A randomised phase III trial of skin closure by subcuticular suture versus skin stapling for prevention of incisional surgical site infection after elective colorectal cancer surgery

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Abstract

Background: Whether subcuticular suture prevents incisional surgical site infection (SSI) after clean-contaminated surgery has not been clarified.

Method: Patients undergoing elective colorectal cancer surgery at one of 16 centers were randomised to receive either subcuticular sutures or skin stapling during the skin closure part of the procedure. The occurrence of incisional SSI was the endpoint of interest. Also accounted for were the time required for wound closure, incidence of wound problems, postoperative length of stay, wound aesthetics, and patient satisfaction.

Results: A total of 1264 patients were enrolled in the study. The cumulative incidence of incisional SSI by day 30 after surgery did not differ significantly between the subcuticular suture group and the staple closure group (8.7% vs 9.8%, respectively; P=0.58 by chi-square test) (odds ratio: 0.88, 95% CI 0.60-1.29). However, a comparison of cumulative incidence curves revealed a significantly longer time to SSI in the subcuticular suture group (P=0.019 by log-rank test) (hazard ratio: 0.66, 95% CI 0.45-0.97). Wound problems (P=0.48), wound aesthetics (P=0.18), and postoperative length of stay (P=0.51) did not differ significantly between groups, and the time required for wound closure was 5 minutes longer in the subcuticular suture group (P<0.001). However, patients in the subcuticular suture group were significantly more satisfied with their wound (52% vs 43%, P=0.002).

Conclusion: Subcuticular suture does not seem to significantly reduce the risk of incisional SSI occurring within 30 days after surgery. Registration number: UMIN000004001.

Introduction

Surgical site infection (SSI) is one of the most common postoperative complications encountered, with a reported incidence of 500,000 cases per year in the United States.[1] SSIs have been reported to account for 15% of all nosocomial infections and up to 38% of such infections in surgical patients.[2] Furthermore, SSIs have been reported to account for 7.3 extra days of hospital stay and for $3,152 in additional costs.[3] Most importantly, 77% of postoperative mortalities have been related to SSIs.[4] Therefore, preventing SSIs is crucial to safeguarding patients and containing medical costs. Incisional SSIs in particular account for two thirds of all SSIs.

Subcuticular suture is a method of wound closure by which the opposing dermal layers at each edge are attached with absorbable sutures buried beneath the skin surface (figure 1a). This method was first described by Halsted in 1890 and has been the preferred method for wound closure in clean surgery.[5] Because no foreign material reaches beyond the epidermis, this method of closure causes no undue skin inflammation, obviates the need for postoperative removal of the suture material, and enhances wound aesthetics.[6-8] The reported rate of incisional SSI is lower with subcuticular suture closure than with staple closure.[6,9,10]

The prevention of incisional SSIs by subcuticular suture was very recently tested in the context of gastroenterological surgery,[11] and the incidence of incisional SSIs appeared to be statistically reduced in cases of colorectal surgery in particular. However, the sample group was relatively small, and the procedures were all open surgeries. The study result pointed to the need for a large-scale randomised controlled trial that would include both open and laparoscopic surgeries to reflect current surgical practice. Thus, the present multi-centre study was conducted to examine whether subcuticular suture, in comparison to metal staple closure, reduces the incidence of incisional SSI after surgery for colorectal cancer.

Methods

Study design

Eligible patients 1) were scheduled for elective colorectal cancer surgery with or without ileostomy or colostomy; 2) had an Eastern Co-operative Oncology Group performance status (ECOG PS) of 0 or 1; and 3) showed adequate organ function according to the following laboratory data: white blood cell count > 3,000 and < 10,000/μL; neutrophil count ≥ 1,500/μL; hemoglobin ≥ 9.0 g/dL; platelet count ≥ 70,000/μL; total bilirubin ≤ 1.5 mg/dL; AST ≤ 100 IU/L; ALT ≤ 100 IU/L; serum creatinine ≤ 1.5 mg/dL; and serum albumin ≥ 2.8 g/dL; and 4) provided written informed consent.

