single-blinded RCT was undertaken at a Japanese university high-volume centre for liver resection. The protocol for this study was approved by the institutional review board (IRB) at Nihon University School of Medicine which includes an external observer (RK170314-02). This study has been registered in the University Hospital Medical Information Network Clinical Trials Registry (UMIN-ID000036670), a member of the Japan Primary Registries Network, which meets the WHO registry criteria. All patients provided written informed consent prior to enrolment and were informed of the right to decline participation in this study at any time.

Study endpoints

The primary endpoint was the incidence of any wound complications within 30 days after surgery. Secondary endpoints were the frequency of surgical site infection (SSI), duration of postoperative hospitalisation and total medical cost. Subset analysis allowed only 3 preoperative allocated factors closely associated with wound complication. This study evaluated the superiority of subcuticular sutures compared to staples.

Definitions

Wound complications were defined as the presence of signs relating to treatment: wound disruption, stitch abscess, abscess, seroma or hematoma or superficial or deep incisional SSI. According to the Centres for Disease Control and Prevention (CDC) guideline, [18] superficial incisional SSI was defined as an infection occurring within 30 days of surgery and arising only in the skin or subcutaneous tissue. Deep incisional SSI was defined as infection occurring within 30 days of surgery and arising only in the fascial or muscle layers. Protocols for wound treatment and drain management against SSI were followed as described elsewhere. [10] After patient discharge, responsible surgeons (S.Y, H.T and T.T) checked for the presence of wound complications on patient follow-up until 30 days after surgery.

Participant eligibility

Eligibility criteria for elective open liver resection included: age, 20–80 years; liver function, Child–Pugh grade A or B; Eastern Cooperative Oncology Group (ECOG) performance status, 0 or 1; and adequate organ function without any severe co-morbidities. Exclusion criteria were: requirement for bilio- or entero-reconstruction during operation; presence of infection within 2 weeks [4]; uncontrolled diabetes mellitus, coagulopathy or any other disorder that would preclude study participation; or allergic reaction to stainless steel or polydioxanone. Patients were informed of their ability to refuse to participate at any time. History of any kind of re-laparotomy was allowed.

Randomisation, allocation and masking

Recruitment of patients was assessed in weekly surgical unit conferences, and allocations were made just after liver resection by a distant and isolated PC-operator who was blinded to patient information. Patients were randomly assigned (1:1) to receive either subcuticular sutures or staples for skin closure. A PC software in Microsoft Excel Visual Basic for Applications was developed for this trial, and computer-generated minimization method was used for randomisation. Patient allocation was performed by randomisation after matching for the 3 risk factors associated with wound complications (presence of diabetes mellitus, liver function; indocyanine green retention rate at 15 min (ICG-R15) and repeat incision).

Postoperative information was written by an independent treatment team on a formatted sheet. The investigator (M.Y) was not associated with treatment and was blinded to group assignment. Complications were only judged by the investigator from the medical records on the formatted sheet. All data were stored in an independent PC, with regular monitoring by the IRB annually and by the department every 3 months. All statistical analyses were performed by an independent researcher (S.Y).

Operative procedure

The basic surgical techniques and perioperative management that we use for OLR are described elsewhere. [19] A J-shaped incision was the most common incision, with thoracotomy added only when the tumour was located in the posterior segment or caudate lobe. [20] Hepatic parenchymal transection was performed using a clamp-crushing method and intermittent blood flow occlusion (Pringle's manoeuvre) was routinely used in all cases. [21, 22].

Surgical gloves and instruments were changed before wound closure and the subcutaneous space was irrigated with saline. An abdominal drain was placed through a separate site away from the operative incision. [19] Routine approximation of the fat layer with 3–0 multifilament absorbable suture (polyglycolic acid, OPEPOLYX® N; Alfresa Pharma Corporation, Tokyo, Japan) was performed before skin closure. Finally, 3–0 monofilament absorbable suture (polydioxanone, MONODIOX®; Alfresa Pharma Corporation) was used for subcuticular suture with both interval and length of bite of sutures at 15 mm. In the staples group, metallic skin staples (Appose ULC 35 W; Medtronic, Tokyo, Japan) 10 mm in size were used.

