厚生労働科学研究費補助金

医療技術実用化総合研究事業

「消化器外科手術における合成吸収糸使用の手術部位感染抑制効果に関する多施設共同並行群間無作為化比較試験」

平成20年度　総括研究報告書

研究代表者　前原　喜彦

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目次

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研究要旨　皮下・腹壁縫合糸については、欧米において絹糸と合成吸収糸の無作為化臨床試験とメタアナリシスで、合成吸収糸の有効性が確立しているが、腹腔内で合成吸収糸を使用することで手術部位感染(Surgical Site Infection：SSI)が減少するというエビデンスは確立していない。本臨床試験の目的は、以下の点である。推奨されている周術期の患者管理を行い、消化器手術の腹腔内での絹糸使用群と合成吸収糸使用群のSSI発生率を比較し、合成吸収糸使用の有効性を検討する。これまでに、上部消化管、下部消化管、肝、膵の臓器別に吸収糸群、非吸収糸群の目標症例数を設定し、2年間の症例登録期間を経てSSI発生率を比較する。effect size（2 群間の治療効果の差）を推定し、将来の大規模臨床第Ⅲ相試験を実施するためにランダム化臨床第Ⅱ相試験を行う。主要評価項目を手術部位感染(SSI)の総発生率とし、副次評価項目は部位別(表層、深部、臓器体腔)感染発生率、SSI発生後治癒確認までの日数、術後在院日数とする。胃切除術270例、大腸切除術270例、肝切除術320例、膵頭十二指腸切除術290例　合計1150例を設定し、2年間の症例登録期間を経てSSI発生率を比較する無作為化臨床第Ⅱ相試験を行う。試験プロトコールの作成の中で、症例の選択基準、除外基準、SSI防止に関する予防策の統一など、試験結果の精度に関する議論を十分に重ねてきた。生物統計家により登録症例数設計を行い、胃切除術270例、大腸切除術270例、肝切除術320例、膵頭十二指腸切除術290例　合計1150例を計画した。インターネットを利用した登録システムであるEDCシステムを準備し、平成21年2月16日より症例登録を開始した。平成21年4月8日現在、胃：39例、大腸17例、肝臓：59例、膵臓：17例、合計132例が登録されている。臨床試験の性格上、結果は症例登録終了、結果解析後である。早期の症例集積に向けて、全施設で登録中である。臓器別で進捗に差が出るが、研究予定期間内の登録は完了し、解析結果を出せる進捗状況である。

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A.　研究目的

欧米先進諸国では、消化器手術において手術用絹糸は使用されなくなっている。これは、合成吸収糸が発売された当初、多くの動物実験と臨床試験において絹糸と合成吸収糸の比較試験が行われ、皮下、腹壁縫合における合成吸収糸の有効性が証明された結果である。米国CDC(Center for disease control and prevention)の手術部位感染(SSI)防止ガイドライン中に多くの参照文献として掲載されており、ガイドラインの本文には、絹糸の存在下では感染の危険性が増加すると記載されている。手術創に絹糸が存在すると、細菌が付着しやすく感染を助長する(Elek et al.,Br J Exp Pathol 1957)。一方わが国では、依然として手術用絹糸が広く使用されている。皮下・腹壁縫合については、欧米において絹糸と合成吸収糸の無作為化臨床試験とメタアナリシスで、合成吸収糸の有効性が確立している(Weilland et al,Am J Surg 1998;Riet,et al,Br J Surg 2001)が、腹腔内で合成吸収糸を使用することで手術部位感染(SSI)が減少するというエビデンスは確立していない。本臨床試験の目的は、以下の２点である。

1) CDCにより推奨されている周術期の患者管理を行い、消化器手術の腹腔内での絹糸使用群と全合成吸収糸使用群のSSI発生率を比較し、合成吸収糸使用の有効性を検討する。

2) 腹腔内感染発症例において、絹糸使用群と合成吸収糸使用群の治癒期間について比較検討する。

これまでに、九州大学第二外科にて腹腔内での結紮・縫合糸に関する調査を盛り込むSSIサーベイランス(総数903例)がプロスペクティブに施行され、特に大腸手術(386例)において吸収糸群のSSIが絹糸群に比べて有意に低率であったと報告し(吸収糸群13.9%、絹糸群22.4% P=0.03)、吸収糸の有用性を示唆している(Watanabe et al,Surgery Today, 2008)。しかしながら、腹腔内の腹腔内の絹糸使用と合成吸収糸使用における手術部位感染についての臨床比較試験は行われておらず、本臨床試験でエビデンスの創出を図る。絹糸がSSI発生の点で劣っていることを示唆する報告は散見されるが、腹腔内での吸収糸・非吸収糸の使用とSSIに関するmega-RCTは存在せず、どの種類の消化器手術で吸収糸使用がどれくらい有用なのか、本臨床試験で明らかにする意義は大きい。