Eligible patients were assigned randomly to skin closure by subcuticular suture or by skin stapling. The primary endpoint was the occurrence of postoperative incisional SSI, and the cumulative incidence of such SSI was determined. Other factors investigated were 1) wound problems, especially excessive exudation or dehiscence; 2) length of postoperative hospital stay; 3) time required to close the wound; 4) wound aesthetics; and 5) patient satisfaction. This study was approved by the institutional review board (IRB) of each center involved and registered in the UMIN Clinical Trials Registry (UMIN000004001).

Randomisation and masking

Patients were recruited by participating surgeons and enrolled preoperatively. Randomisation was done at a 1:1 allocation ratio to balance treatment over the following factors: institution, type of surgery (open vs. laparoscopic), and location of the tumour (colon vs. rectum). Surgeons were notified of the allocation by telephone before surgery; neither the patient nor the investigators were blinded to the allocation. These processes were managed by the data center located at National Cancer Center Hospital East.

Surgical procedure

After fascial closure, the incision was irrigated with the appropriate amount of warm saline, approximately 500 mL for open surgery and 100 mL for laparoscopic surgery. The incision was then

closed with either subcuticular sutures or skin staples. When subcuticular sutures were used, the dermal layers of each edge were properly attached to each other with suture strings buried beneath the skin surface (figure 1a); 4-0 or 5-0 absorbable mono-filament suture material was used. When skin staples were used, the dermis of each edge was properly attached at intervals of 10-15 mm (figure 1b). For standardisation, the participating surgeons were requested to learn the procedures described above through lectures and by viewing an instructional video provided by the authors before the start of the study.

Perioperative care

Because the study was a multi-institutional trial, perioperative care was not exactly the same from centre to centre. The institutions were surveyed before the trial by means of a questionnaire, and it was confirmed that each institution largely follows the Centers for Disease Control and Prevention (CDC) guideline for perioperative care.[4] The approach to standard perioperative care as described in the CDC guideline was also provided to each institution at conferences and in the study protocol.

SSI surveillance

Patients' surgical wounds were inspected daily during the period of hospitalisation. Incisional SSI was suspected if there was any purulent discharge, pain or tenderness, localised swelling, redness, or heat. The fluid or tissue was aesceptically obtained and cultured, and if infectious organisms were isolated, SSI was diagnosed, and the superficial incision was opened by the surgeon.[4] An SSI was identified by a surgeon other than the patient's primary surgery or by the institution's infection control team. Each participating surgeon attended lectures, meetings, and discussions to learn to identify SSIs on the basis of the CDC criteria. These sessions were held to standardise the surgeons' interpretation of the SSI definition as well as the surveillance at each institution. Upon hospital discharge, each patient was asked to respond to a questionnaire regarding his or her wound, and the incision was re-inspected at the outpatient clinic approximately 30 days after surgery. Therefore, the possibility of post-discharge SSI was tracked both by questionnaire and out-patient examination. The total number of incisional SSIs detected overall within 30 days after surgery, both during and after hospitalisation, was

determined.

Evaluation of other factors

Wound problems, particularly exudation and dehiscence, were surveyed in the same way as SSI. The total number of patients with excessive exudate or dehiscence within 30 days after surgery, both during and after hospitalisation, was recorded. Each patient's wound was inspected for aesthetics in the outpatient clinic 30 days after surgery by the nurse and surgeon and judged in accordance with a validated scar evaluation scale ranging from 1 (least aesthetic) to 6 (most aesthetic).[12] Patient satisfaction was self-reported on a scale ranging from 1 (least possible satisfaction) to 5 (greatest possible satisfaction).[13]

Statistical analysis

The study was first designed to detect a 6.0% reduction in the incidence of SSI from 14.0% in the staple group to 8% in the subcuticular suture group, with a two-sided significance level of 0.10 and power of 80%. Accordingly, the initial target sample size was 800 patients. However, upon consultation with a biostatistician (T.Y.), it was recommended that we change the two-sided significance level to 0.05 and the power to 90% to obtain a definitive result. This change necessitated enrollment of 1206 patients. We thus planned a sample size of 1240 patients. Between-group difference in the incidence of incisional SSI was analysed by chi-square test. Differences between numerical variables and binary variables were analysed by Mann-Whitney U-test and chi-square test, respectively. Between-group difference in the incidence of incisional SSI over time was analysed by log-rank test. All P values are two-tailed, and $P < 0.05$ was considered statistically significant. Statistical analyses were performed with SAS for Windows ver. 9.3 and SPSS 11.0 J for Windows.