As all lead surgeons had experienced at least 100 hepato-biliary pancreatic surgeries annually and were familiar with both procedures, no specific training was undertaken before this trial. Postoperative treatment was provided in accordance with guidelines for the prevention of SSI issued by the CDC as much as possible. [18] An independent hospital infection control team conducted monthly monitoring of the incidence of any kind of infection and was able to stop the study when specific infections were observed during this study.

Statistical analysis

We calculated that a sample size of 265 patients per treatment group would be needed. This sample size provided statistical power of 80% with the risk of type I error set at 0.05 (two-sided) to detect superiority in reducing the frequency of wound complications. Wound complications were anticipated to be encountered in 13.1% [10] of patients in the staples group and 5.4% [4] in the subcuticular sutures group according to positive results of clean surgery, allowing for a roughly 10% rate of loss to follow-up. The projected accrual period was three years, and no interim analyses were allowed in the event of a major incident identified by the monitoring team. Subset analysis allowed only three preoperative allocated factors closely associated with wound complication. Uni and multivariate analyses were performed for risk of all wound complications. The factors into multivariate analysis were selected in accordance with the results from univariate analysis or from known as a risk for wound complication in previous studies. [1–3, 10] To lessen confounding among these variables, factors in multivariate analysis were reduced as much as possible.

Statistical analysis was performed on an intention-to-treat basis. Data are expressed as percentages for categorical variables and as medians with ranges for continuous numerical variables. We used Fisher's exact test to compare categorical variables and the Mann–Whitney U test to compare continuous variables. All values of p <0.05 were considered statistically significant. All statistical analyses

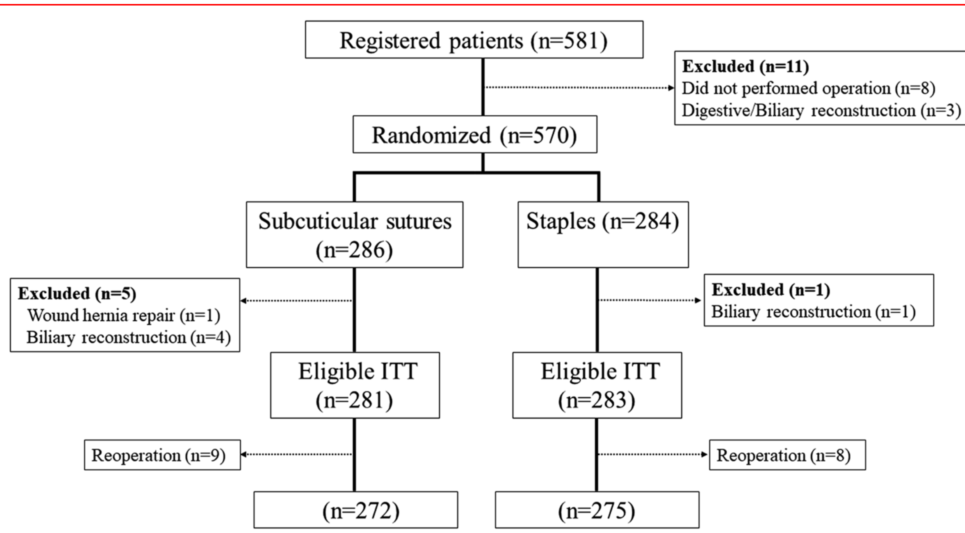

Fig. 1 Flow diagram of patients. A total of 581 patients were registered, and 570 patients were randomly allocated to receive subcutaneous suture or staples. Reoperation was performed after skin closure, modified intention-to-treat analysis was performed

