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Postoperative Changes in Body Composition After Gastrectomy

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Nutritional status is one of the most important clinical determinants of outcome after gastrectomy. The aim of this study was to compare changes in the body composition of patients undergoing laparoscopy-assisted gastrectomy (LAG), distal gastrectomy (DG), or total gastrectomy (TG). Total body protein and fat mass were measured by performing a multifrequency bioelectrical impedance analysis using an inBody II machine (Biospace, Tokyo, Japan) in 108 patients (72 men, 36 women) who had undergone LAG (n = 24), DG (n = 39), or TG (n = 45). Changes between the preoperative data and results obtained on postoperative day 14 and 6 months after surgery were then evaluated. The mean preoperative body weight of the subjects was 57.6 ± 10.7 kg, the mean body mass index was 22.5 ± 3.4 kg/m^2, and the mean fat % was 24% ± 7%. In the immediate postoperative period (14 days), the body weight loss in the LAG group was significantly lower than in the DG and TG groups (2.5 ± 0.9 kg vs. 3.5 ± 1.8 kg and 4.0 ± 1.9 kg, respectively; $P < 0.0001$). The body composition studies demonstrated a loss of total body protein rather than fat mass. Six months after surgery, body weight was not significantly different from preoperative values in the LAG and DG groups (−1.2 ± 3.8 kg and −1.8 ± 4.7 kg, respectively), but had decreased by 8.9 ± 4.9 kg in the TG group ($P = 0.0003$). A body composition analysis revealed a loss of fat mass in the DG and TG groups. The patients who underwent gastrectomy lost body protein mass during the early postoperative period. The type and extent of surgery has an effect on long-term body mass and composition. Bioelectric impedance analysis can be used to assess body composition and may be useful for nutritional assessment in patients who have undergone gastrectomy. (J Gastrointest Surg 2005;9:313–319) © 2005 The Society for Surgery of the Alimentary Tract

Key words: Body composition, gastrectomy, bioelectrical impedance analysis

Weight loss is a common problem after gastrectomy; the main mechanisms implicated include impaired food intake and malabsorption.[1,2] Weight loss occurs principally during the first 3 months after surgery.[3] Patients who undergo a subtotal gastrectomy consume fewer calories during the first 3 months after surgery, after which their intake improves.[4] Nutritional status is one of the most important clinical determinants of outcome after gastrectomy.

The body can be divided into two or more compartments based on its anatomic, fluid, or chemical components.[5] The most commonly used body composition model is a two-component model, in which the body is divided into fat mass and lean body mass (Fig. 1). Multicomponent techniques allow the lean body mass to be broken down into as many as four components, such as extracellular water, total body water, body protein mass (muscle mass), and bone.

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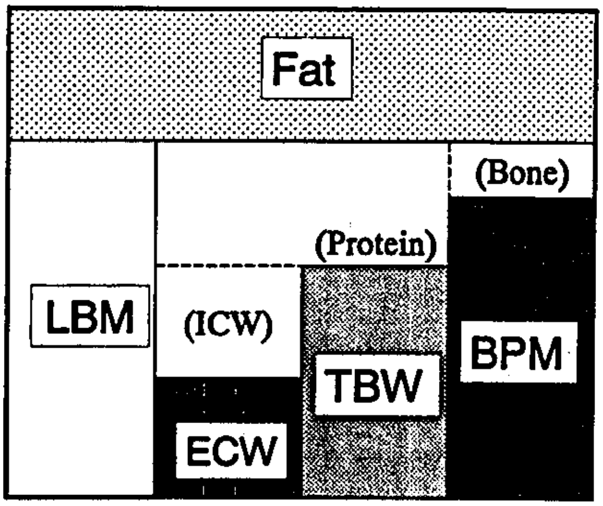

Fig. 1. Graphic representation of two-compartment and multicompartment models. According to this approach, fat is considered to be an extractable lipid and the remainder of the body weight is regarded as the lean body mass (LBM). Water is the single largest compartment, and total body water (TBW) is divided into intracellular water (ICW) and extracellular water (ECW). The lean body mass is also the sum of two fat-free components: body protein mass (BPM) and bone.

Bioelectrical impedance appears to provide a noninvasive, safe, rapid, and accurate method for evaluating body composition.[6] The method is based on the bioelectrical principle of impedance, the vector sum of resistance and reactance. Resistance is the opposition to electrical current in relation to the length and diameter of a cylinder. The human body resembles a set of serially connected cylinders (arms, trunk, and legs) with a known height and relatively constant diameter. As a result, height^2/resistance is proportional to hydrated portion of the body, such as total body water and lean body mass. By subtracting the lean body mass from the weight, the fat mass (the nonhydrated portion of the body) can be calculated.

Reactance reflects the component of impedance resulting from the presence of capacitive elements, such as the cell membrane. Multifrequency bioelectrical impedance analysis operates on the principle that the body's resistance is dependent on the frequency of the applied alternating current. Total body water is distributed between intracellular water and the extracellular water spaces, which are separated by the cell membranes. At a low frequency, the cell membranes act as capacitors, and the amount of extracellular water is predominantly measured. At a higher frequency, however, the membranes become permeable, and the total amount of body water can be measured. The ratio of extracellular water to total body water (edema index) is correlated with the ratio of the resistance at a high frequency to the resistance at a low frequency.[7] Segmental bioelectrical impedance of the arms and limbs enables the segmental body protein mass (muscle mass), as well as total body protein, to be precisely determined.[8]

Body composition is altered after surgery, and the metabolically active body mass is diminished (catabolic phase).[9] Once the patient recovers from the surgical insults, positive nitrogen balance and weight gain occur (anabolic phase). However, few body composition studies have been carried out following gastrectomy; furthermore, there is no data regarding the impact of various types of gastrectomy on body composition alterations.[10-12] The aim of this study was to compare postoperative changes in body composition in patients undergoing laparoscopic-assisted gastrectomy, distal gastrectomy, or total gastrectomy.

PATIENTS AND METHODS

The nutritional status of 108 patients with gastric cancer (72 men, 36 women) was evaluated at the Nippon Medical School Hospital between January 2002 and September 2003. Twenty-four patients underwent laparoscopy-assisted gastrectomy (LAG), 39 patients underwent distal gastrectomy (DG), and 45 patients underwent total gastrectomy (TG). LAG was indicated for the resection of T1 (mucosa or submucosa) N0 tumors and included partial gastrectomies (n = 2), segmental gastrectomies (n = 8), and distal gastrectomies (n = 14). DG with gastroduodenal or gastrojejunal anastomosis was performed for cancers located in the distal or middle third regions of the stomach. TG was carried out for lesions larger than 3 cm in diameter located in the proximal or middle third of the stomach; Roux-en-Y antecolic reconstruction was performed using a 40 to 50 cm jejunal limb. The degree of lymph node dissection varied from D0 to D2 in the surgery for stage IA and IB tumors; D2 nodal dissection was used routinely for stage II or higher stages.[13,14]

Patients were managed postoperatively according to an established clinical pathway. This included provision of drinking water (500 ml/day) on the fourth postoperative day. Food ingestion progressed every 2 days in four steps from liquid meals to solids starting on the fifth postoperative day to achieve a targeted energy intake of 1450 kcal. Hospital discharge was routinely planned for the 14th postoperative day, although earlier discharge was permitted if more than 1000 kcal/day intake had been achieved.