Results

In total, 1264 patients were enrolled from 16 centers in Japan between August 2010 and April 2012. Of these patients, 629 were allocated to abdominal closure by stapling and 635 to closure by subcuticular suture. Thirty-two patients, because of re-operation (staple group, n=16; subcuticular suture group, n=8), major protocol violation (subcuticular suture group, n=3), cancelled surgery (staple group, n=1; subcuticular suture group, n=2), withdrawn consent (subcuticular suture group, n=1), or ineligibility (subcuticular suture group, n=1) were excluded from the analysis (figure 2). The ineligibility was due to anemia (hemoglobin < 9.0 g/dL). Thus, the full analysis set comprised 612 patients in the staple group and 620 in the subcuticular suture group. Baseline demographics and operative and postoperative characteristics of patients were well-balanced between the two groups (Table 1).

The study results are shown in Table 2. The incidence of incisional SSI at 30 days after surgery was 9.8% in the staple group and 8.7% in the subcuticular suture group. This difference was not statistically significant (P=0.58). However, a significant between-group difference was found in the time to occurrence of SSI (figure 3; P=0.019), with a hazard ratio of 0·659 (95% CI, 0.449-0.968). The incidence of wound problems (6.9% vs. 5.8%; P=0.48), the postoperative length of stay (9 days vs. 9 days; P=0.51), and wound aesthetics (proportion of patients with highest possible score: 78% vs. 80%; P=0.18) did not differ significantly between the two groups, but the time required to close the wound was significantly longer in the subcuticular suture group than in the staple group (1 minute vs. 6.5 minutes; P<0.001). Regarding patient satisfaction, the proportion of patients giving the highest possible score was greater in the subcuticular suture group than in the staple group (P=0.002). In our subset analysis, subcuticular suture tended to be favored, but the difference was not significant (figure 4).

Discussion

Subcuticular suture is a skin closure method that involves properly attaching opposite dermal layers with absorbable sutures buried beneath the skin surface. It is widely accepted as the procedure of choice in clean surgery because it is good for simple postoperative care, wound aesthetics, and wound scar prevention, and there is no need for removal of the stitches.[5-7] Subcuticular suture has been shown to be significantly better than stapling for preventing wound problems including incisional SSI after cardiovascular and orthopaedic surgery.[6,9,14] A group of gastrointestinal surgeons in Japan recently found and reported no difference between subcuticular suture and stapling in the incidence of wound problems after open gastrointestinal surgery.[11] However, a subcuticular suture-based decrease was found in the incidence of incisional SSI after open colorectal surgery in particular, although the number of colorectal surgeries was relatively low (n=277) and the procedure was limited to open surgery. We designed a large randomised controlled trial that would include both open and laparoscopic colorectal surgery to clarify whether subcuticular suture is of clinical benefit for preventing incisional SSI in cases of colorectal surgery. The present study was conducted in the context of colorectal surgery because the incidence of incisional SSI is higher in this context than in others.

Physiologically, wound healing involves re-epithelialisation that is completed within 24-48 hours after skin closure, and dermal reconstruction takes place through angiogenesis and fibrogenesis within 3-4 days.[15-17] We believe that subcuticular suture promotes attachment of each dermal layer, supports dermal reconstruction, and subsequently enhances wound healing. This series of proper wound healing events prevents tissue hypoxia and dead space formation, which encourage infection; thus, the surgical incision is protected from contamination. Therefore, we predicted subcuticular suture to be effective in preventing incisional SSI in colorectal surgery.