Table 1 Baseline demographic and clinical characteristics

	Subcuticular stures (*n* = 281)	Staples (*n* = 283)	*p* value
Age (year)	68 (34–80)	68 (26–80)	0.559
Sex (male)	220 (78.3%)	220 (72.4%)	0.107
Body mass index	23.1 (14.9–32.5)	23.2 (14.5–36.2)	0.983
Wound length (cm)	34 (16–53)	34 (16–53)	0.193
Wound thickness (mm)	22 (5–56)	22 (7–48)	0.796
Repeat incision with same wound	82 (29.2%)	85 (30.0%)	0.824
Repeat liver resection	53 (18.9%)	57 (20.1%)	0.701
Diabetes mellitus	89 (31.7%)	95 (33.6%)	0.631
Anticoagulation therapy	33 (11.7%)	38 (13.4%)	0.547
Preoperative chemotherapy	40 (14.2%)	37 (13.1%)	0.688
ICG-R15 (%)	11.3 (1.6–69)	11.1 (1.7–35.1)	0.885
Viral infection			
HBV	59 (21.0%)	46 (16.3%)	0.148
HCV	62 (22.1%)	71 (25.1%)	0.398
ASA grade			0.331
1	6 (2.1%)	2 (0.7%)	
2	252 (89.7%)	260 (91.9%)	
3	23 (8.2%)	21 (7.4%)	
Total-bilirubin (mg/dl)	0.64 (0.2–1.69)	0.61 (0.23–1.78)	0.384
Prothrombin time (%)	100 (27–100)	100 (30–100)	0.482
Albumin (g/dl)	4.3 (2.5–5.2)	4.2 (2.8–5.7)	0.303
Child–pugh class			0.852
A	269 (95.7%)	270 (95.4%)	
Bile leakage	12 (4.3%)	13 (4.6%)	
HbA1c (%)	5.9 (4–9.7)	5.8 (4.6–10.9)	0.929
Platelet count (10^4µl)	17.8 (4.7–52.7)	18.8 (4.7–49.2)	0.389
Creatinine (mg/dl)	0.78 (0.37–1.45)	0.75 (0.31–1.44)	0.0113
Diseases			0.515
Primary liver tumour	195 (69.4%)	198 (70.0%)	
Metastatic liver cancer	81 (28.8%)	83 (29.3%)	
Gallbladder cancer	5 (1.8%)	2 (0.7%)	
Operation related variables			
Partial or wedge resection	212 (75.4%)	204 (72.1%)	0.365
Segmentectomy	44 (15.7%)	40 (14.1%)	0.611
Lobectomy or extented lobectomy	25 (8.9%)	40 (14.1%)	0.052
Operation time (min)	329 (157–661)	325 (115–805)	0.866
Blood loss (ml)	230 (2–2935)	260 (0–3513)	0.205
Subcutaneous drainage	28 (10.0%)	28 (9.9%)	0.978
With thoracotomy	105 (37.4%)	117 (41.3%)	0.334
Intraoperative transfusion	8 (2.9%)	11 (3.9%)	0.494
Specimen weight (g)	73 (6–1900)	70.5 (5.5–2861)	0.643
Pathological background liver			
F3,4*	77 (27.4%)	91 (32.2%)	0.217

ICG-R15, indocyanine green retention rate at 15 min; *ASA,* American Society of Anesthesiologists; *HBV,* Hepatitis B virus; *HCV,* Hepatitis C virus; *C-D* Clavien-Dindo classification

*according to the Inuyama classification

Table 2 Primary and key secondary outcomes outcome and its components in modified intention-to-treat population