Body protein mass, fat mass, and the ratio of extracellular water to total body water (edema index) were measured using a segmental multifrequency bioelectrical impedance analysis performed with an inBody II machine (Biospace, Tokyo, Japan), which was developed by Cha et al. to determine the physical fitness and body shape of healthy people.[8] Patients stood upright, stepping on the foot electrodes and loosely gripping the hand electrodes, with their arms held vertically. In this manner, the eight tactile electrodes were placed in contact with the thumb and palm of each hand and the front and rear soles of each foot. The microprocessor-controlled switches and impedance analyzer were started to measure the segmental resistances of the arms, trunk, and legs without accounting for fluid redistribution. Alternating currents with a magnitude of 100 μA and frequencies of 5 to 500 kHz were used. The height and weight of each patient was measured using electric scales. The body mass index (BMI) was calculated as body weight/height^2 (kg/m^2), and the degree of obesity was calculated as body weight/ideal body weight (%). All assessments were obtained preoperatively, on the 14th postoperative day (before hospital discharge), and at 6 to 12 months after surgery in the outpatient clinic.

All data are expressed as mean ± SD. Statistical analysis employed a paired Student's t test for each of the patients and one-factor ANOVA with a post hoc test for the operative procedures using StatView software (SAS Institute, Cary, NC). A P value of <0.05 was considered to be statistically significant.

RESULTS

The clinical characteristics of the patients in each of the three study groups were comparable, although the patients allocated to the LAG group were significantly older than those in the other groups (Table 1). Coexisting diseases were present in 30% of the patients. There was no in-hospital mortality and all patients were available for follow-up examination at 6 to 12 months. Postoperative complications occurred in seven cases (6.5%): two cases of pneumonia, two wound infections, two anastomotic strictures, and one heart failure. The length of hospital stay was longest in the TG group (19.9 ± 8.5 days); the LAG and DG groups hospital stays were 13.7 ± 1.9 and 16.7 ± 5.5 days, respectively. Distribution of cases by cancer stage is shown in Table 2. The LAG group consisted of patients with only stage IA or IB tumors.

The preoperative nutritional evaluations indicated that body size and degree of obesity were similar in all groups (Table 3). The mean preoperative body weight of all subjects was 57.6 ± 10.7 kg, the mean BMI was 22.5 ± 3.4 kg/m^2, and the mean fat % was 24% ± 7%. The mean degree of obesity was 109% ± 17 %.

Table 1. Clinical status

	LAG (n = 24)	DG (n = 39)	TG (n = 45)
Age (y)	72.0 ± 6.8*	64.3 ± 9.4	63.3 ± 12.3
Male (no.)	15	25	32
Length of hospital stay (days)	13.7 ± 1.9	16.7 ± 5.5	19.9 ± 8.5†
Coexisting disease			
DM	1	6	11
Ischemic heart disease	2	3	1
CHF	1	1	1
COPD	1	0	3
Comorbid disease			
Pneumonia		1	1
Wound infection			2
Anastomotic stricture	1		1
Heart failure			1

LAG = laparoscopy-assisted gastrectomy; DG = distal gastrectomy; TG = total gastrectomy; DM = diabetes mellitus; CHF = chronic heart failure; COPD = chronic obstructive pulmonary disease.
*P = 0.005 vs. DG; P = 0.001 vs. TG.
†P = 0.0003 vs. LAG; P = 0.025 vs. DG.

In the immediate postoperative period (14 days), body weight loss was significantly lower in the LAG group compared to the DG and TG groups (2.5 ± 0.9 kg vs. 3.5 ± 1.8 kg and 4.0 ± 1.9 kg, respectively; $P < 0.05$) (Fig. 2). Body composition analysis revealed a loss of body protein mass rather than fat mass in all groups. Body protein or fat loss did not differ among the groups, although the changes in fat loss ranged from 0.6 ± 1.0 kg in the LAG group to 1.5 ± 2.7 kg in the TG group. The mean BMI had decreased in all three groups on the 14th postoperative day (Table 4). The ratio of extracellular water to total body water (edema index) was similar in the LAG and DG groups, but was higher in the TG group on the 14th postoperative day (Table 5).

Table 2. Clinical stages of gastric cancers*

	LAG (n = 24)	DG (n = 39)	TG (n = 45)
IA	21	20	5
IB	3	8	6
II	0	3	9
IIIA	0	1	6
IIIB	0	3	11
IV	0	4	8

LAG = laparoscopy-assisted gastrectomy; DG = distal gastrectomy; TG = total gastrectomy.
*According to Japanese Classification of Gastric Carcinoma.[11]

Table 3. Preoperative nutritional assessment

	LAG (n = 24)	DG (n = 39)	TG (n = 45)
Body weight (kg)	54.4 ± 9.1	57.2 ± 11.3	59.6 ± 10.1
Degree of obesity (%)	106 ± 19	108 ± 16	112 ± 17
Body protein (kg)	38.6 ± 7.3	40.8 ± 8.0	42.6 ± 8.3
Fat (kg)	13.5 ± 5.2	13.9 ± 5.5	14.5 ± 5.8
BMI (kg/m^2)	21.8 ± 3.5	22.3 ± 3.2	23.2 ± 3.4

LAG = laparoscopy-assisted gastrectomy; DG = distal gastrectomy; TG = total gastrectomy; BMI = body mass index.

At 6 months after surgery, mean body weight had returned to its preoperative values in the LAG and DG groups (−1.2 ± 3.8 kg and −1.8 ± 4.7 kg, respectively) (Fig. 3), but had decreased by 8.9 ± 4.9 kg in the TG group ($P = 0.0003$). A body composition analysis revealed that the mean fat mass had decreased in the DG group (−1.5 ± 2.9 kg), but both the mean body protein and the mean fat mass had decreased in the TG group (−3.6 ± 1.8 kg and −5.2 ± 4.2 kg, respectively). The mean BMI was similar to the preoperative value in the LAG and DG groups, but had decreased in the TG group (Table 4). The ratio of extracellular water to total body water (edema index) 6 months after surgery was similar to the preoperative value in the LAG group, but had increased in the DG and TG groups (Table 5).

From the 14th postoperative day to 6 to 12 months after surgery, a gain in the mean body protein mass was observed in the LAG and DG groups (1.1 ± 1.1 kg and 1.3 ± 1.5 kg, respectively) (Fig. 4). In the TG group, no difference in the mean body protein mass was observed between those two time periods, but the

Table 4. Postoperative changes in body mass index

	LAG (n = 24)	DG (n = 39)	TG (n = 45)
14 d	−0.8 ± 0.7*	−1.0 ± 0.7*	−1.4 ± 1.0*
6 mo	−0.3 ± 1.4	−0.3 ± 1.8	−3.4 ± 2.4†

LAG = laparoscopy-assisted gastrectomy; DG = distal gastrectomy; TG = total gastrectomy.
*$P < 0.0001$.
†$P = 0.0072$.

mean body weight and mean fat mass had decreased (−4.1 ± 3.4 kg and −3.5 ± 3.2 kg, respectively). The edema index increased in the TG group only after the patients were discharged.

