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Subcuticular Absorbable Suture with Subcutaneous Drainage System Prevents Incisional SSI after Hepatectomy for Hepatocellular Carcinoma

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Abstract
Background The effectiveness of subcuticular absorbable suture with subcutaneous drainage to decrease the risk of postoperative incisional surgical site infection (SSI) in hepatocellular carcinoma (HCC) patients was evaluated.
Methods A total of 149 patients with HCC who underwent hepatectomy (Hx) were retrospectively investigated. Patients were divided into two groups: the patients with subcuticular suture combined with subcutaneous drainage (the drainage group; 61 patients) and the patients with nylon suture without subcutaneous drainage (the nylon group; 88 patients). After the operations, the complication rate of postoperative incisional SSI was analyzed and compared between the two groups.
Results In the drainage group the rate of incisional SSI was significantly lower compared to the nylon group: 14–3 % ($p = 0.033$), respectively. Patients with incisional SSI needed significantly longer postoperative hospital care than the patients without incisional SSI: 28 versus 15 days ($p < 0.005$). Multivariate analysis revealed that subcuticular absorbable suture with subcutaneous drainage significantly reduced the occurrence of incisional SSI (odds ratio; 0.15; $p = 0.034$).
Conclusions We have demonstrated that the subcuticular suture with subcutaneous drainage is effective in preventing incisional SSI in patients undergoing Hx for HCC.

Introduction

In recent decades, hepatectomy (Hx) for hepatocellular carcinoma (HCC) has become safer as a result of advances in perioperative management [1]. However, in contrast to Hx for metastatic liver cancer, strict perioperative management is required for Hx for HCC, because it usually develops from chronic hepatitis or cirrhosis. It has been reported that the mortality rate is substantially higher in patients with cirrhosis (8.7 %) than in patients with a normal liver (1 %) [2].

Incisional surgical site infection (SSI) is not a lethal disease by itself. However, it can lead to increased medical costs, longer hospitalization, and a reduced quality of life in the postoperative course [3, 4]. The incidence of incisional SSI in hepatobiliary surgery has been reported at 30.9 % [5]. There are several methods used for skin closure after abdominal operations. The choice of method or material is often based on a surgeon's personal experience. The suture material used most commonly in skin closure is nonabsorbable nylon [6]. Recently, subcuticular suture with subcutaneous drainage has been reported to be highly effective for preventing incisional SSI, especially in gynecological [7–10] and colorectal surgery [11].

The present study was designed to examine the effectiveness of subcuticular absorbable suture with subcutaneous drainage in decreasing the risk of postoperative incisional SSI after Hx in patients with HCC. The risk factors for incisional SSI for Hx in HCC were also evaluated.

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Methods

Patient eligibility

From 2009 to 2011, a total of 149 consecutive patients underwent Hx for primary and recurrent HCC at the Department of Surgery, Hiroshima Red Cross and Atomic Bomb Survivor Hospital (Hiroshima, Japan). The patients were divided into a consecutive series of two groups based on the time of the patient's admission, the skin closure used: transdermal nylon suture (the nylon group; from April 2009 to May 2010, 88 patients) and the subcuticular suture and subcutaneous drainage group (the drainage group; from June 2010 to May 2011, 61 patients). Thus, this study was nonrandomized, and the backgrounds of the patients in the two groups were not completely equal. The selection of type of Hx was made on the basis of liver function and tumor location [12]. Liver function was assessed by the Child-Pugh classification [13] and indocyanine green retention rate at 15 min (ICG-R15). Child-Pugh class C was regarded as a contraindication for Hx. The evaluating system of the Liver Cancer Study Group of Japan [14] was used to categorize histological findings. The indication for Hx for patients with HCC throughout the period of the present study did not change.

The skin of the abdomen was prepared before the procedure by the application of a povidone-iodine solution. All operations were performed and incisions were made and closed with the same surgeons (Y.Y. and E.T.). After closure of the fascia with continuous 0 (3.5 metric) Biosyn absorbable sutures prepared from a synthetic polyester composed of glycolide, dioxanone, and trimethylene carbonate (Covidien, Japan), the surgical incisions in all patients were irrigated with saline solution. In the nylon group, wounds were closed with interrupted transdermal vertical mattress sutures with monofilament 2/0 (3 metric) nylon. The use of 2/0 monofilament nylon was selected because of its inertness and the ease with which it slides through the skin. Skin sutures and dressings were removed on the ward on postoperative day 7–10, depending on the surgeon's professional opinion. The subcutaneous tissue of nylon group was not closed or reapproximated. The wounds of patients in the drainage group were closed with a subcuticular suture [15] procedure with 4/0 (1.5 metric) PDS II suture material (Ethicon, Japan). All knots were buried in the wound. A 3.5-mm Argyle Multi-Channel Drainage Set (MCDS) (Covidien, Japan) (Fig. 1) was placed in the subcutaneous tissue and brought out through a separate stab wound incision. This subcutaneous drain was left in place longer than 72 h, until drainage measured <10 ml for 24 h.