All patient	Subcuticular sutures ($n = 281$)	Staples ($n = 283$)	Odds ratio (95% CI)	p value
Primary outcome				
Wound complication	35 (12.5%)	45 (15.9%)	1.33 (0.83–2.15)	0.241
Detail of wound complication				
Incisional SSI	30 (10.7%)	37 (13.1%)	1.26 (0.76–2.11)	0.379
Organ space SSI	20 (7.1%)	23 (8.1%)	1.15 (0.62–2.17)	0.651
Non-SSI	6 (2.1%)	7 (2.5%)	1.16 (0.38–3.65)	0.789
Wound separation	1 (0.4%)	3 (1.1%)	3.00 (0.38–60.82)	0.319
Heaematoma	1 (0.4%)	3 (1.1%)	3.00 (0.38–60.82)	0.319
Seroma	3 (1.1%)	2 (0.7%)	0.66 (0.09–4.01)	0.675
Complications				
C–D grade ≧ IIIa	18 (6.4%)	18 (6.4%)	0.99 (0.51–1.95)	0.983
Bile leakage	25 (8.9%)	33 (11.7%)	1.35 (0.78–2.34)	0.280
Postoperative hospital days ≧ 2 weeks	111 (39.5%)	126 (44.5%)	1.23(0.88–1.72)	0.227
Medical Cost (US$) ≧ 7000	142 (50.5%)	152 (53.7%)	1.14(0.82–1.58)	0.450

SSI, surgical site infection; *C-D* Clavien-Dindo classification

*at least 2 times using same wound when incision

were performed using JMP version 13.1 statistical software (SAS Institute Inc., Cary, NC, USA).

Results

Study flow

A total of 581 patients were potentially available for enrolment during the study period (Fig. 1). Among these, a total of 11 patients were excluded from participation (8 patients with no liver resection due to wider tumour invasion, and 3 patients who underwent digestive or biliary tract reconstruction). Of the remaining 570 patients, 286 patients were assigned to receive subcuticular sutures, and 284 patients were assigned to receive staples. Assessment of postoperative records found that 6 patients (1.0%) did not meet the inclusion criteria, due to 5 cases of miss-judged allocation (biliary tract anastomosis during operation) and 1 case of simultaneous abdominal wall hernia repair. Nine patients (3 cases of abdominal bleeding, 2 cases of bile leakage and 1 case each of deep incisional SSI, intraabdominal abscess, ileus and subcutaneous hematoma) in the subcuticular sutures group and 8 patients (3 cases of bile leakage, 2 cases of abdominal bleeding and 1 case each of deep incisional SSI, intraabdominal abscess and wound disruption) in the staples group required reoperation within 30 days. However, these patients were analysed on a modified intention-to-treat basis. The final groups thus comprised 281 patients in the subcuticular sutures group and 283 patients in the staples group.

Baseline characteristics of patients

No significant differences in baseline characteristics (such as nutrition status or history of preoperative chemotherapy) were seen between the two groups, with the exception of the serum concentration of creatinine (Table 1). No treatment-related adverse events were seen for either stapling or subcuticular suturing. There was no missing patient's date during follow-up.

Endpoints and risk analysis

Wound complications developed in 80 (14.1%) of the 564 patients. Regarding the primary outcome, subcuticular sutures did not significantly reduce wound complication rate within 30 days after surgery in the overall cohort [35 patients (12.5%) vs. 45 patients (15.9%), odds ratio (OR), 1.33; 95% confidence interval (CI), 0.83–2.15; $p = 0.241$] (Table 2). Rates of types of wound complications likewise did not differ significantly between procedures.

In terms of secondary outcomes, no significant differences in wound SSI rate, duration of postoperative hospitalisation or total medical cost were identified between the two procedures in the overall cohort (Table 2). Multivariate analysis showed five independent predictors for wound complication in the overall cohort. Serum albumin level (OR, 3.52; 95% CI, 1.38–8.97; $p = 0.008$), operation time