DISCUSSION

This study investigated changes in the body composition of patients undergoing laparoscopy-assisted gastrectomy, distal gastrectomy, or total gastrectomy. Body weight, body protein, and fat mass decreased during the immediate postoperative period. Laparoscopy-assisted gastrectomies resulted in a smaller loss of body weight and a shorter hospital stay compared with open surgeries. Laparoscopic procedures represent a less invasive approach for the treatment of gastric cancer, similar to laparoscopic cholecystectomies.[15,16] Many organs and cells of the body use glucose, not fat, as their primary fuel.[17] Although fat is the largest deposit of energy in the body, fat cannot be effectively converted to carbohydrates in mammalian tissues. Fat is composed of fatty acid, which is used as a substrate for the synthesis of ketone bodies as fuel in the liver, and glycerol, which can be used for gluconeogenesis. Body protein constitutes the next

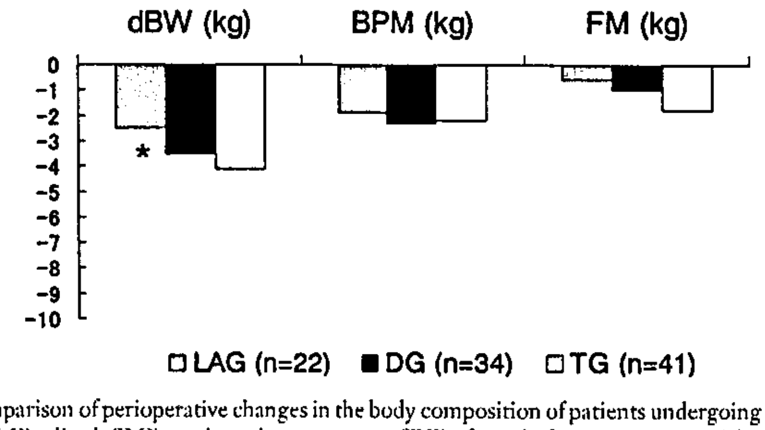

Fig. 2. Comparison of perioperative changes in the body composition of patients undergoing laparoscopy-assisted (LAG), distal (DG), and total gastrectomy (TG), from before surgery to 14th postoperative day. *$P = 0.039$ vs. DG and $P = 0.002$ vs. TG. dBW = change in body weight; BPM = body protein mass; FM = fat mass.

Table 5. Edema index

	LAG (n = 24)	DG (n = 39)	TG (n = 45)
Preoperative	0.341 ± 0.013	0.340 ± 0.016] *	0.336 ± 0.013] †] **
14 d postoperative	0.344 ± 0.011	0.342 ± 0.012	0.344 ± 0.014] ‡
6 mo postoperative	0.346 ± 0.015	0.343 ± 0.010]	0.355 ± 0.014] ‡]

LAG = laparoscopy-assisted gastrectomy; DG = distal gastrectomy; TG = total gastrectomy; edema index = extracellular fluid/total body water.
*P = 0.0006 vs. preoperative.
†P = 0.0001 vs. preoperative.
‡P = 0.0095 vs. 14 d postoperative.
**P = 0.0003 vs. preoperative.

largest mass of usable energy. Following surgery, proteolysis is accelerated to generate amino acids for the support of gluconeogenesis and other key synthetic processes. Therefore, endogenous protein must be broken down for conversion to glucose after surgery. This results in the simultaneous, rather than sequential, depletion of body protein and fat mass.[18]

In this study, the body weight loss that occurred during the immediate postoperative period consisted mainly of body protein loss rather than fat loss. The changes in body composition after surgery were characterized by a loss of body protein and fat mass and the expansion of the extracellular fluid compartment.[7] Although no differences in body protein or fat loss were seen among the three groups, the edema index of the TG group, but not that of the LAG or DG groups, increased during the early postoperative period. Within the confines of the multicomponent model, the body protein mass includes extracellular water as well as total body water. These findings suggest that the increase in interstitial water after a total gastrectomy may result in an underestimation of the decrease in the body protein mass during this altered state, compared with the results for patients who have undergone other surgical procedures. On the other hand, the serum albumin levels were similar among the groups before surgery and 6 months after surgery (mean value of 4.1 ± 0.5 and 4.3 ± 0.3 g/dl, respectively). Only in the immediate postoperative period were the levels of the TG group (3.6 ± 0.4 g/dl) lower than the levels of the LAG (4.0 ± 0.2 g/dl) and DG (3.9 ± 0.4 g/dl) groups.

The anabolic phase starts 3 to 6 days after an operation with a high level of insult, such as gastrectomy, and often coincides with the commencement of oral feeding.[7] In this study, the length of the hospital stay was longer in the TG group because adequate food intake was often delayed in this group. After the start of the anabolic phase, the patient enters a prolonged period of early anabolism, characterized by a positive nitrogen balance and weight gain. In the postoperative period, from the time of hospital discharge until 6 months after surgery, the patients in the LAG and DG groups regained their body protein mass, but no gain in body protein mass occurred in the TG group. The edema index of the TG group also increased, so the active body protein mass was likely diminished. Moreover, losses of body weight and fat mass were recorded in the TG group during

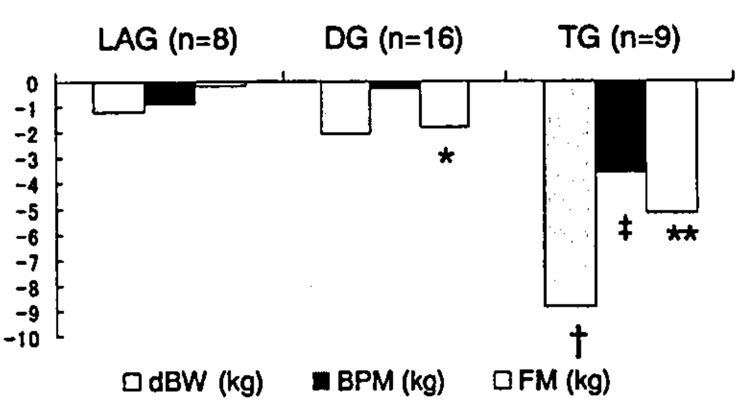

Fig. 3. Overall changes in the body composition of patients undergoing laparoscopy-assisted (LAG), distal (DG), and total gastrectomy (TG), from before surgery until 6 months after surgery. *P = 0.031, †P = 0.0003, ‡P = 0.0001, **P = 0.0038. dBW = change in body weight; BPM = body protein mass; FM = fat mass.

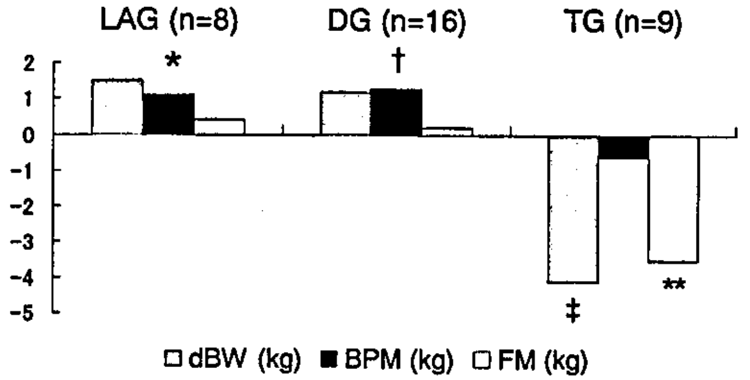

Fig. 4. Postoperative changes in body composition of patients undergoing laparoscopy-assisted (LAG), distal (DG), and total gastrectomy (TG), from the 14th postoperative day until 12 months after surgery. **P* = 0.020, †*P* = 0.0027, ‡*P* = 0.0036, ***P* = 0.0077. dBW = change in body weight; BPM = body protein mass; FM = fat mass.

this period, although protein synthesis may have been increased as a result of sustained oral feeding.