Among our patients, the incidence of incisional SSI after subcuticular suture as of postoperative day 30 did not differ significantly from that after stapling (8.7% vs. 9.8%, P=0.58 by chi-square test, odds ratio: 0.88, 95% CI 0.60-1.29). Subset analysis also indicated that subcuticular suture was not superior

over stapling for preventing SSI (figure 4). However, the cumulative risk of incisional SSI within 30 days was shown to be significantly lower in the subcuticular suture group than in the staple group (figure 3) (P=0.019 by log-rank test, hazard ratio: 0.66, 95% CI 0.45-0.97). These data indicate that subcuticular suture prevents incisional SSI to some extent but not unequivocally within the first 30 days after surgery. Because the cumulative risk was shown to be lower in the subcuticular suture group, it is possible that the incidence of incisional SSI in the subcuticular suture group would also have been lower if the incisions had been judged beyond postoperative day 30. In the very least, it is evident that subcuticular suture is a feasible method of wound closure not only after clean surgery but also after colorectal surgery, for which the incidence of incisional SSI is relatively high.

Wound problems including exudation and dehiscence, wound aesthetics, and postoperative hospital stay did not differ significantly between the two methods (Table 2). However, patient satisfaction, judged by the percentage of patients giving the highest possible score, was significantly greater in the subcuticular suture group than in the staple group (P=0.002). Although wound aesthetics did not differ between the two groups, patients were more satisfied with subcuticular suture, probably because it does not require removal of the stitches or because of its natural appearance without foreign objects like staples. The longer time required to close the wounds by subcuticular suture was not unexpected, but the difference was only 5 minutes in an operation that was longer than 200 minutes. Given the context, this difference is minor.

Tsujinaka and colleagues conducted the first randomised controlled trial investigating the influence of subcuticular suture on wound complications in gastrointestinal surgery.[11] Subcuticular suture was shown to decrease the incidence of incisional SSI in colorectal surgery in particular. However, the trial included only open surgeries, wound closure allocations were not well-balanced (n=176 vs. 101), and tumour location was not considered among the allocation factors even though it is a significant prognostic factor for incisional SSI.[18] In comparison, the present study focused on colorectal cancer, involved both open and laparoscopic surgery, and balanced the patient allocation in terms of tumour location and type of surgery, both of which are significant factors related to the risk of incisional

SSI.[18,19] The proportion of laparoscopic surgeries was high in the present study, which was reflective of current surgical practice. Therefore, we believe that the study described herein clearly elucidates the influence of subcuticular suture on SSI following colorectal surgery. We believe this study to be complementary to the trial conducted by Tsujinaka and colleagues, which dealt only with open surgery. Together, the two studies show clearly that subcuticular suture is equivalent to skin stapling in terms of the risk of incisional SSI after gastrointestinal surgery.

One of the limitations we face in discovering SSIs is post-discharge surveillance. Delgado-Rodriguez et al. reported development of SSIs in as many as 45.6% (103/226) of patients after discharge.[20] However, in some centres, post-discharge SSI surveillance is based solely on a review of medical records or on a one-time medical examination in the outpatient clinic.[6-10,14,21] With the trend towards shorter hospital stays, some infections may be missed unless special attention is paid to post-discharge surveillance. However, in the present study, post-discharge SSI surveillance was achieved by means of patient questionnaire, outpatient medical examination, and review of the patient's medical records, which increased the reliability of the results. Another limitation was that the response to the patient questionnaire was 81.6%. However, this rate was fairly high in comparison to rates obtained in other surgical randomised controlled trials,[22-24] and it did not differ significantly between our two procedure groups (P=0.44). Therefore, we believe that this limitation did not substantially affect the interpretation of our data. The other limitation was that perioperative factors that affect the incidence of SSI were not exactly the same among the participating institutions. However, each institution was involved in several joint meetings to standardise the subcuticular suture technique, the perioperative care, and the SSI surveillance. Furthermore, institution was used as a stratification factor before randomisation. Therefore, the effects of inter-institutional inconsistencies were minimised.