Table 3 Logistic regression analysis for the risk of wound complication

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*p* value	Odds ratio	95% CI	*p* value
Patient's related variables						
Age ≥ 75	1.09	0.60–1.98	0.766	1.19	0.63–2.23	0.596
Sex(male)	1.15	0.65–2.02	0.631			
Body mass index ≥ 25	2.11	1.31–3.42	0.002			
Wound length(cm) ≥ 35	3.02	1.82–5.01	< 0.0001	2.09	1.18–3.69	0.011
Wound thickness(mm) ≥ 30	2.10	1.23–3.58	0.006	1.77	1.00–3.12	0.490
Repeat incision with same wound	0.98	0.58–1.64	0.934			
ASA grade 3	1.16	0.50–2.70	0.733	0.97	0.40–2.33	0.941
Albumin(g/dl) < 3.5	3.71	1.58–8.71	0.001	3.52	1.38–8.97	0.008
Child–pugh A	1.98	0.77–5.13	0.150			
Creatinine(mg/dl) ≥ 1.00	0.96	0.44–2.12	0.928			
Presence of diabetes mellitus	1.21	0.73–1.98	0.455			
ICG-R15 (%) ≥ 15	1.26	0.75–2.12	0.387			
Preoperative chemotherapy	1.01	0.51–2.01	0.978			
Operation related variables						
Lobectomy or extented lobectomy	1.27	0.63–2.55	0.501	0.87	0.40–1.88	0.715
Operation time(min) ≥ 300	3.06	1.74–5.39	< 0.0001	2.03	1.01–4.08	0.048
Blood loss(ml) ≥ 300	2.30	1.42–3.73	0.001	1.38	0.80–2.41	0.250
Wound closure (Staples)	1.33	0.83–2.15	0.241	1.20	0.73–1.99	0.471
Subcutaneous drainage	1.56	0.77–3.15	0.217			
With thoracotomy	2.23	1.38–3.60	0.001			
Intraoperative transfusion	0.33	0.04–2.49	0.257			
Bille leakage	1.13	0.53–2.39	0.759			
Pathological background liver						
F3,4*	1.82	1.11–2.96	0.016	1.79	1.05–3.05	0.033

ICG-R15, indocyanine green retention rate at 15 min; *ASA* American Society of Anesthesiologists; *C-D* Clavien-Dindo

*according to the Inuyama classification

(OR, 2.03; 95% CI, 1.01–4.08; $p = 0.048$),wound length (OR, 2.09; 95% CI, 1.18–3.69; $p = 0.011$), pathological F3 and F4 in Inuyama classification (OR, 1.79; 95% CI, 1.05–3.05; $p = 0.033$) and wound thickness (OR, 1.77, 95% CI, 1.00–3.12; $p = 0.049$) (Table 3).

In subset analysis by the 3 allocated factors, subcuticular sutures were significantly associated with a reduced frequency of wound complications in repeat incision, whereas liver function and presence of diabetes mellitus were not (Fig. 2). Regarding repeat incision, subcuticular sutures were associated with significantly reduced rates of wound complications [7 patients (8.5%) vs. 17 patients (20.0%); OR, 2.68; 95% CI, 1.08–7.29; $p = 0.035$] and incisional SSI [5 patients (6.1%) vs. 14 patients (16.5%); OR, 3.04; 95% CI, 1.10–9.79; $p = 0.035$], but not with primary incision (Table 4). In univariate analysis, body mass index (BMI) ($p = 0.034$), wound length ($p = 0.021$) serum albumin value ($p = 0.031$) and closure with skin staples ($p = 0.026$) were the factors predicting wound complications (Table 5). In multivariate analysis, the only factor showing a negative independent association with wound complications was closure with skin staples (OR, 2.93; 95% CI, 1.18–7.99, $p = 0.038$).

Discussion

To the best of our knowledge, this trial represents the largest RCT of liver resection as a clean-contaminated surgery. The unique feature of this study was the focus on repeat incision, which has been considered one of the highest risk factors for wound complications. [23] Separate treatment teams, a remote assignment system and independent surveillance of complications were all used in this study to minimise possible information biases. Regarding to the primary endpoint, no significant differences were