The overall changes in body composition from before surgery to 6 months after surgery showed that the body weight loss that occurred during the immediate postoperative period was recovered in the LAG and DG groups, although a loss of fat mass was recorded in the DG group. This finding may reflect the fact that patients undergoing partial and segmental gastrectomy (LAG group) had larger remnant stomach than patients who underwent a distal gastrectomy (DG group). In the TG group, overall losses of 15% body weight, 8% body protein, and 36% fat were recorded during this period. These results are consistent with the findings of previous studies in which weight loss (10% of preoperative weight) occurred early after total gastrectomy and body fat decreased by 40% during the first 6 months after gastrectomy.[19] In a long-term follow-up study, the weight loss consisted mainly of the depletion of body fat stores, whereas no significant decrease in lean body mass was observed.[10] Similar changes in body composition, including an increase in interstitial fluid (edema), were observed in the TG group during the postoperative period in the present study. Fat loss may be correlated with insufficient food intake after surgery.

Presumably, patients in the LAG and DG groups were able to regain their body protein mass during the postoperative period and return to their previous quality of life earlier after surgery.[20] The patients in the DG and TG group may have impaired nutritional intake, which seems to be associated with fat loss. Clearly, the small size of the residual gastric pouch and the absence of the stomach limit the amount of food consumed at one sitting. However, gastrectomy patients are expected to increase the frequency and caloric density of their meals postoperatively. In contrast, individuals who have undergone a Roux-en-Y gastric bypass typically eat fewer meals and voluntarily restrict their consumption of calorie-dense foods.[21,22] These alterations arise in part from a generalized loss of hunger that extends beyond postprandial satiety. One hypothesis explaining this phenomenon is that the procedure affects gut-derived factors involved in appetite regulation. Patients who have undergone a Roux-en-Y gastric bypass have markedly lower ghrelin levels and do not exhibit any of the meal-related oscillations observed in control subjects.[23] Future studies are required to define the clinical significance of ghrelin and develop nutritional interventions to prevent the depletion of body fat.

CONCLUSION

Patients who underwent a gastrectomy lost body protein during the perioperative period, and the resulting loss of body weight was significantly smaller in the LAG group than in the DG or TG groups. Six months after surgery, the body weight of the patients in the LAG and DG groups had recovered to the preoperative level, but a further decrease was observed in the TG group. The main postoperative change in body composition was a loss of fat mass in the DG and TG groups. Multifrequency bioelectrical impedance analyses can be used to assess body composition and may be useful for performing nutritional assessments in patients who have undergone a gastrectomy.

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クリニカルパス適用胃切除患者における Cefazolin (CEZ) と Sulbactam/Ampicillin (SBT/ABPC) の術後感染発症阻止効果並びに費用対効果の比較

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Comparison of the Effects of Prophylactic Antibiotic Therapy and Cost-effectiveness between Cefazolin (CEZ) and Sulbactam/Ampicillin (SBT/ABPC) in Gastric Cancer Surgery Employing Clinical Pathway

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The present study was designed to investigate the effects of prophylactic antibiotic therapy and the cost-effectiveness of Cefazolin (CEZ) and Sulbactam/Ampicillin (SBT/ABPC) in gastric cancer surgery employing clinical pathway. 157 patients (62 in the CEZ group and 95 in the SBT/ABPC group), who underwent surgery for gastric cancer at the First Department of Surgery of our hospital, were investigated. There was no significant difference between the groups with regard to sex, age, incidence of complication, stage of cancer, surgical method, operative time and blood loss, length of hospitalization, the appearance of systemic inflammatory response syndrome (SIRS), changes body tempreture, white blood cell count (WBC), C-reactive protein (CRP), or clinical outcome of postoperative care by a nurse during post-operation for 7 days. The prophylactic effect of infection was also no different between the CEZ (69.4%) and SBT/ABPC (69.5%) groups. In contrast, decision analysis strongly indicated that the anticipate cost of antibiotics was higher in the latter group (¥20402) than in the CEZ group (¥15556), suggesting that the prophylactic effect of CEZ may be more cost-effective. Thus, evaluations of pharmacotherapy from the aspect of cost may be one of the important responsibility of hospital pharmacists in the future.

Key words——clinical pathway; gastric cancer; prophylactic antibiotic therapy; cost-effective analysis; Cefazolin (CEZ); Sulbactam/Ampicillin (SBT/ABPC)

緒　　論

米国では 1983 年より Medicare の入院医療費の支払い方法として，医療費の診断群別定額支払い制度 (Diagnosis Related Group/Prospective Payment System; DRG/PPS) が導入されているが，わが国でも平成 15 年 4 月より診断群分類 (Diagnosis Procedure Combination; DPC) に基づく包括支払い制度が大学病院，国立がんセンター，国立循環器病センターなどの特定機能病院計 82 施設での入院医療において開始された．その結果，入院患者の在院期間の短縮と入院費用の削減並びに患者満足度の向上などを目的として，クリニカルパス (Clinical Pathway; CP) が日本の医療においてさらに注目されるようになった．日本医科大学付属病院（以下「当院」という）では 1998 年に「CP 研究会」が設立され，

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患者ケアを医療スタッフがチームとなって行うシステムの構築を検討してきた.[1] 薬剤部では，その中でも胃癌の切除術患者CPに積極的に携わり，同CPに薬剤管理指導業務を導入することによる有用性並びにその費用対効果についての検討を行い，数多くの知見を得ている.[2-5]

現在，手術方法や術後管理，術後感染発症阻止薬の投与方法の確立などにより術後感染の発症割合は以前と比較し急速に減少したが，完全に排除することはできず，約1–3割の胃切除患者に術後感染症が発症することが報告されている.[6,7] 術後感染症は入院期間の延長並びにそれに伴う医療費の増加につながるばかりか，場合によっては患者の生命を危険にさらすことにもなりかねない．そのため，感染予防の目的で投与される術後感染発症阻止薬の臨床評価を行うことは感染対策の一環として非常に重要な事項であると考える．事実，胃癌手術では術後感染発症阻止薬の選択により術後感染の発症率に差が生じることが報告されている.[7] しかしながら，胃癌の術後感染発症阻止薬を感染が発症した際の治療薬まで含めて薬剤経済学的な観点から臨床的に詳細に評価した報告はまだない．そこで本研究では，当院における胃切除患者CPで用いられているCefazolin (CEZ) とSulbactam/Ampicillin (SBT/ABPC) の術後感染発症阻止効果並びに費用対効果について検討し，知見を得たので報告する．