外科術後感染症で最も多い感染症が手術部位感染(SSI)であり、その発生は患者満足度を低下させるだけでなく入院期間の延長を伴い、医療経済上も大きなマイナスインパクトを与える。本研究は開腹消化器手術における吸収糸の使用が手術部位の感染症発症を抑えるという効果の臨床的エビデンス創出に関する研究である。本研究で手術部位感染症が予防できれば術後の合併症を減らすことが可能となり、消化器手術を受ける国民の医療が安全に行え、在院日数が短縮し、通常の包括医療で済む患者の割合が増す。本臨床試験の結果は、科学的な根拠に基づいた質の高い医療の国民への提供と医療経済の効率化に貢献できると考える。

B. 研究方法

上部消化管、下部消化管、肝、膵の臓器別に吸収糸群、非吸収糸群について目標症例数を設定し、２年間の症例登録期間を経てSSI発生率を比較する。effect size(2群間の治療効果の差)を推定し、将来の大規模臨床第Ⅲ相試験を実施するために臨床第Ⅱ相試験を行う。

「消化管外科手術における合成吸収糸使用の手術部位感染抑制効果に関する多施設共同並行群間無作為化比較試験」

「肝切除および膵頭十二指腸切除における合成吸

収糸使用の手術部位感染抑制効果に関する多施設共同並行群間無作為化比較試験」
上記二つの臨床第Ⅱ相試験を行う。
(1) 研究計画および方法
1) 多施設共同並行群間無作為化比較試験
2) 試験材料：滅菌済み手術用絹糸、合成吸収性縫合糸(Polyglactin910,Polydioxanone)
3) 対象疾患：本研究の対象疾患は、以下の通りとする。
胃部分切除術：胃全摘術
合成吸収糸群135例、絹糸群135例
結腸・直腸切除術：
合成吸収糸群135例、絹糸群135例
肝切除手術：
合成吸収糸群160例、絹糸群160例
膵頭十二指腸切除手術：
合成吸収糸群145例、絹糸群145例
割り付け因子
消化管：施設、術式、腹腔鏡補助
肝膵：施設、　（肝）肝硬変の有無、
（膵）糖尿病の有無
4) 周術期管理法を下記の項目について規定する。
術前の患者準備、抗菌薬の予防投与を統一する。
手術手技：筋膜には合成吸収糸を使用し、閉鎖式(吸引)ドレーンを用いる。
術後の管理法：手術部位感染が疑われた場合には必ず細菌培養検査を提出する。
5) 評価項目
主要評価項目：手術部位感染(SSI)の総発生率
副次評価項目：部位別(表層、深部、臓器体腔)感染発生率、SSI発生後治癒確認までの期間術後在院日数
6) 手術部位感染(SSI)の評価基準：CDCによる手術部位感染の定義に準拠
①表層切開部創感染
②深部切開部創感染
③臓器体腔創感染
7) 登録の手順
施設登録及び症例登録は、データセンターにおける中央登録制とする。
8) 症例登録期間：平成21年2月16日～
追跡終了日：最終症例登録の1ヶ月後
全研究期間：2年1ヶ月
(2) 研究体制：研究代表者および研究分担者の施設で対象患者の登録をEDCシステムを用いて登録・データセンターに行う。無作為
化割付された術式を行い、決められた術後管理を行い手術部位感染率を比較する。割り付け結果の施行確認を手術室で第三者施行。通常直接介助の看護師を想定する。SSIの判定は、割り付け結果を知らないSSI判定能力のある主治医・術者以外の医療者が行う（他の外科医、ICTリンクナース、ICTメンバー）

（倫理面への配慮）本試験に関与するすべての者は「世界医師会ヘルシンキ宣言」、および「臨床研究に関する倫理指針」に従う。

説明文書・同意書(様式)および同意撤回書は試験責任医師が作成する。また、作成した説明文書・同意書(様式)は試験開始前に所属する医療機関の倫理審査委員会に提出し、その承認を得る。試験に携わる関係者は被験者の個人情報保護に最大限の努力をはらう。

データセンターが医療機関へ照会する際の被験者の特定は、試験責任医師および試験分担医師が管理する被験者識別コードまたはデータセンターが発行した登録番号を用いて行う。原資料の直接閲覧を行ったモニタリング担当者、監査担当者、規制当局の担当者などは、そこで得られた情報を外部へ漏洩しない。

主任研究者等が試験で得られた情報を公表する際には、被験者が特定できないよう十分に配慮する。

C. 研究結果

＜プロトコル＞

平成20年度の当該研究課題「消化器外科手術における合成吸収糸使用の手術部位感染抑制効果に関する多施設共同並行群間無作為化比較試験」の採択に際して、当研究のプロトコルの細部に関して推敲を重ねてきた。平成20年9月9日に東京で開催された班会議において、研究代表者、研究分担者により具体的なプロトコル内容について審議を行い、最終的には平成20年11月6日にプロトコルが完成した。各研究分担者へ発送し、現在、各研究分担者施設の倫理審査委員会へ申請中である。また審議の過程で、消化管領域の参加施設が１１施設、肝・胆・膵領域の参加施設が１７施設へと拡大し、より迅速な症例の集積が可能となった。