Skin closure was not timed in this series. Both skin closure techniques were commonly used at our hospital before the trial commenced. For routine antimicrobial prophylaxis (AMP), administration of second-generation cephem antibiotics was initiated 30 min before skin incision with another dose administered 3 h later. When the operation lasted more than 3 h, additional doses were given every 3 h thereafter during the operation. After Hx, additional AMP was administered for 3 days. Postoperative bile leakage was defined as the drainage of macroscopic bile from the surgical drains for >7 days postoperatively and was managed as described previously [16]. Postoperative hyperglycemia was defined as over 200 mg/dl within 72 h after hepatectomy [17].

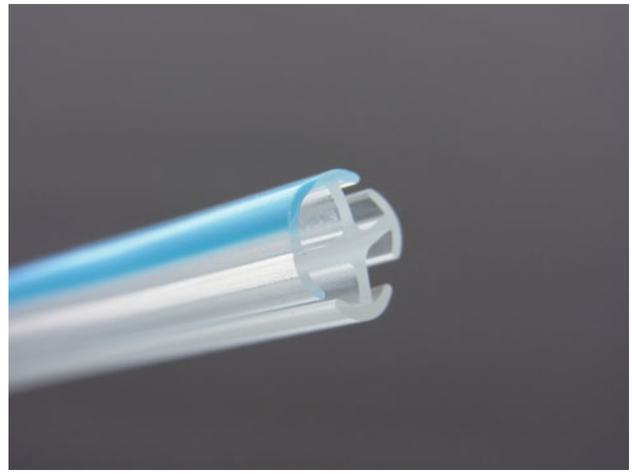

Fig. 1 Argyle multi-channel drainage set with combination of three fluted channels and one open-tip lumen

As stated, the outcome of interest was the development of an incisional SSI, as defined by the U.S. Department of Health and Human Services and Centers for Disease Control and Prevention [18]. Briefly, an incisional SSI occurs within 30 days of surgery and only involves the skin and subcutaneous tissue.

Statistical analysis

Statistical analysis was performed on the following variables: AST, ALT, ICG-R15, tumor size, blood loss, and operative time were assessed with the Mann-Whitney *U* test, and other continuous variables were evaluated with the unpaired Student's *t* test. Where appropriate, variables are expressed as means ± SD. Categorical data were compared with the Chi-square test. Only significant variables in univariate analysis were admitted in the multivariate analysis using the logistic regression model. Statistical analysis was performed with Stat View software (Abacus Concepts, Inc., Berkeley, CA). A p value of <0.05 was considered significant.

Disclosures and freedom of investigation

All aspects of this study, including, but not limited to its design, the methods used, outcome variables, analysis of data, and production of the written report, were under the direct control of the investigators, with no input (financial or otherwise) from any sources. None of the authors have received any (financial or otherwise) incentive, including honoraria or consultancy fees.

Results

As shown in Table 1, the incisional SSI rate in patients with Hx for HCC was significantly lower in the drainage group than in the nylon group, 14–3 %. There was no significant difference in factors such as age, gender, body mass index (BMI), history of Hx, presence of diabetes, American Society of Anesthesiologists (ASA) Score [19], Child-Pugh classification, total lymphocyte count, type IV collagen 7S domain levels, and blood transfusion rate, except for blood loss and operative time. Performance of the study at a single institution over a short period of time assured relative uniformity of care to minimize confounders.