対象と方法

1. 対象　2002年1月から2003年9月までに当院第一外科において胃癌のため胃切除又は胃全摘術がCPを用いて施行された患者157名を対象とした．

2. 調査項目　当院第一外科では，胃癌の術後感染発症阻止薬は「CEZ 1 g 又はSBT/ABPC 1.5 gを加刀直後より投与し，手術時間が3時間を超える場合は追加投与する．手術終了後6時間以内に術後感染発症阻止薬を投与し，以後術後3日目（2003年8月に行われたCP改定後は術後2日目）まで1日2回CEZ 1 g 又はSBT/ABPC 1.5 gを追加投与する」というプロトコールに従い投与されている (Table 1)．まず，胃切除CPが施行された症例をCEZ投与群とSBT/ABPC投与群に分け，それぞれの群についてレトロスペクティブにカルテ調査を行い，性別，年齢，術前併存疾患（高血圧，糖尿病，虚血性心疾患，不整脈，脳血管障害，肝機能障害，腎機能障害）の有無，胃癌のstage，術式，手術時間及び術中出血量，入院日数，検出された細菌（培地の1/3以上の検出）並びに感染部位，治療抗菌薬の種類・投与日数並びに費用，全身性炎症反応症候群 (Systemic Inflammatory Response Syndrome; SIRS) 陽性症例数，全症例及び術後感染発症症例の体温・白血球 (White Blood Cell Count; WBC)・C反応性蛋白 (C-Reactive Prorein; CRP)

Table 1. Schedule of Clinical Pathway in Gastrectomy Patients

	Drugs	Dose	Use	Day ( ) −6	Day ( ) −5	Day ( ) −4	Day ( ) −3	Day ( ) −2	Day ( ) −1	Day ( ) OPE	Day ( ) 1	Day ( ) 2	Day ( ) 3	Day ( ) 4	Day ( ) 5	Day ( ) 6	Day ( ) 7	Day ( ) 8
1	Mageorol P		1×						1									
2	Parsennid (12)		1×						2T									
3	Rhythmy (2)		1×						1T									
4	Excelase	3C	3×														3C	3C
5	Magmitt (330)	3T	3×														3T	3T
1	Glycerin enema (120)									1	*							
2	Voltaren supposhitory ( )									*	*							
1	CEZ (1 g) or SBT/ABPC (1.5 g)									3V	2V	2V						
2	Vitamin B_1 (50)									1A	1A	1A	1A					
3	Vitamin B_2 (30)									1A	1A	1A	1A					
4	Vitamin B_6 (30)									1A	1A	1A	1A					
5	Vitamin C (500)									1A	1A	1A	1A					
6	KN3B (500)									2	2	2	2	2	2	2		
7	Physio 140 (500)									1								
8	Aminofluid (500)										2	2	2	2	2	2	2	2
9	Lepetan (0.2)		EPI							*	*							
10	Sosegon (15)		I.m							*	*							
11	Atarax-P (25)		I.m							*	*							

CEZ: Cefazolin, SBT/ABPC: Sulbactam/Ampicillin, *: Rescue.

の経時変化（術後1，3，7日後の値），看護到達目標達成度（1日目：重症看護チャートを用いた1—2時間毎のバイタルサインのチェック不要，3日目：看護師の補助による歩行可能，7日目：流動食摂取）の経時変化（術後1，3，7日後の値）のデータを収集・解析した．なお，CEZ及びSBT/ABPCは医師の判断により投与された．術後感染症については，CP担当医師と相談し，担当医が患者の臨床所見（肺炎，腹腔内感染等）及び検査値（体温・WBC・CRP等）から術後感染症の可能性ありと評価し，術後感染発症阻止薬を治療抗菌薬に変更した症例及び細菌培養結果が陽性であった症例を術後感染症ありとして評価した．また，CP患者の看護は，いずれの病棟の看護師も消化器外科手術の術後管理について十分な経験があるため，病棟間における看護技術の差はないとして評価した．抗菌薬の薬剤費は平成14年3月版の保険薬事典収載の薬価基準を用いた．なお，費用対効果分析は支払い者の立場で行った．

3. 費用対効果の算出　収集したデータに基づき判断樹（Decision tree）を作成した．先述したように，術後感染発症阻止効果は担当医が患者の臨床所見及び検査値から術後感染症の可能性ありと評価し，術後感染発症阻止薬を治療抗菌薬に変更した症例及び細菌培養結果が陽性であった症例を感染症ありとして評価したため，各群ともこれらの因子をモデルに組み入れた．術後感染発症阻止薬を治療抗菌薬に変更した確率を1回目の治療の確率，及び1回目の治療抗菌薬投与では感染症が改善せず，2回目以降の抗菌薬治療を行った確率を2回目以降の治療の確率とした．なお，治療抗菌薬は抗菌薬使用のガイドライン[12]に基づき投与された．

副作用・有害事象については，SBT/ABPC群で1例皮膚障害が認められたが，治療を行うことなく，投与中止により改善したことからモデルに組み入れなかった．それぞれの分岐点の確率は臨床試験成績等に基づいたものでなく，本研究データに基づいた確率とした．それぞれのシナリオの抗菌薬費用に発現確率を掛け合わせることで患者1人当たりの期待抗菌薬費用を算出し，その期待抗菌薬費用の合計金額を術後感染発症阻止率で割ることにより各術後感染発症阻止薬の費用対効果比を算出した．

4. 統計解析　年齢，手術時間，術中出血量，入院日数，術後患者体温，CRP，WBCの値は平均値±標準偏差（S.D.）で示し，両群の比較にはMann–WhitneyのU検定を用いた．なお，術後患者体温，CRP，WBCは各術後日の両群間を比較検討した．また，性別，術前併存疾患患者数，胃癌のstage及び術式の分散，SIRS陽性症例数，看護到達目標達成度の比較にはχ^2検定を用い，いずれも，$p<0.05$を有意性ありとして評価した．なお，統計解析ソフトはStat View-J 5.0 for Macintoshを用いた．

結　果

1. CEZとSBT/ABPCの術後感染発症阻止効果の比較　CEZ群の使用バイアル数（平均値±S.D.）は8.7±1.4，使用日数（平均値±S.D.）は3.9±0.7であった．また，SBT/ABPC群の使用バイアル数（平均値±S.D.）は8.8±1.1，使用日数（平均値±S.D.）は3.9±0.5であった．両群間で使用バイアル数，使用日数は有意な差を認めず，CPに基づいて術後感染発症阻止薬の投与が行われた．なお，その他の注射剤，内服剤もほぼCP通りに投与された．

CEZ投与群及びSBT/ABPC投与群の患者特性因子をTable 2に示す．CEZ投与群の症例数は62名（男/女＝38/24），平均年齢は64.4±11，術前併存疾患患者数は29名（46.8％），Stage Iが36名（58.1％），Stage II 6名（9.7％），Stage IIIA 7名（11.3％），Stage IIIB 4名（6.5％），Stage IV 6名（9.7％），GIST 3名（4.8％）であった．また，SBT/ABPC投与群の症例数は95名（男/女＝69/26），平均年齢は67.2±11，術前併存疾患患者数は57名（60.0％），Stage Iが34名（35.8％），Stage II 23名（24.2％），Stage IIIA 10名（10.5％），Stage IIIB 13名（13.7％），Stage IV 12名（12.6％），GIST 3名（3.2％）であった．これらすべてにおいて両群間に有意な差を認めなかった．

胃切除患者の臨床指標データをTable 3に示す．CEZ投与群では幽門側胃切除手術が30名（同時手術として胆摘出手術2名，胆肝切除手術1名を含む），腹腔鏡補助下胃部分切除手術3名（同時手術として胆摘手術1名を含む），胃全摘出手術22名（同時手術として胆摘出手術3名，脾摘出手術1名，膀卵巣摘出手術1名，脾摘出・肝部分切除手術

Table 2. Clinical Characteristics, Diagnosis and Stage of Gastric Cancer in Gastrectomy Patients

Surgical prophylaxis		CEZ	SBT/ABPC	P value
Number of patients		62	95	—
Sex (M/F)		38/24	69/26	0.1359
Age (mean±S.D.)		64.4±11	67.2±11	0.1202
Number of patients with complication*		29(46.8%)	57(60.0%)	0.3724
Gastric cancer stage	I	36(58.1%)	34(35.8%)	0.0542
	II	6(9.7%)	23(24.2%)	
	IIIA	7(11.3%)	10(10.5%)	
	IIIB	4(6.5%)	13(13.7%)	
	IV	6(9.7%)	12(12.6%)	
	GIST	3(4.8%)	3(3.2%)	

* Hypertension, diabetes mellitus, ischemic heart disease, cardiac arrhythmia, cerebrovascular accident, liver dysfunction, renal dysfunction.