In conclusion, we found that the incidence of incisional SSI in patients treated by elective colorectal surgery does not differ significantly between closure of the skin by subcuticular suturing and closure by stapling. However, patients are more satisfied with wounds closed by subcuticular suture than with those closed with staples. Considering the increased patient satisfaction, we recommend subcuticular

suturing as the procedure of choice for skin closure after gastroenterological surgery.

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Figure legends

Figure 1: Schematic drawings of skin closure

1-a) Subcuticular suturing

The opposing skin layers are properly attached to each other by subcuticular suture.

1-b) Skin stapling

The opposing skin layers are attached to each other with skin staples.

Figure 2: Study enrollment and randomisation

A total of 1,264 patients were enrolled, 1,232 of whom were included in the final analysis.

Figure 3: Cumulative risk of incisional SSI within 30 days after surgery

Figure 4: Subset analysis of the relative risk of incisional SSI

Note that the relative risk of incisional SSI did not differ significantly between any of the subgroups.

Figure 1a

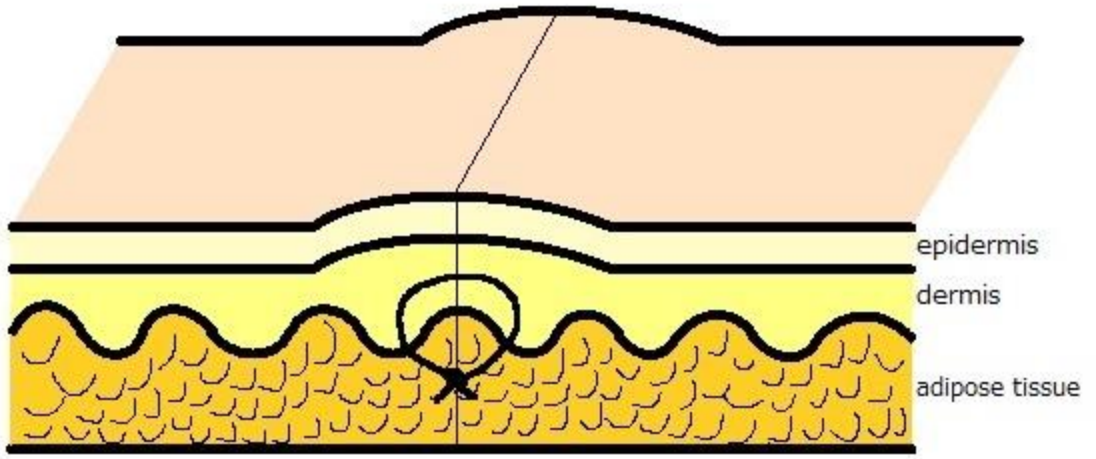

Figure 1b

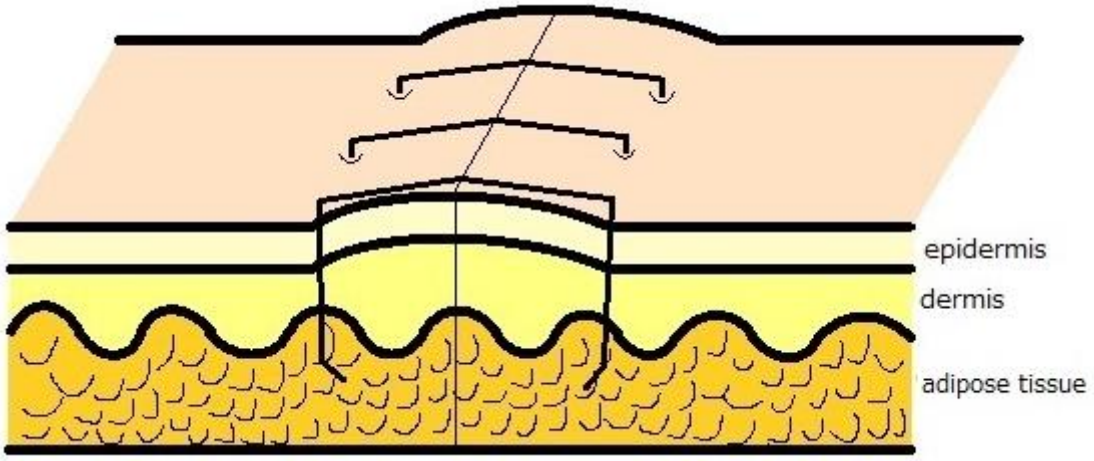

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Figure 2 Study enrolment and randomisation