Table 2 summarizes the results of the univariate analysis conducted to determine the relationship between the clinical variables and the incisional SSI. The pathogenic bacteria for incisional SSI were 3 species, methicillin-resistant *Staphylococcus epidermidis* ($n = 6$), methicillin-resistant *Staphylococcus aureus* ($n = 4$), and *Enterococcus faecalis* ($n = 2$). The pathogen-positive rate was 79 %. Factors such as age, gender, operative time, blood loss, history of Hx, BMI, total lymphocyte count, and postoperative morbidity—i.e., bile leakage or hyperglycemia—were not predictors of incisional SSI. Factors that were associated with incisional SSI in the univariate analysis and were of statistical significance are (1) the presence of a subcutaneous drain, (2) a poor ASA score, (3) the presence of diabetes, (4) higher preoperative type IV-collagen 7S domain levels, and (5) Child-Pugh classification. Postoperative hospital stay in the SSI group was significantly longer than in the group of patients without SSI (28 days vs. 15 days; $p < 0.005$). Multivariate subgroup analysis of the association between the above factors and incisional SSI showed that the presence of a subcutaneous drain was independently associated with incisional SSI (odds ratio: 0.15; $p = 0.034$) (Table 3).

Discussion

Many surgeons believe that nonabsorbable suture material is preferable, as it is easier to tie, and is more cost-effective. Others feel that these issues are of minor importance and prefer absorbable sutures because their removal is not necessary, saving the surgeon time and

Table 1 Comparison of patient background characteristics, operative procedures, and perioperative outcomes between the nylon group and the subcuticular suture with subcutaneous drainage group

Characteristics	Nylon group ($n = 88$)	Subcuticular suture with subcutaneous drainage group ($n = 61$)	p Value
Preoperative parameters			
Age, years[a,b]	69.3 ± 9.3	69.3 ± 11.1	0.947
Gender, male/female[c]	62/26	37/24	0.213
Hepatitis type, n (%)[c]			
HBV+	14 (16%)	11 (18%)	0.733
HCV+	57 (65%)	42 (69%)	0.604
ASA score (2:3), n[c]	57:31	42:19	0.604
BMI, kg/m^2[a,b]	23.0 ± 3.1	23.6 ± 3.2	0.223
Smoking, n (%)[c]	15 (17%)	10 (16%)	0.917
Primary or repeat hepatectomy, n[c]	59:29	33:28	0.138
Laboratory data			
Total lymphocyte count/μl [a,b]	1,305.2 ± 631.7	1,372.2 ± 641.0	0.533
Hemoglobin, g/dl [a,b]	12.9 ± 1.7	12.9 ± 1.8	0.876
Platelets × 10^4/μl [a,b]	14.1 ± 7.2	13.5 ± 6.9	0.617
AST, U/l [a,d]	39.1 ± 27.2	39.8 ± 19.8	0.415
ALT, U/l [a,d]	36.1 ± 28.9	35.6 ± 25.5	0.690
ICG-R15, %[a,d]	18.8 ± 10.4	22.1 ± 12.0	0.085
Type IV-collagen 7S domain levels, ng/ml[a,b]	5.8 ± 1.7	6.0 ± 1.7	0.354
Child-Pugh classification[e] (A:B), n[c]	84:4	57:4	0.604
Co-morbid condition, n (%)[b]			
Hypertension	41 (47%)	38 (62%)	0.069
Diabetes mellitus	27 (31%)	20 (33%)	0.786
Tumor size, cm[a,d]	2.5 ± 1.6	2.3 ± 1.4	0.533
pStage[f] (I:II:III:IV), n[c]	10:25:27:23	9:18:15:15	0.846
Pathological liver cirrhosis, n (%)[c]	45 (51%)	41 (67%)	0.060
Blood loss, g[a,d]	607.6 ± 578.1	511.3 ± 734.6	0.014
Transfusion, n (%)[c]	9 (10%)	4 (7%)	0.435
Operative time, min (median, range)[d]	268 (89, 586)	219 (110, 586)	0.006
Operative methods, n[c] (less than subsegmentectomy: segmentectomy or more)	65:23	52:9	0.317
Postoperative morbidity, n (%)[c]			
Bile leakage	4 (5%)	8 (13%)	0.062
Hyperglycemia	39 (44%)	24 (39%)	0.546
Incisional SSI	12 (14%)	2 (3%)	0.033

Table 1 continued

Characteristics	Nylon group($n = 88$)	Subcuticular suture with subcutaneous drainage group($n = 61$)	*p* Value
Postoperative hospital stay, days (median, range)[b]	16 (8, 189)	15 (7, 80)	0.409