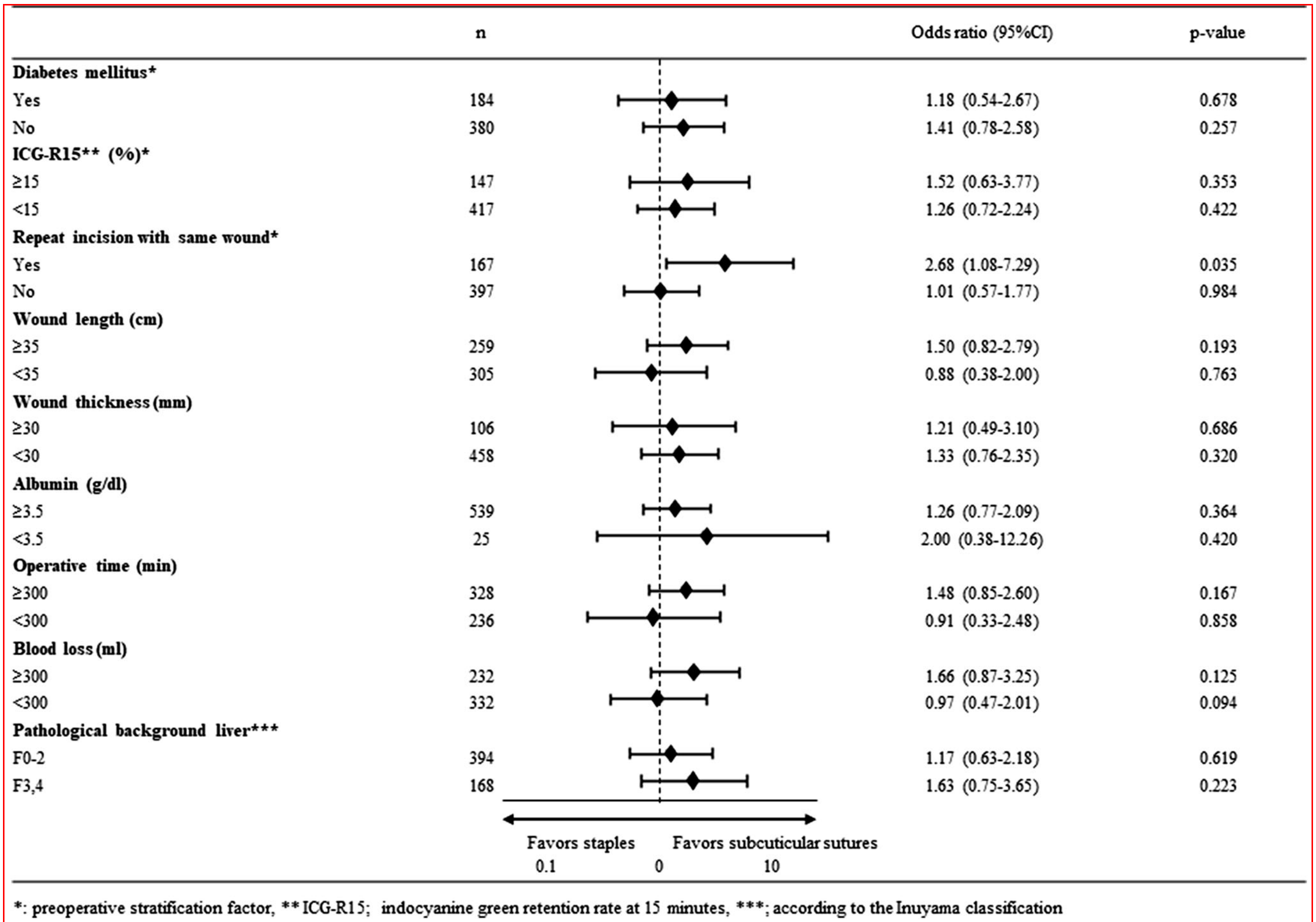

Fig. 2 Forest plot of wound complications in the modified intention-to-treat population. No significant difference otherwise wound complication rate for repeat incision was seen between the subcutaneous suture and staple groups in wound complication rates from the modified intention-to-treat analysis

evident between subcuticular sutures and staplers for all wound complications in the overall cohort. This means that this trial failed to prove the superiority of subcuticular sutures as a standard procedure for skin closure in open liver resection.