＜症例登録およびデータマネジメント＞

上記プロトコルの検討・確定とともに、臨床試験遂行にあたり症例登録・データマネジメントを外部機関に委託することを決定した。データマネジメント部分を研究担当者から
切り離し、データの質および信頼性を確保する目的である（品質保証・管理）。イーピーエス株式会社と契約を進め、Ｗｅｂシステム（ＥＤＣシステム）による症例登録、データ収集管理構築を鋭意進めている。また、臨床試験のプロトコルは大学病院医療情報ネットワーク（UMIN）「臨床試験登録システム」に登録を行った。

上記進捗状況を踏まえて平成21年2月16日から症例登録、試験治療を開始した。平成21年4月8日現在、胃：39例、大腸17例、肝臓：59例、膵臓：17例、合計132例が登録されている。臨床試験の性

格上、結果は症例登録終了、結果解析後である。

D. 考察

臨床試験の性格上、結果は症例登録終了、結果解析後である。

E. 結果

早期の症例集積に向けて、全施設で登録中である。臓器別で進捗に差が出るが、研究予定期間内の登録は完了し、解析結果を出せる進捗状況である。

F. 健康危険情報

特記すべきことなし。

G. 研究発表

論文発表（外国語論文）

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Risk Factors Associated with Surgical Site Infection in Upper and Lower Gastrointestinal Surgery. ***Surgery Today 38:404-412***

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
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渡辺　昭博	Risk Factors Associated with Surgical Site Infection in Upper and Lower Gastrointestinal Surgery	Surgery Today	38	404-412	2008

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Risk Factors Associated with Surgical Site Infection in Upper and Lower Gastrointestinal Surgery

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Abstract

Purpose. To assess the risk factors of surgical site infection (SSI) in gastrointestinal surgery.
Methods. Surgical site infection surveillance was conducted in 27 hospitals.
Results. The incidence of SSI in the 941 patients studied was 15.5%. The factors associated with SSI were body mass index (BMI), comorbidity, emergency procedures, wound classification, blood loss, the suture material used for intra-abdominal ligation, the method of subcutaneous incision, the frequency of glove changes, and the absence of subcutaneous sutures. In lower alimentary tract procedures, additional factors influencing the incidence of SSI were sex, smoking status, operating time, the suture material used for abdominal wound closure and seromuscular sutures, and the combined resection procedures. According to a multiple logistic regression analysis, the independent risk factors for SSI were as follows: the type of operation, blood loss, wound classification, emergency procedures, the frequency of glove changes, the use of subcutaneous sutures, combined resection procedures, and the material used for seromuscular suturing.
Conclusion. Strict asepsis and minimal blood loss were associated with a lower incidence of SSI following gastrointestinal surgery. The use of absorbable suture material may be involved in reducing the risk of SSI.

Key words SSI · Gastrointestinal surgery · Surveillance

Introduction

Surgical site infection (SSI) accounts for about 15% of all nosocomial infections and occurs in 10%–30% of all patients undergoing gastrointestinal surgery.[1,2] Surgeons either tend to ignore or are unaware of these data because of the minor impact these infections have on postoperative recovery, especially incisional SSIs. Nevertheless, a considerable number of patients suffer from the unexpected and painful complications of an SSI. Thus, surgeons should be made aware of the high incidence and costs of managing SSIs.[1,3]

In 1970, the Centers for Disease Control and Prevention (CDC) in US set up the National Nosocomial Infection Surveillance (NNIS) system and established the guidelines for the prevention of SSI.[4] The CDC also reported that surveillance plays an important role in decreasing the incidence of SSI. In 1998, almost 30 years after the NNIS system was established, the Japanese Nosocomial Infection Surveillance (JNIS) system was started.[5] Most Japanese surgeons now recognize the importance of preventing SSI. We founded the SSI study group in Kyushu University to decrease the rate of SSIs and to investigate the factors influencing it. This report presents our preliminary results of SSI surveillance of gastrointestinal surgery in the Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, and its 26 affiliated hospitals in the Kyushu, Shikoku, and Chugoku districts. We focused on the operative procedures, including the materials used in abdominal closure, seromuscular suturing, and intra-abdominal ligation.

Methods

Between October 1, 2004 and January 31, 2005, we collected and analyzed data prospectively from patients who underwent operations for gastrointestinal disease

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in the Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, and its 26 affiliated hospitals. The subjects of this study consisted of patients who underwent operations in the intra-abdominal alimentary tract, such as procedures for gastroduodenal, small intestinal, and colorectal diseases, and appendicitis. Patients who underwent esophageal, anal, pancreatic, and biliary tract operations were not included in this surveillance. Records of both elective and emergency procedures were collected preoperatively, intraoperatively, and during 1 month of postoperative follow-up. No recommendations were made prior to or during this study to decrease the incidence of SSI. There was no protocol for the administering of antibiotics, including preoperative preparations for colorectal operations.