ALT alanine aminotransferase, *AST* aspartate transaminase, *ASA* American Society of Anesthesiologists, *BMI* body mass index, *HBV* hepatitis B surface antigen, *HCV* anti-hepatitis C virus antibody, *ICG-R15* indocyanine green retention rate at 15 min, *n* number of patients

[a] Values are expressed as mean ± SD

[b] Unpaired Student's *t* test

[c] Chi-square test

[d] Mann-Whitney *U* test

[e] Child-Pugh classification [12]

[f] Pathologic TNM staging [13]

reducing the patient's discomfort [20]. Even though the incidence of incisional SSI after Hx has been decreased through progress in perioperative management and improvements in surgical procedure [1], there is still cause for concern. The effect on incisional SSI of the type of skin closure used in the large incision for Hx is not well established. Our incisional SSI rate in patients with nylon sutures was 14 %, which was no higher than the occurrence rates of 5.5–19.2 % reported in other series [17, 21–25]. Although comparable, the definition of incisional SSI differs between different studies. It has been reported that old age [21], BMI [17], prolonged operative time [22], use of silk sutures [22], elevated blood loss [17, 26], and postoperative complications—i.e., hyperglycemia [17] and bile leakage [17, 22]—were risk factors for postoperative incisional SSI. However, those previous studies did not refer to the skin closure methods. In our multivariate analysis, these factors were not related to the incidence of incisional SSI.

We found a significantly lower incidence of incisional SSI in wounds closed by subcuticular absorbable suture with subcutaneous closed suction drain than in those closed with transdermal nylon sutures. Interrupted transdermal nylon sutures may permit escape of exudates, but they produce a potential communication between the skin and subcutaneous tissues, and they require costly time for their removal.

Hepatocellular carcinoma usually develops from chronic hepatitis or cirrhosis. Pessaux et al. [27], reported liver cirrhosis is one of the risk factors for SSI in abdominal surgery. The high prevalence of infectious complications in cirrhosis can be explained by the presence of various dysfunctions in the mechanisms of defense against infection [28]. Additionally, patients with cirrhosis often have associated disorders such as malnutrition, acute hypovolemia,

Table 2 Comparison of clinicopathological features, operative procedures, and perioperative outcomes between the no SSI group and the SSI group

Characteristics	Without SSI group ($n = 135$)	With SSI group ($n = 14$)	*p* Value
Preoperative parameters			
Age, years[a,b]	69.4 ± 10.2	68.4 ± 8.9	0.706
Gender, male/female[c]	87/48	12/2	0.109
Hepatitis type, *n* (%)[c]			
HBV+	24 (18%)	1 (7%)	0.310
HCV+	92 (68%)	7 (50%)	0.171
ASA score (2:3), *n*[c]	93:42	6:8	0.049
BMI, kg/m^2[a,b]	23.2 ± 3.2	24.1 ± 3.0	0.289
Smoking, *n* (%)[c]	23 (17%)	2 (14%)	0.793
Primary or repeat hepatectomy, *n*[c]	83:52	10:4	0.453
Laboratory data			
Total lymphocyte count /μl[a,b]	1,350 ± 652	1,179 ± 410	0.341
Hemoglobin, g/dl[a.b]	12.9 ± 1.8	13.2 ± 0.8	0.643
Platelet × 10^4/μl[a,b]	13.8 ± 6.8	14.9 ± 9.0	0.596
AST, U/l[a.d]	39.0 ± 25.2	42.6 ± 14.6	0.126
ALT, U/l[a.d]	35.2 ± 27.9	42.6 ± 22.9	0.107
ICG-R15, %[a.d]	19.9 ± 11.0	23.9 ± 13.2	0.257
Type IV-collagen 7S domain levels, ng/ml[a.b]	5.8 ± 1.7	7.0 ± 1.8	< 0.01
Child-Pugh classification[e] (A : B), *n*[c]	129 : 5	11 : 3	<0.01
Co-morbid condition, *n* (%)[c]			
Hypertension	70 (52%)	9 (65%)	0.230
Diabetes mellitus	38 (28%)	9 (64%)	<0.01
Tumor size, cm[a,d]	2.4 ± 1.6	2.6 ± 1.3	0.743
p stage[f] (I:II:III:IV), *n*[c]	18:40:39:31	1:3:3:7	0.227
Pathological liver cirrhosis, *n* (%)[c]	76 (56%)	10 (71%)	0.288
Blood loss, g[a,d]	564.4 ± 663.9	601.6 ± 465.0	0.352
Transfusion, *n* (%)[c]	12 (9%)	1 (7%)	0.826
Operative time, min (median, range)[d]	245 (110, 586)	248 (89, 465)	0.387
Operative methods, *n*[c] (less than subsegmentectomy : segmentectomy or more)	108 : 27	9 : 5	0.127
Subcuticular suture with subcutaneous drainage, *n* (%)[c]	59 (44%)	2 (14%)	0.033
Postoperative morbidity, *n* (%)[c]			
Bile leakage	12 (9%)	0 (0%)	0.243
Hyperglycemia	54 (40%)	9 (64%)	0.080