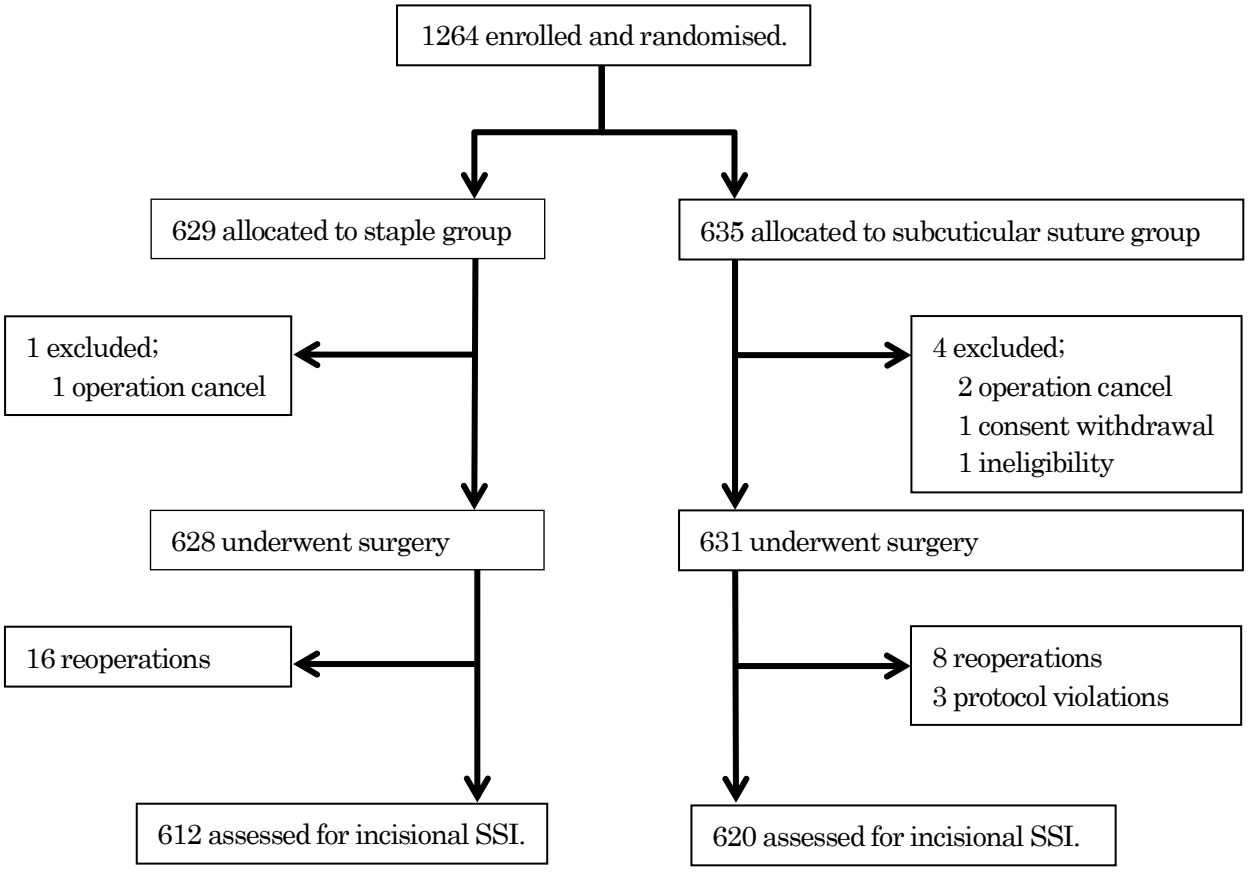