Compared to other organs, repeat surgery rates are much higher for liver resection for HCC (6–53%) [7, 16, 23–25] and colorectal cancer liver metastasis (9–37%). [17, 26, 27] We used three specific factors (repeat incision, diabetes mellitus, ICG-R15 as a marker of liver functional reserve) known as risk factors for wound complications in the allocation process to allow independent analyses. No studies have shown which type of closure is better in cases of repeat incision, because such investigations require large numbers of participants. The wound complications occurred with the primary incision in 28/199 patients (14.1%) with subcuticular sutures as compared to 28/198 patients (14.1%) with staples (OR, 1.01; 95% CI, 0.57–1.77; $p = 0.984$). In contrast, subcuticular sutures successfully reduced the occurrence of wound complications (7/82 patients, 8.5%) in repeat incisions compared to staples (17/85 patients, 20.0%; OR, 2.68; 95% CI, 1.08–7.29; $p = 0.035$). Even in subset analysis ($n = 167$), subcuticular sutures reduced the rate (11.5%) of wound complications from repeat incisions and thus appeared preferable for this situation.

In multivariate analysis for wound complications in our total cohort used five host-related factors (age; serum albumin level < 3.5 g/dl; patient's activity; background liver fibrosis F3 or F4; wound thickness ≥ 30 mm) and four operation related factors (wound length ≥ 35 cm; procedure; operation time ≥ 300 min; intraoperative blood loss ≥ 300 ml), Wound length and operation time were the strongest predictors of wound complications. This means that minimum invasive hepatobiliary surgeries such as laparoscopic liver resection represent one possible option to reduce wound complication rates. Indeed, the rate of severe complications was similar between open and

Table 4 Primary and key secondary outcomes outcome and its components in modified intention-to-treat population

Primary incision	Subcuticular sutures (n = 199)	Staples (n = 198)	Odds ratio (95% CI)	p value
Primary outocome				
Wound complication rate	28 (14.1%)	28 (14.1%)	1.01 (0.57–1.77)	0.984
Detail of wound complication				
Incisional SSI	25 (12.6%)	23 (11.6%)	0.92 (0.50–1.68)	0.772
Organ space SSI	14 (7.0%)	20 (10.1%)	1.49 (0.73–3.09)	0.275
Non-SSI	3 (1.5%)	4 (2.0%)	1.35 (0.29–6.91)	0.698
Wound separation	1 (0.5%)	3 (1.5%)	3.05 (0.39–61.85)	0.312
Heaematoma	0 (0%)	2 (1.0%)	0	0.155
Seroma	2 (1.0%)	0 (0%)	0	0.157
Repeat incision*	(n = 82)	(n = 85)		
Primary outocome				
Wound complication rate	7 (8.5%)	17 (20.0%)	2.68 (1.08–7.29)	0.035
Detail of wound complication				
Incisional SSI	5 (6.1%)	14 (16.5%)	3.04 (1.10–9.79)	0.035
Organ space SSI	6 (7.3%)	3 (3.5%)	0.46 (0.10–1.82)	0.279
Non-SSI	3 (3.7%)	3 (3.5%)	0.96 (0.17–5.34)	0.964
Wound separation	0 (0%)	0 (0%)	0	1.000
Heaematoma	1 (1.2%)	1 (1.2%)	0.96 (0.04–24.64)	0.980
Seroma	1 (1.2%)	2 (2.4%)	1.95 (0.18–42.45)	0.581

SSI, Surgical site infection

*at least 2 times using same wound when incision

laparoscopic surgeries in a recent RCT [28], while the total wound complication rate was lower, and operation time was shorter with laparoscopic surgery, reflecting this speculation. In contrast, regarding management for patients who have previously undergone open liver surgery, our results show an apparent contribution to improved outcomes in such instances with the use of subcuticular sutures.