Table 2 continued

Characteristics	Without SSI group ($n = 135$)	With SSI group ($n = 14$)	p Value
Postoperative hospital stay, days (median, range)[b]	15 (7, 189)	28 (11, 154)	<0.005

[a] Values are expressed as mean ± SD

[b] Unpaired Student's t test

[c] Chi-square test

[d] Mann-Whitney U test

[e] Child-Pugh classification [13]

[f] Pathologic TNM staging [14]

Table 3 Multivariate analysis of risk factors for incisional SSI after hepatectomy

Variables	Odds ratio	p Value
Subcuticular suture with subcutaneous drainage	0.15	0.034
Diabetes mellitus	3.41	0.067
Child-Pugh score	3.27	0.267
ASA score	2.07	0.302
Type IV-collagen 7S domain levels	1.23	0.314

and hypoalbuminemia [29], which can worsen pre-existing immune dysfunction [30]. Sorg et al. [31], working with a mouse model, revealed wound closure in hepatectomized animals was delayed compared to control and sham animals, as indicated by significantly lower values of epithelialization and neovascularization over 10 days. Their wounds had reduced bursting strength coexisting with significantly decreased collagen content. Zografos et al. [32] reported the subcuticular suture promised higher blood flow in wounds in comparison with transdermal suture. The method may augment the relationship of blood flow to wound healing. We chose 4/0 PDS II as our material for subcuticular sutures because it is an absorbable monofilament suture [33]. PDS II retains 74 % of its tensile strength at 2 weeks; 50 %, after 4 weeks. Thus, this suture is a good choice for wounds that require prolonged tensile strength after Hx.

A few trials have reported that a subcutaneous drain is effective for reducing the incidence of incisional SSI [7–11]. In contrast with the above reports, two randomized controlled trials found the use of a subcutaneous drain was not effective for the prevention of incisional SSI [34, 35]. These two studies used staples for skin closure, different from our subcuticular absorbable sutures. In a comparative study, Johnson et al. [36] reported that the use of subcuticular sutures reduced the rate of SSI compared with staples. According to a study by Ramsey et al. [34], the BMI in the suture alone group was significantly lower than that in the suture and drain group, but, as in the present study, the backgrounds of two groups were not completely equal. Both studies used closed suction drainage of the subcutaneous space with a Jackson-Pratt (JP) drain. The JP drain has multiple holes to discharge fluid. In general, because suction pressure is dependent on a suction area, fatty tissue might be damaged while the JP drain is in place, a result of the higher power on the small suction holes. Conversely, the MCDS used in our study is made from soft medical polyurethane and has a unique shape with a combination of 3 fluted channels and 1 open-tip lumen. Polyurethane material enables creation of a wide inner cavity for efficient drainage, and the distinct shape provides a large surface area for drainage. Furthermore, the drains were removed at 72 h, or earlier if output was less than 30 ml/24 h [34] or less than 50 ml per 24 h up to a maximum of 4 days [35]. The subcutaneous drain serves several purposes: it decreases the dead space in the fat layer, it adheres to the fat layer, and it drains serous effusion. We have never removed a drain within 72 h postoperatively, even when there was no discharge or when drainage was <10 ml for 24 h. These differences, more strict criteria for removal of the drain and use of the new material for the drain, might contribute to a further reduction of incisional SSI.

Of course, the surgeon must be concerned about operative time, the need for blood transfusions, and other technical aspects of the procedure that may influence the development of incisional SSI. These technical factors, however, did not demonstrate any significance in our study. Continuous efforts should be made to develop additional new strategies to prevent postoperative incisional SSI until it disappears. The new methods used in this study for skin closure were effective in preventing incisional SSI in HCC patients undergoing Hx. Larger clinical trials using subcuticular sutures and subcutaneous drainage in Hx, such as randomized control trials, are required to confirm our findings.

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