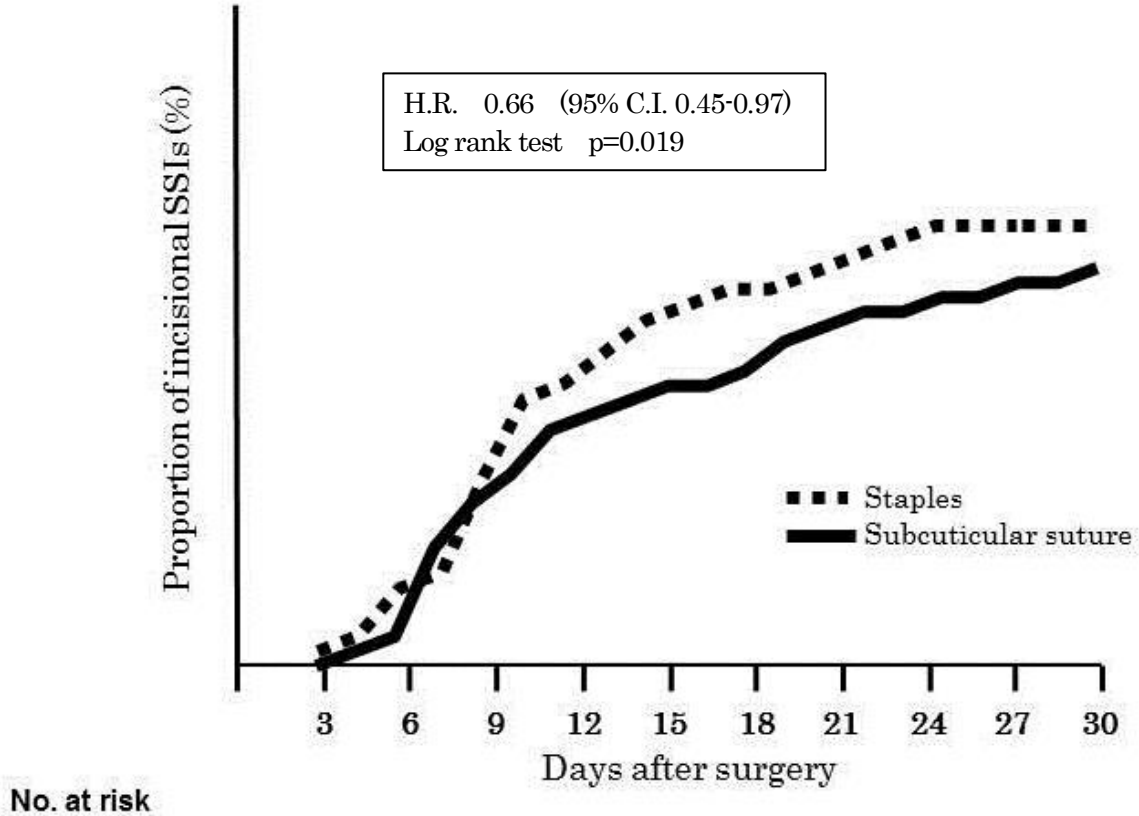