The preoperative data, including body weight, height, smoking habits, and the method of hair removal, were collected from responses to a questionnaire given to the patients. The American Society of Anesthesiologists (ASA) score was calculated by the anesthesiology team when requested by the attending physician. The diagnosis and classification of SSI, namely, superficial incisional, deep incisional, or organ/space SSI, and the surgical wound classification, namely, Class I (clean), Class II (clean-contaminated), Class III (contaminated), or Class IV (dirty-infected), were based on the CDC definitions.[4] Patients with delayed primary sutures were excluded from the superficial SSI assessment. All data were collected by the attending physician or the SSI staff, namely, surgeons who were responsible for data accumulation and SSI evaluation. The data files were sent to the secretary of the SSI study group at the Department of Surgery, Fukuoka Dental College, Fukuoka, Japan.

Univariate statistical analyses were conducted using chi-square tests and unpaired, one-tailed t tests. Yates correction was done if there was a number lower than 10 in the chi-square test. Multivariate regression analysis was conducted for gastrectomy, colectomy, rectal resection or amputation, and appendectomy, using a BMDP package program (The BMDP PLR program; BMDP Statistical Software, Los Angeles, CA, USA) for an IBM (IBM, Armonk, NY, USA) 3090 mainframe computer, employing Cox's proportional hazard model[6] to determine the independent factors for SSI. Stoma operations (including Hartmann's operation), bypass procedures, perforation closure, adhesiolysis, wedge resection, and other miscellaneous procedures were excluded from the analysis. The covariates studied are listed in Tables 4 and 5.

Results

Patient Characteristics

We analyzed 941 patients. Table 1 summarizes the patient characteristics and incidences of SSI. The age distribution was 11–98 years, and 63.7% of the patients were men. The SSI-positive group had a significantly higher mean body mass index (BMI) than the SSI-negative group ($P = 0.046$). Patients with comorbidity had a higher incidence of SSI than those without comorbidity ($P = 0.045$). Within the comorbidity group, patients with chronic lung disease such as asthma had a higher incidence of SSI than those without comorbidity ($P = 0.003$). According to the questionnaire, 28.6% of the patients were smokers, consistent with the current smoking rate in Japan. The group who either quit smoking for less than a month before their operation or were still smoking at the time of their operation had a relatively higher SSI rate (18.4%) than the non-smokers or the patients who had quit smoking for more than a month (14.9%). Hair on the skin over the operative site was either not removed (35.5%) or was removed using clippers or a depilatory agent (52.8%) in majority of patients. Only 29 (3%) patients had the preoperative area shaved, and because of this low percentage, there was no significant difference in SSI rates between shaved patients and those who were not shaved. Regarding the timing of hair removal, 334 (35.5%) patients were prepared on the day prior to surgery, contrary to the current CDC guidelines.[4]

Incidence of SSI According to the Type of Operation

The incidence of SSI following upper alimentary tract operations, which consisted of partial and total gastrectomy, including total resection of the gastric remnant, was 8% (26/326). Conversely, the incidence of SSI following lower alimentary tract operations, which consisted of small-intestinal and colorectal surgery, appendectomy, and stoma operations including Hartmann's operation, was as high as 20%–30% (Table 2).

Operative Variables and SSI

The relationships between operative variables and SSI are summarized in Table 3. The incidence of SSI was significantly associated with such factors as elective or emergency surgery, wound classification, blood loss, the suture material used for intra-abdominal ligation, the method of subcutaneous incision, the frequency of glove changes, and the presence of subcutaneous sutures (Table 3). The incidence of SSI was lower following the procedures in which absorbable sutures were used than the procedures in which non-absorbable sutures were

Table 1. Patient characteristics and surgical site infection

Characteristics	No. of patients	SSI (+) (%)	SSI (−)	*P*
Age	941	64 ± 17	64.4 ± 17	NS
Sex				
Male	599	103 (17.2)	496	NS
Female	342	43 (12.6)	299	
BMI	923	22.5 ± 3.7	21.8 ± 3.5	0.046
ASA score				
1 and 2	775	113 (14.6)	662	NS
≥3	164	33 (20.1)	131	
Comorbidity				
Absent	542	73 (13.5)	469	0.045
Present	388	71 (18.3)	317	
Diabetes mellitus	113	16 (14.2)	97	NS[b]
Cardiovascular disease	112	21 (18.8)	91	NS[b]
Lung disease	13	6 (46.2)	7	0.003[b]
Renal failure	18	4 (22.2)	14	NS[b]
Albumin < 3 g/dl	50	9 (18)	41	NS[b]
Hemoglobin < 10 g/dl	79	14 (17.7)	65	NS[b]
Others[a]	117	22 (18.8)	95	NS[b]
Smoking				
None/cessation ≥ a month	747	111 (14.9)	636	NS
Cessation < a month/smoking	185	34 (18.4)	151	
Hair removal				
None	334	47 (14.1)	287	NS
Depilatory agent/clipper	497	76 (15.3)	421	
Razor shaving	29	3 (10.3)	26	