Table 3. Operative Procedures, Time, Blood Loss and Length of Hospitalization of Gastrectomy Patients

Surgical prophylaxis		CEZ (n=62)	SBT/ABPC (n=95)	P value
Surgical method	Distal gastrectomy	30	45	0.0602
	+gallbladder extirpation	(2)	(3)	
	+gall and liver extirpation	(1)	—	
	+liver extirpation	—	(1)	
	Laparoscopy assisted distal gastrectomy	3	16	
	+gallbladder extirpation	(1)	(1)	
	Total gastrectomy	22	29	
	+gallbladder extirpation	(3)	(3)	
	+splenectomy	(1)	(2)	
	+ovariotomy	(1)	—	
	+splenectomy, liver extirpation	(1)	—	
	+splenectomy, pancreatectomy	—	(1)	
	+splenectomy, intestinal extirpation	—	(1)	
	+splenectomy, gall extirpation, esophagectomy	—	(1)	
	Pylorus gastrectomy	3	0	
	Partial gastrectomy	1	3	
	Others	3	2	
Operative intervention	Operative time (mean: hr±S.D.)	3.3±1.1	3.5±1.2	0.2523
	Blood loss (mean: ml±S.D.)	313.1±373.3	380.4±347.5	0.3524
LOS	Total LOS (mean: day±S.D.)	26.1±8.1	28.5±10.9	0.2637
	Preoperative LOS (mean: day±S.D.)	8.6±4.6	9.4±4.7	0.3897
	Postoperative LOS (mean: day±S.D.)	17.6±6.6	19.0±9.6	0.3081

LOS: Length of hospital stay.

1名を含む)，噴門部胃切除手術3名，胃部分切除手術1名，その他の手術3名であった．平均手術時間（hr）は3.3±1.1，平均術中出血量（ml）は313.1±373.3であった．全入院日数は26.1±8.1，術前入院日数は8.6±4.6，術後入院日数は17.6±6.6であった．また，SBT/ABPC投与群では幽門側胃切除手術が45名（同時手術として胆摘出手術3名，肝切除手術1名を含む)．腹腔鏡補助下胃部分切除手術16名（同時手術として胆摘出手術1名を含む)．胃全摘出手術29名（同時手術として胆摘出手術3名，脾摘出手術2名，脾摘出・膵摘出手術1名，脾摘出・腸切除手術1名，脾摘出・胆摘出・食道切除手術1名を含む)．胃部分切除手術3名，その他の手術2名であった．平均手術時間（hr）は

3.5±1.2，平均術中出血量（ml）は380.4±347.5であった．全入院日数は28.5±10.9，術前入院日数は9.4±4.7，術後入院日数は19.0±9.6であった．これらすべてにおいて両群間に有意な差を認めなかった．

CEZ投与群及びSBT/ABPC投与群での術後感染発症症例の感染部位，検出細菌治療抗菌薬の種類，投与日数及び投与費用をそれぞれTable 4及びTable 5に示す．CEZ投与群での術後感染発症症例数は19名，分離された細菌は27種，SBT/ABPC投与群での術後感染発症症例数は29名，分離された細菌は41種であった．その結果，CEZの術後感染発症阻止率は69.4%（43/62），SBT/ABPCは69.5%（66/95）であり，両群間で有意な差を認め

Table 4. The Cases of Postoperative Infection in Gastrectomy Patients Pretreated with Cefazolin (CEZ)

CEZ	Infecting region	Infecting agent	Antibiotics	Using period	Drug cost (Yen)
1	Drain	Staphylococcus			
2	Drain	Staphylococcus			
3		Fungus			
4	Drain	Staphylococcus	PAPM/BP 0.5 g×1/day	1	18189
			PAPM/BP 0.5 g×2/day	4	
5	Gauze in wound	Acinetobacter	FMOX 1 g×2/day	2	7616
	Drain	Enterococcus			
		Staphylococcus			
		Bacillus			
6			MEPM 0.5 g×2/day	9	35460
7			IPM/CS 0.5 g×1/day	1	31755
			IPM/CS 0.5 g×2/day	7	
8	Arterial blood	Staphylococcus	MEPM 1 g×2/day	2	437185
	Drain	MRSA	MEPM 0.5 g×2/day	2	
	Gauze in wound	Enterococcus	FOM 1 g×1/day	1	
	Sputum	Candida	FOM 1 g×2/day	20	
			ABK 200 mg×1/day	1	
			ABK 400 mg×1/day	2	
			CPFX 300 mg×2/day	1	
9	Drain	Enterococcus	PAPM/BP 0.5 g×2/day	16	64672
	Gastric juice	Klebsiella			
	Purulence	Serratia			
	C-tube	Pseudomonas			
		Escherichia			
10			CTRX 1 g×2/day	3	6930
11	Bile	Aeromonas hydrophila group	FMOX 1 g×2/day	3	11424
12	Drain	Enterococcus	CTRX 1 g×2/day	4	9240
13	Drain	Staphylococcus			
14	Drain	Staphylococcus			
15	Arterial blood	Staphylococcus	FMOX 1 g×2/day	3	28896
			SBT/CPZ 1 g×2/day	6	
16	Drain	Staphylococcus	PIPC 1 g×2/day	1	6898
			CMZ 1 g×2/day	4	
17	Drain	Staphylococcus	CFPN-PI (100 mg)3 T/day	2	6898
18	Gauze in wound	Enterococcus	CMZ 1 g×2/day	6	8676
		MRSA			
19	Secretion of urinary system	Streptococcus			

CEZ: Cefazolin sodium hydrate, PAPM/BP: Panipenem/Betamipron, FMOX: Flomoxef sodium, MEPM: Meropenem trihydrate, IPM/CS: Imipenem/Cilastatin sodium, FOM: Fosfomycin, ABK: Arbekacin sulfate, CPFX: Ciprofloxacin, CTRX: Ceftriaxone sodium, SBT/CPZ: Sulbactam/Cefoperazon sodium, PIPC: Piperacillin sodium, CMZ: Cefmetazole sodium, CFPN-PI: Cefcapene Pivoxil hydrochloride.