Figure 3 Cumulative risk of incisional SSI within 30 days after surgery



No. at risk											
Staples	612	611	590	571	563	558	554	554	553	553	553
Subcuticular suture	620	620	604	589	583	577	573	572	570	568	567

Figure 4 Subgroup analysis

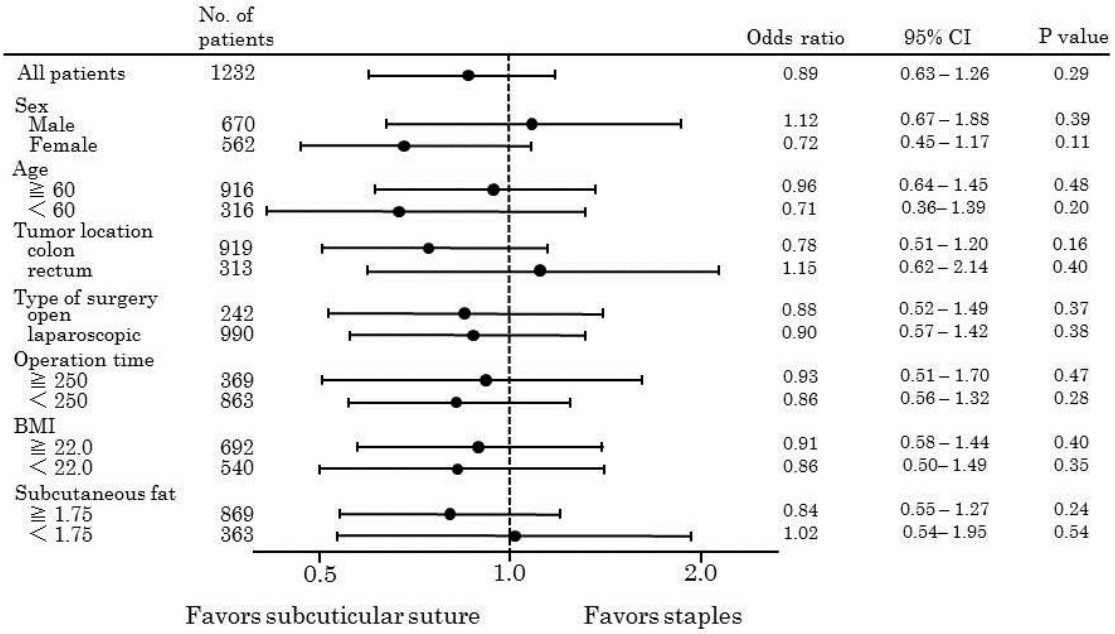


Table 1. Patient characteristics per study group

Characteristic		Staples (n=612)		Subcuticular suture (n=620)	
Age (years)	median (range)	67	(25-91)	65	(30-91)
Gender (male)	n, (%)	335	(55%)	335	(54%)
BMI (kg/m2)	median (range)	22.6	(14.3- 38.2)	22.3	(14.6-34.3)
PS (0)	n, (%)	569	(93%)	577	(93%)
ASA score					
1, 2	n, (%)	595	(97%)	600	(97%)
3	n, (%)	17	(3%)	20	(3%)
DM	n, (%)	47	(8%)	64	(10%)
History of smoking	n, (%)	80	(13%)	66	(11%)
Type of surgery					
Open	n, (%)	121	(20%)	121	(20%)
Laparoscopic	n, (%)	491	(80%)	499	(80%)
Tumour location					
Colon	n, (%)	462	(76%)	457	(74%)
Rectum	n, (%)	150	(24%)	163	(26%)
Lowest body temperature during surgery (℃)	median (range)	35.8	(31.9-37.2)	35.9	(31.9-37.7)
Surgical drains	n, (%)	467	(76%)	469	(76%)
Prophylactic cephalosporin	n, (%)	609	(99%)	619	(99%)
Depth of subcutaneous fat tissue (cm)	median (range)	1.8	(0-5)	1.8	(0-5)
Operation time (min)	median (range)	206	(60-690)	213	(81-621)
Blood loss (mL)	median (range)	29	(0-4700)	25	(0-3575)

BMI: body mass index, PS: performance status, ASA: American society of Anesthesiology, DM: diabetes mellitus

Table 2 Postoperative outcomes according to the type of skin closure

Outcome		Staples (n=612)		Subcuticular suture (n=620)		P value
Incisional SSI	n, (%)	60	(9.8%)	54	(8.7%)	0.58
Wound problem	n, (%)	42	(6.9%)	36	(5.8%)	0.48
Postoperative hospital stay (days)	median (range)	9	(4-77)	9	(5-76)	0.51
Wound aesthetics	n, (%) of patients with highest score	475	(78%)	500	(80%)	0.18
Patient satisfaction*	n, (%) of patients with highest score	211	(43%)	268	(52%)	0.002
Time to close wound (min)	median (range)	1	(0.5-25)	6.5	(0.5-30)	< 0.001

SSI: surgical site infection
*total n=1005