Values are expressed as mean ± SD
SSI, surgical site infection; BMI, body mass index; ASA, American Society of Anesthesiologists; NS, non-significant
[a]Others include liver cirrhosis or chronic hepatitis, steroid usage, infection, and other diseases
[b]Versus comorbidity absent cases

Table 2. Type of operation and surgical site infection

Operation	Type of SSI: Superficial incisional[a]	Deep incisional	Organ/space	Total	SSI (%)
Gastrectomy: proximal and distal	5 (220)	2 (222)	8 (222)	15 (222)	6.8
Gastrectomy: total and gastric remnant	5 (104)	0 (104)	6 (104)	11 (104)	10.6
Resection: small intestine	4 (33)	1 (35)	2 (35)	7 (35)	20
Resection: colon	35 (235)	6 (238)	9 (238)	50 (238)	21
Resection: rectum	6 (96)	1 (98)	6 (98)	13 (98)	13.3
Rectal amputation and total pelvic exenteration	5 (30)	2 (30)	2 (30)	9 (30)	30
Stoma and Hartmann's operation	9 (36)	0 (38)	1 (38)	10 (38)	26.3
Bypass	4 (19)	0 (20)	1 (20)	5 (20)	25
Closure of perforation	0 (17)	2 (20)	2 (20)	4 (20)	20
Appendectomy	8 (92)	2 (99)	6 (99)	16 (99)	16.2
Adhesiolysis	0 (12)	2 (12)	0 (12)	2 (12)	16.7
Wedge resection	0 (12)	0 (13)	0 (13)	0 (13)	0
Others	3 (12)	1 (12)	0 (12)	4 (12)	33.3

Numbers in parentheses indicate the number of operations
SSI, surgical site infection
[a]Delayed primary suture cases were excluded

used for abdominal wound closure and seromuscular suturing, although the difference was not significant. Regarding the drainage type, open drainage was associated with an 18.1% incidence of SSI, which was higher than that associated with other types of drainage. The association of patient characteristics and operative variables with the incidence of SSI was assessed separately in relation to upper and lower alimentary tract operations because of the differences in the SSI rates (Tables 4, 5). In upper alimentary tract surgery, significant

Table 3. Operative variables and surgical site infection

Operative variable	No. of patients	SSI (+) (%)	SSI (−)	*P*
Emergency				
Elective	732	94 (12.8)	638	<0.001
Emergency	207	51 (24.6)	156	
Wound classification				
Classes I and II	812	96 (11.8)	716	<0.001
Classes III and IV	129	50 (38.7)	79	
Laparoscopic or assisted surgery				
No	836	133 (15.9)	703	NS
Yes	106	13 (12.3)	93	
Blood loss	941	234 ± 317	415 ± 594	<0.001
Operation time	932	198 ± 109	185 ± 88	NS
Abdominal wound closure				
Intermittent or continuous				
Intermittent	609	93 (15.3)	516	NS
Continuous	330	53 (16.1)	277	
Suture material				
Absorbable	808	119 (14.7)	689	NS
Non-absorbable	131	27 (20.6)	104	
Intra-abdominal suture material				
Seromuscular suture				
Absorbable	260	31 (11.9)	229	NS
Non-absorbable	570	92 (16.1)	478	
None	91	19 (20.9)	72	
Ligation				
Absorbable	154	16 (10.4)	138	0.047[a]
Non-absorbable	739	124 (16.8)	615	
None	33	2 (6.1)	31	
Subcutaneous incision				
By surgical knife	120	8 (6.7)	112	0.006
By electric cautery	821	138 (16.8)	683	
Drainage				
No drain	134	18 (13.4)	116	NS
Closed (suction)	132	21 (15.9)	111	
Closed (non-suction)	244	29 (11.9)	215	
Open	431	78 (18.1)	353	
Frequency of glove changes				
None	255	24 (9.4)	231	0.002
One or more	685	122 (17.8)	563	
Subcutaneous suture				
No	741	129 (17.4)	612	0.002
Yes	199	17 (8.5)	182	

Values are expressed as mean ± SD
SSI, surgical site infection
[a]Absorbable versus non-absorbable

relationships were observed between the incidence of SSI and blood loss as well as combined resections. The incidence of SSI was lower when absorbable sutures had been used for abdominal wound closure, seromuscular sutures, and intra-abdominal ligations, than when non-absorbable sutures had been used, although the differences were not significant.