Table 5. The Cases of Postoperative Infection in Gastrectomy Patients Pretreated with Sulbactam/Ampicillin (SBT/ABPC)

SBT/ABPC	Infecting region	Infecting agent	Antibiotics	Using period	Drug cost (Yen)
1			IPM/CS 0.5 g×1/day IPM/CS 0.5 g×2/day	1 6	27521
2	Drain	Staphylococcus			
3	Drain	Enterococcus Staphylococcus	IPM/CS 0.5 g×2/day	17	71978
4			IPM/CS 0.5 g×2/day	7	29638
5	Purulence	Candida	PAPM/BP 0.5 g×2/day	4	16168
6			PAPM/BP 0.5 g×3/day	5	94037
7	Drain	Klebsiella Stenotrophomonas	IPM/CS 0.5 g×3/day IPM/CS 0.5 g×2/day MINO 100 mg×2/day	8 1 7	
8	Sputum	Staphylococcus			
9	Sputum	Klebsiella Candida			
10	Arterial blood Catheter tip	Enterobacter Serratia	SBT/CPZ 1 g×2/day	4	11648
11	Arterial blood Catheter tip	Acinetobacter	FMOX 1 g×2/day	3	11424
12	Sputum Urine	Klebsiella Pseudomonas aeruginosa	FMOX 1 g×1/day FMOX 1 g×2/day CFPN-PI (100 mg) 3 T/day CLDM 600 mg×2/day PIPC 1 g×2/day PAPM/BP 0.5 g×2/day	1 3 7 3 4 4	40264
13	Drain Bile	Staphylococcus Staphylococcus Enterobacter	PAPM/BP 0.5 g×2/day SBT/CPZ 1 g×2/day	7 4	39942
14	Drain	Staphylococcus Enterococcus Candida Micrococcus	FMOX 1 g×2/day CTRX 0.5 g×2/day	8 6	44324
15	Drain Bowel movement Catheter tip Purulence	Serratia Candida MRSA Staphylococcus Streptococcus milleri group	FMOX 1 g×2/day MEPM 0.5 g×2/day CZOP 1 g×2/day	8 2 3	49894
16	Drain	Staphylococcus			
17			PAPM/BP 0.5 g×2/day	4	16168
18	Sputum	Klebsiella Candida Enterobacter Stenotrophomonas Pseudomonas			
19	Sputum	Escherichia Candida	ABK 200 mg×1/day	4	48808
20			FMOX 1 g×2/day	4	15232
21			IPM/CS 0.5 g×2/day	4	16936
22			IPM/CS 0.5 g×3/day	4	25404
23	Arterial blood	Klebsiella	FLCZ 100 mg×1/day CPFX 300 mg×2/day IPM/CS 0.5 g×2/day	6 4 4	81400
24	Sputum	Klebsiella	IPM/CS 0.5 g×1/day IPM/CS 0.5 g×2/day PIPC 1 g×2/day	1 6 4	31977
25			IPM/CS 0.5 g×1/day IPM/CS 0.5 g×2/day FMOX 1 g×2/day	1 3 4	30051
26			IPM/CS 0.5 g×2/day	4	16936
27	Gauze in wound	MRSA Bacillus			
28			MEPM 0.5 g×2/day	4	7700
29	Sputum	Pseudomonas aeruginosa Serratia Candida	IPM/CS 0.5 g×2/day	12	50808

SBT/ABPC: Sulbactam/Ampicilin sodium, IPM/CS: Imipenem/Cilastatin sodium, PAPM/BP: Panipenem/Betamipron, ABK: Arbekacin sulfate, MINO: Minocycline hydrochloride, FMOX: Flomoxef sodium, FLCZ: Fluconazole, ABK: Arbekacin sulfate, MEPM: Meropenem trihydrate, CFPN-PI: Cefcapene Pivoxil hydrochloride, CLDM: Clindamycin phosphate, CTRX: Ceftriaxone sodium, CZOP: Cefozopran hydrochloride.

なかった．CEZ 投与群のグラム陽性菌発現率は 70.4% (19/27)，グラム陰性菌発現率は 22.2% (19/27)，真菌発現率は 7.2% (2/27) であった．一方，SBT/ABPC 投与群のグラム陽性菌発現率は 41.5% (17/41)，グラム陰性菌発現率も 41.5% (17/41)，真菌発現率は 17.1% (7/41) であり，有意な差は認められなかったが，CEZ 投与群の方が SBT/ABPC 投与群と比較してグラム陽性菌発現率が高く，逆にグラム陰性菌発現率は SBT/ABPC 投与群の方が高い傾向が認められた．術後感染症の中で特に臨床的に問題となっているメチシリン耐性黄色ブドウ球菌 (Methicillin－Resistant Staphylococcus Aureus; MRSA) 及び緑膿菌による術後感染症発症率を Table 6 に示す．CEZ 投与群での MRSA 発現率は 7.4% (2/27)，SBT/ABPC 投与群は 4.9% (2/41) であった．また，CEZ 投与群での緑膿菌発現症例数は 0% (0/27)，SBT/ABPC 投与群では 4.9% (2/41) であり，有意差は認められないものの，CEZ 投与群の方が MRSA 発現率が高く，逆に緑膿菌発現率は SBT/ABPC 投与群の方が高い傾向が認められた．

術後 24 時間後の SIRS 陽性症例数を Table 7 に示す．CEZ 投与群での陽性症例数は 7 名 (11.1%)，SBT/ABPC 投与群では 17 名 (17.9%) であった．なお，発現頻度は両群間で有意な差を認めなかった．

CEZ 投与群及び SBT/ABPC 投与群での術後体温，CRP 値及び白血球数の経時変化（全症例及び術後感染発症例）を Fig. 1 に示す．いずれの値も有意な差を認めなかった．なお，看護到達目標達成率も両群間で有意な差を示さなかった．

2. CEZ と SBT/ABPC の費用対効果の比較

CEZ 投与群と SBT/ABPC 投与群の判断分析モデルを Fig. 2 に示す．CEZ 群と SBT/ABPC 群の 1 回目の治療抗菌薬の平均費用はそれぞれ 17535 円及び 25825 円，2 回目以降の治療抗菌薬の平均費用はそれぞれ 144303 円及び 23516 円であった．このモデルを基にして算出された患者 1 人当たりの期待抗菌薬費用の合計及び費用対効果比（患者 1 人当たりの期待抗菌薬費用の合計/術後感染発症阻止率）を Table 8 に示す．患者 1 人当たりの期待抗菌薬費用の合計は CEZ 投与群で 15556 円，SBT/ABPC 投与群で 20402 円であった．また，費用対効果比は CEZ 投与群で 22565，SBT/ABPC 投与群で 29355 であった．

Table 6. The Number of MRSA and *Pseudomonus aeruginosa* Isolated from Postoperative Patients of Gastric Cancer

	CEZ	SBT/ABPC
Occurrence rate of MRSA	7.4% (2/27)	4.9% (2/41)
Occurrence rate of Pseudomonas aeruginosa	0% (0/27)	4.9% (2/41)

Occurrence rate = (number of occurrence case) / (number of occurrence case in total isolated bacilli).