The limitations of this study were that: (1) wound dressings could not be blinded for the treatment team; (2) wound pain was not evaluated; and (3) laparoscopic surgeries were not included. Regarding to the difference of wound complication of repeat incision, the significant difference observed in total wound complication between two groups. It is mainly depended on the rate of incisional SSI. In our previous study, we focused on reducing the subcutaneous accumulation of effusions to reduce wound complication. [10] However, we found no preventive effects of subcutaneous drain placement against wound infection and drain. Because the effusion of subcutaneous tissue was smaller than we expected. We routinely performed subcutaneous suturing of the fat layer using absorbable sutures before skin closure to achieve reduced wound complications. However, only the tighten fixation by subcuticular sutures cannot explain about the difference. The tightened tissue space with subcuticular sutures may have contributed to reduced bacterial penetration into the subcutaneous tissue, especially with thick and long incisions. We speculated that peripheral blood circulation in the scar tissue was poor and may thus create poor conditions for tissue adaption. In such situations, the tighten fixation achieved with subcuticular sutures may contribute to a reduction in wound complications.

The positive results of randomised trials using subcuticular sutures to reduce wound complications have been confirmed only for clean surgery. [1–3] It is uncertain the reason why the subcuticular sutures have positive impact on wound complication only in clean surgery. We speculated that the most different point was longer wound incisions that exceed 30 cm in open liver resection. Moreover, most of participants have chronic liver disease such as hepatitis or receiving chemotherapy. These factors might have negative impact on wound healing either skin staples or subcuticular sutures.

Table 5 Logistic regression analysis for the risk of wound complication in repeat resection

Risk factor	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*p* value	Odds ratio	95% CI	*p* value
Patient's related variables						
Age ≥ 75	1.36	0.47–3.92	0.586	1.93	0.56–6.41	0.281
Sex(male)	2.34	0.72–8.61	0.147			
Body mass index ≥ 25	2.61	1.07–6.39	0.034			
Wound length(cm) ≥ 35	2.93	1.14–7.41	0.021	2.11	0.66–6.19	0.213
Wound thickness(mm) ≥ 30	1.56	0.48–5.22	0.458	0.91	0.27–3.39	0.911
ASA grade 3	0.52	0.07–4.21	0.518			
Albumin(g/dl) < 3.5	4.71	1.10–22.18	0.031	4.31	0.79–26.19	0.111
Child–pugh A	3.09	0.53–17.90	0.187			
Creatinine(mg/dl) ≥ 1.00	0.98	0.27–3.57	0.958			
Presence of diabetes mellitus	1.29	0.53–3.21	0.611			
ICG-R15 (%) ≥ 15	2.42	0.97–5.96	0.052			
Preoperative chemotherapy	1.02	0.34–2.89	0.971			
Operation related variables						
Lobectomy or extented lobectomy	1.51	0.31–7.48	0.617	0.96	0.17–5.58	0.961
Operation time(min) ≥ 300	2.47	0.89–6.84	0.081	2.41	0.63–10.01	0.199
Blood loss(ml) ≥ 300	2.12	0.88–5.11	0.085	1.68	0.63–4.49	0.288
Wound closure (Staples)	2.81	1.11–7.21	0.026	2.93	1.18–7.99	0.038
Subcutaneous drainage	1.22	0.46–3.02	0.761			
With thoracotomy	1.89	0.81–4.51	0.161			
Bille leakage	0.81	0.18–3.91	0.784			
Pathological background liver						
F3,4*	1.76	0.69–4.49	0.234	1.54	0.53–4.49	0.426

ICG-R15, indocyanine green retention rate at 15 min; *ASA,* American Society of Anesthesiologists

*according to the new Inuyama classification

In conclusion, either subcuticular sutures or staple can be standard method for skin closure in OLR. However, the results of this RCT suggest that use of subcuticular sutures is warranted in cases of repeat incision.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no funding or conflicts of interest to disclose with respect to this manuscript.

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