In the lower alimentary tract operations, significant relationships were observed between the incidence of SSI and sex, BMI, smoking status, emergency procedures, wound classification, blood loss, operating time, abdominal wound suture material, seromuscular suture materials, ligation suture material, combined resection operations, frequency of changing gloves, and the presence of subcutaneous sutures. A higher incidence of SSI was seen in patients who underwent a functional end-to-end anastomosis than in those who underwent an ordinary hand-sewn anastomosis, although the difference was not significant.

The protocol for antibiotic prophylaxis was not fixed, but we investigated it in this surveillance of SSI. Cefazolin was given to 68.3% of the patients who underwent upper alimentary tract operations, and the duration of administering was not longer than 3 days in 88.1%.

Table 4. Characteristics of the patients who underwent upper versus those who underwent lower abdominal operations and their effect on surgical site infection

Characteristics	Upper (n = 312)				Lower (n = 401)			
	No. of patients	SSI (+)	SSI (−)	P	No. of patients	SSI (+)	SSI (−)	P
Age	310	69.8 ± 12	65.8 ± 11	NS	397	66.5 ± 13.2	69.5 ± 12	NS
Sex								
Male	206	19 (9.2)	187	NS	240	56 (23.3)	184	0.026
Female	106	5 (4.7)	101		161	23 (14.3)	138	
BMI	308	22.2 ± 3.6	22.2 ± 3.6	NS	393	22.9 ± 3.3	22.0 ± 3.3	0.025
ASA								
1 and 2	272	18 (6.6)	254	NS	331	65 (19.6)	266	NS
≥3	40	6 (15)	34		70	14 (20)	56	
Comorbidity								
Absent	176	10 (5.7)	166	NS	222	44 (19.8)	178	NS
Present	129	14 (10.9)	115		173	33 (19.1)	140	
Diabetes mellitus	43	3 (7.0)	40	NS[b]	47	9 (19.1)	38	NS[b]
Cardiovascular disease	32	3 (9.4)	29	NS[b]	52	13 (25.0)	39	NS[b]
Lung disease	5	3 (60.0)	2	NS[b]	3	1 (33.3)	2	NS[b]
Renal failure	3	0 (0)	3	NS[b]	9	1 (11.1)	8	NS[b]
Albumin <3 g/dl	11	2 (18.2)	9	NS[b]	20	4 (20.0)	16	NS[b]
Hemoglobin <10 g/dl	13	2 (15.4)	11	NS[b]	50	9 (18.0)	41	NS[b]
Others[a]	24	3 (12.5)	21	NS[b]	49	7 (14.3)	42	NS[b]
Smoking status								
None/cessation ≥ a month	243	17 (7)	226	NS	330	57 (17.2)	273	0.018
Cessation < a month/smoking	68	7 (10.3)	61		67	21 (31.3)	46	
Hair removal								
None	131	11 (8.4)	120	NS	110	17 (15.4)	93	NS
Depilatory agent/clipper	150	10 (6.7)	140		247	50 (20.2)	197	
Razor shaving	9	1 (11.1)	8		14	2 (14.2)	12	

Values are expressed as mean ± SD
SSI, surgical site infection; NS, non-significant
[a] Others include liver cirrhosis or chronic hepatitis, steroid usage, infection, and other diseases
[b] Versus comorbidity absent cases

Cefmetazole and flomoxef sodium were given to 44.1% and 28.7% of the patients who underwent lower alimentary tract operations, respectively, and the duration of administering was not longer than 3 days in 77.1%. There was no significant difference in the incidence of SSI according to the type of antibiotics or their duration.

Multivariate Analysis

Gastric surgery, colorectal surgery, and appendectomy (excluding minor operations such as wedge resection, stoma operation, and bypass operations) were analyzed by a multivariate analysis in relation to SSI (Table 6); 48 (6.1%) of the 791 patients were excluded from the analysis because of incomplete data. The type of operation, blood loss, wound classification, emergency procedures, frequency of changing gloves, subcutaneous sutures, combined resection procedures, and the type of seromuscular suture material were identified by multivariate analysis as independent factors influencing the incidence of SSI.

Discussion

The CDC classified postoperative infections as either SSI or remote infection. SSI was further categorized into superficial, deep incisional, and organ/space infection.[4] These definitions are useful for infection identification and data comparison among hospitals. The CDC guidelines also provided much evidence for specific perioperative management strategies, which have been adopted by surgeons throughout the world. There is considerable evidence that SSI surveillance itself decreases the rate of infection (category IB).[3,7,8] Therefore, we established our SSI study group and started to perform surveillance to decrease the rate of SSI. We investigated operative procedures such as laparoscopy, methods of closing the abdomen, suture materials, methods of subcutaneous incision, drainage methods, frequency of glove changing, presence of subcutaneous sutures, and anastomotic techniques, in addition to the usual factors included in SSI surveillance.

Our surveillance revealed that the overall incidence of SSI, including post-emergency procedures, was 15.5%

Table 5. Operative variables of upper versus lower abdominal operations and their effect on surgical site infection

	Upper (n = 312)				Lower (n = 401)			
Operative variable	No. of patients	SSI (+)	SSI (−)	P	No. of patients	SSI (+)	SSI (−)	P
Emergency								
Elective	307	20 (6.5)	287	NS	342	61 (17.8)	281	0.024
Emergency	5	4 (80)	1		59	18 (30.5)	41	
Wound classification								
Classes I and II	306	24 (7.8)	282	NS	351	56 (16)	295	<0.0001
Classes III and IV	6	0	6		50	23 (46)	27	
Laparoscopic or assisted surgery								
No	27	0	27	NS	36	8 (22.2)	28	NS
Yes	286	24 (8.4)	262		365	71 (19.5)	294	
Blood loss	312	657 ± 766	334 ± 370	<0.001	397	489 ± 629	224 ± 286	<0.0001
Operation time	307	239 ± 71	240 ± 71	NS	398	222 ± 115	180 ± 73	<0.001
Abdominal wound closure								
Intermittent or continuous								
Intermittent	186	12 (6.5)	162	NS	251	53 (21.1)	198	NS
Continuous	126	12 (9.5)	102		150	26 (17.3)	124	
Suture material					401			
Absorbable	275	19 (6.9)	256	NS	343	61 (17.8)	282	0.019
Non-absorbable	37	5 (13.5)	32		58	18 (31)	40	
Intra-abdominal suture material								
Seromuscular suture								
Absorbable	82	5 (6.1)	77	NS	100	12 (12)	88	0.035[a]
Non-absorbable	225	19 (8.4)	206		248	54 (21.8)	194	
None	3	0	3		46	10 (21.7)	36	
Ligation								
Absorbable	44	2 (4.5)	42	NS	59	4 (6.8)	55	<0.001[a]
Non-absorbable	261	22 (8.4)	239		338	74 (21.9)	264	
None	2	0	2		2	0	2	
Combined resection								
No	238	14 (5.9)	224	<0.001	374	67 (17.9)	307	<0.001
Yes	70	10 (14.3)	60		27	12 (44.4)	15	
Subcutaneous incision								
By surgical knife	48	2 (4.5)	46	NS	51	3 (5.9)	48	NS
By electric cautery	264	22 (8.4)	242		350	76 (21.5)	274	
Drainage								
No drain	9	1 (11.1)	8	NS	19	1 (5.3)	18	NS
Closed (suction)	47	4 (8.5)	43		70	14 (20)	56	
Closed (non-suction)	123	9 (7.3)	114		96	17 (17.7)	79	
Open	132	10 (7.6)	122		216	47 (21.8)	169	
Frequency of glove changes								
None	59	5 (8.5)	54	NS	74	6 (22.4)	68	0.009
One or more	253	19 (7.5)	234		326	73 (8.1)	253	
Subcutaneous suture								
No	250	21 (8.4)	229	NS	315	72 (22.9)	243	0.024
Yes	61	3 (4.9)	58		86	7 (8.1)	79	
Functional end to end								
No					333	61 (18.3)	272	NS
Yes					68	18 (26.5)	50	

Numbers in parentheses indicate percentages; values are expressed as mean ± SD
SSI, surgical site infection; NS, non-significant
[a] Absorbable versus non-absorbable

and that it was higher following the small-intestinal and colorectal surgical procedures than following gastric surgery. Moreover, univariate analysis revealed that BMI, emergency procedures, wound classification, blood loss, the suture material used for intra-abdominal ligation, the method of subcutaneous incision, the frequency of changing gloves, and the presence of subcutaneous sutures were significantly associated with SSI. Wound classification, emergency procedures, and blood loss were the risk factors most strongly associated with SSI ($P < 0.001$), in accordance with the findings of earlier reports.[2,9,10] Thus, surgeons should practice all measures

Table 6. Multivariate analysis

Variables	Coefficient	S.E.	Odds ratio	95% CI	P
Operation					
Gastric surgery	0		1.0		0.0003
Colorectal surgery	1.312	0.304	3.71	2.0400–6.7400	
Appendectomy	0.7916	0.64	2.21	0.6280–7.7500	
Blood loss	0.001146	0.000315	1	1.0000–1.0000	0.0007
Wound classification	1.193	0.359	3.3	1.6300–6.6700	0.0021
Emergency	1.217	0.451	3.38	1.3900–8.1800	0.0122
Changing gloves	1.102	0.348	3.01	1.5200–5.9700	0.0033
Subcutaneous suture	−1.091	0.351	0.336	0.1690–0.6690	0.0039
Combined resection					
None	0		1.0		0.0365
One organ	1.088	0.374	2.97	1.4200–6.1900	
Two organs	0.2647	0.731	1.3	0.3110–5.4700	
Seromuscular suture					
None	0		1.0		0.0203
Absorbable	−0.8057	0.457	0.447	0.1820–1.1000	
Non-absorbable	0.8057	0.457	2.24	0.9120–5.4900	

Complete data for 741 patients were analyzed

to avoid contamination of the operative field and minimize blood loss to prevent SSI.

The CDC guidelines[4] recommend that surgeons minimize devitalized tissue and foreign bodies such as sutures, charred tissue, necrotic debris, and dead space at the surgical site (category IB). Using a surgical knife during subcutaneous incisions can reduce tissue burn and necrosis, which might explain the lower incidence of SSI associated with the use of a surgical knife than with electric cautery. To reduce necrosis and charred tissue in the incisional wound, surgeons should avoid making slow incisions when using electric cautery. The rate of SSI also decreases if subcutaneous tissue is closed with an absorbable suture to eradicate the dead space.[11]

Less frequent glove changing was associated with a lower incidence of SSI, which may be owing to the procedural background: operative procedures with less contamination such as adhesiolysis and wedge resection do not require glove changing, whereas procedures with more contamination such as colorectal surgery, and stoma operations do require frequent glove changing.

In contrast to upper alimentary tract operations, in which only two factors, namely, blood loss and the additional resection of another organ, were associated with SSI, the patient's sex, smoking habits, operative time, suture material used in both abdominal and seromuscular closure, and the additional resection of another organ were significant univariate factors associated with the incidence of SSI following lower alimentary tract operations. The incidence of SSI was higher when a functional end-to-end anastomosis was performed using suturing instruments[12] than when this technique was not used. Multifiring of the suturing instrument, which is inserted into the intestinal lumen, might be responsible for the higher SSI incidence. The surgical team must therefore pay careful attention to any type of potential contamination during this procedure.

A preoperative smoking habit was found to be a significant risk factor for SSI following lower alimentary tract surgery, and this tendency was also observed in patients who underwent upper alimentary tract surgery. Hypovolemia and hypoxia are believed to be responsible for SSI.[2,10] Smoking causes constriction of the peripheral blood vessels,[13] the possible consequence of which is tissue hypovolemia and hypoxia, creating an environment conducive to SSI.[14] Ideally, patients should refrain from smoking for at least 4 weeks prior to surgery;[15] however, there is usually no time for this, especially when emergency surgery is indicated or the patient has malignant disease. Interestingly, Bluman et al.[16] observed an almost sevenfold increase in postoperative pulmonary complications in smokers who tried to quit smoking prior to surgery in comparison with patients who did not stop smoking. The transient increase in the sputum volume in smokers who stopped smoking several days prior to surgery might be related to this phenomenon.[17,18] A prophylactic strategy should be established for current smokers who are unable to stop smoking for 4 weeks prior to their operations. According to our surveillance protocol, we focused on the type of suture material used for abdominal wall closure, seromuscular sutures, and intra-abdominal ligations. In Japan, silk is still often used for intra-abdominal suturing and ligation because it is less expensive and easier to handle than absorbable synthetic suture material. However, foreign materials, especially silk, are known to accelerate infection.[4,19] In the CDC guidelines,[4] monofilament sutures were recommended to reduce SSI.[4] We investigated the use of suture materials during abdominal wound closure, seromuscular approximation, and ligation. In all cases, absorbable sutures were associated with a lower incidence of SSI than non-absorbable sutures in intra-abdominal ligation ($P = 0.047$). This association was also evident in lower alimentary tract operations involving abdominal wound closure ($P = 0.019$), seromuscular suturing ($P = 0.035$), and ligation ($P < 0.001$). Although the differences were not significant, the same tendencies were observed in the upper alimentary tract procedures. Furthermore, multivariate analysis revealed that the odds ratio of absorbable suture material in seromuscular suturing was lower than that of non-absorbable suture material. These facts suggest the superiority of absorbable suture material in gastrointestinal surgical procedures to reduce the risk of SSI. A well-designed randomized controlled trial is needed to prove this assumption.

The development of a suture sinus, which is a superficial incisional SSI, often involves non-absorbable suture material during abdominal wound closure.[20,21] Thus, absorbable suture material is now widely used for abdominal closure in Japan. According to our surveillance protocol, absorbable sutures were used in 86% of the patients. Polydioxanone (PDS-II), an absorbable suture material, was used in 57% of these patients because of its durability and lower wound failure rate in comparison with polygractin 910 (Vicryl), and polyglycoric acid (Dexon).[22-24] However, braided nylon (Surgilon) and silk were still used in 13% of the patients in this study. Surgeons should be made aware of the evidence demonstrating a better surgical outcome associated with the use of absorbable sutures.[25]

In summary, our study showed that cleaner procedures and reduced blood loss can decrease the incidence of SSI following gastrointestinal surgery. The cessation of smoking for more than a month prior to surgery might also reduce the risk of an SSI, especially in patients undergoing elective lower alimentary tract surgery. Moreover, the use of absorbable suture materials might play an important role in reducing the incidence of SSI. Further study is needed to provide evidence on the use of specific types of intra-abdominal suture materials. In conclusion, SSI surveillance should be conducted and maintained in all hospitals to promote better surgical outcomes.

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