Table 7. The Number of Systemic Inflammatory Response Syndrome (SIRS) Positive Patient in Gastric Cancer

	CEZ (n=62)	SBT/ABPC (n=95)	P value
Number of patients with SIRS positive	7 (11.1%)	17 (17.9%)	0.3321

Table 8. Cost/Effective Analysis of Cefazolin (CEZ) and Sulbactam/Ampicillin (SBT/ABPC) in the Prophylactic Antibiotic Therapy after Gastric Cancer Surgery

Prophylactic drugs	CEZ (n=62)	SBT (n=95)
% of prophylactic effect	69.4% (43/62)	69.5% (66/95)
Total anticipated therapeutic cost/patient (Yen)	15556	20402
Cost-effectiveness	22565	29355

考　察

上部消化管手術時には一般的にグラム陽性菌を考慮した術後感染発症阻止薬の選択がなされる．当院における胃切除術 CP でも，術後感染発症阻止薬として第 1 世代セフェム系である Cefazolin (CEZ) 又はペニシリン系の合剤である Sulbactam/Ampicillin (SBT/ABPC) を使用することが規定されている．[2-5] SBT/ABPC は 1 バイアル当たりの薬価は CEZ と比較し高価であるが (SBT/ABPC：1385 円，CEZ：559 円)，*in vitro* の試験において CEZ よりグラム陽性菌，特に MRSA に対する抗菌活性が強いことが報告されている．[8,9] 本研究では CEZ と SBT/ABPC は無作為に投与されているが，この抗菌活性の差が症例数に差が生じた原因かもしれない．しかし，これら 2 剤を感染が発症した際の治療薬まで含めて薬剤経済学的な観点から詳細に評価した報告はまだない．そこで本研究では CEZ と SBT/ABPC の術後感染発症阻止効果並びに費用対効果について比較検討を行った．

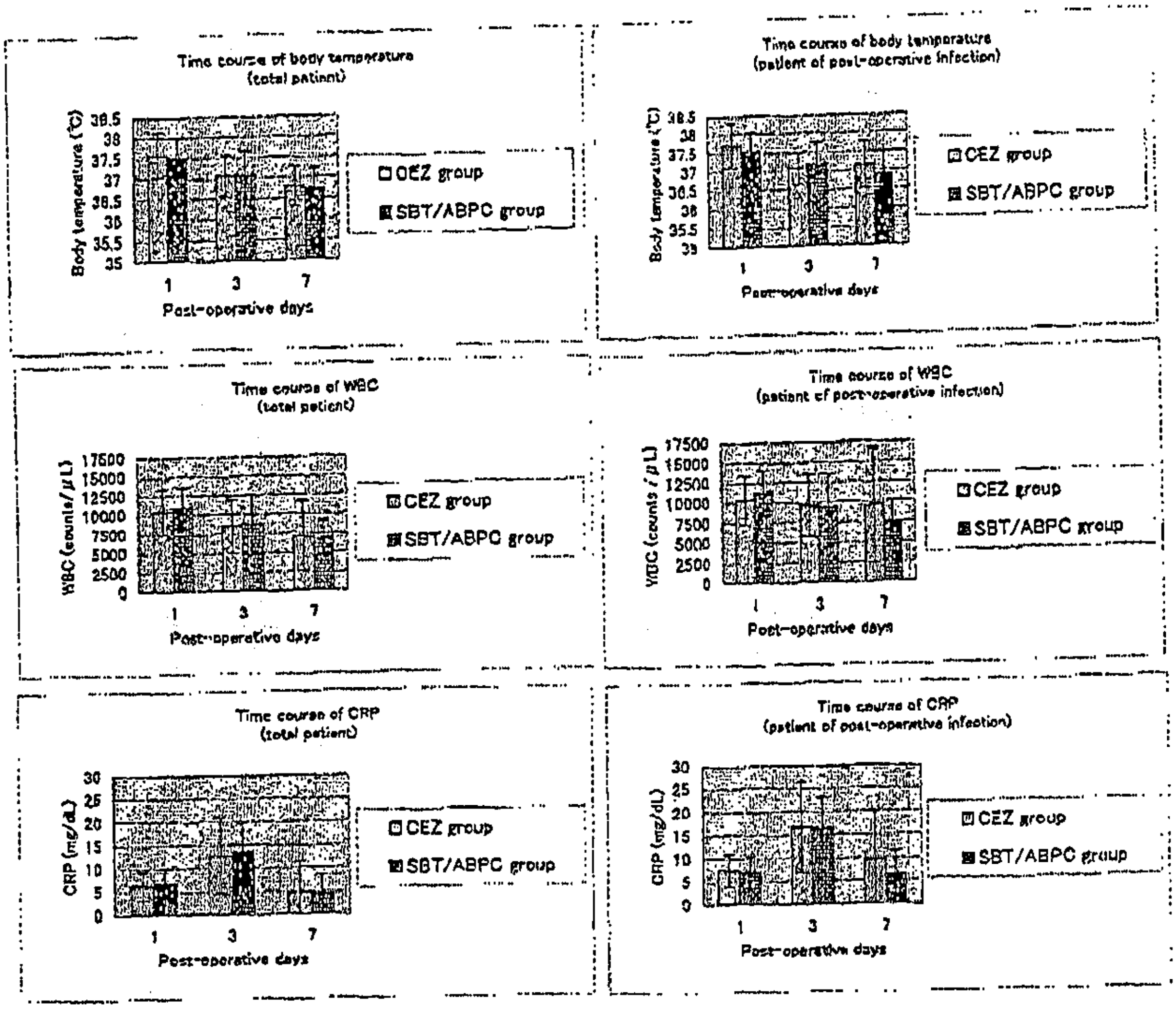

Fig. 1. Time Course of Body Temperature, White Blood Cell Count (WBC) and C-Reactive Protein (CRP) in Postoperative Patients of Gastric Cancer

性別，年齢，術前併存疾患患者数，胃癌のstage，手術時間，術中出血量，入院日数，SIRS陽性患者数，術後体温・CRP・白血球の経時変化は両群間で有意な差を認めなかった．術式において腹腔鏡補助下胃部分切除手術数は両群間で差が認められたが，全体の分布には差がなく，術後感染リスクに影響するとされる手術侵襲（手術時間及び術中出血量の増加）[10]においても両群間で差が認められなかった．また，データとして示さなかったが，術後感染発症例の手術侵襲（術中出血量及び手術時間）も両群間で有意な差を認めなかった．したがって，今回生じた術後感染の差は，2つの術後感染発症阻止薬の効果の差として妥当であると考える．また，術後感染を発症した症例の術後体温・CRP・白血球の経時変化も両群間で有意な差を認めなかったことから，少なくともこれらの値を指標とした感染の重症度はCEZ群とSBT/ABPC群とで差はなかったと考える．また，術後感染を発症した場合，入院日数が有意に延長することが報告されているが，両群間において術後感染症発症例の術後入院日数は有意な差を認めなかったことから（CEZ群：21.1±9.4，SBT/ABPC：24.2±15.4）本分析では術後入院日数について考慮しなかった．

術後感染発症阻止率を比較すると，両群間において有意な差を認めなかった．分離された菌株を比較すると，CEZ投与群の方がSBT/ABPC投与群と比較してグラム陽性菌の検出率が高く，逆にグラム陰性菌はSBT/ABPC投与群の方が検出率が高い傾向が認められた．MRSA検出率もCEZ投与群の方が高く，逆に緑膿菌はSBT/ABPC投与群の方が高い傾向が認められた．先述したように，*in vitro*の試験においてSBT/ABPCはCEZよりMRSAを含

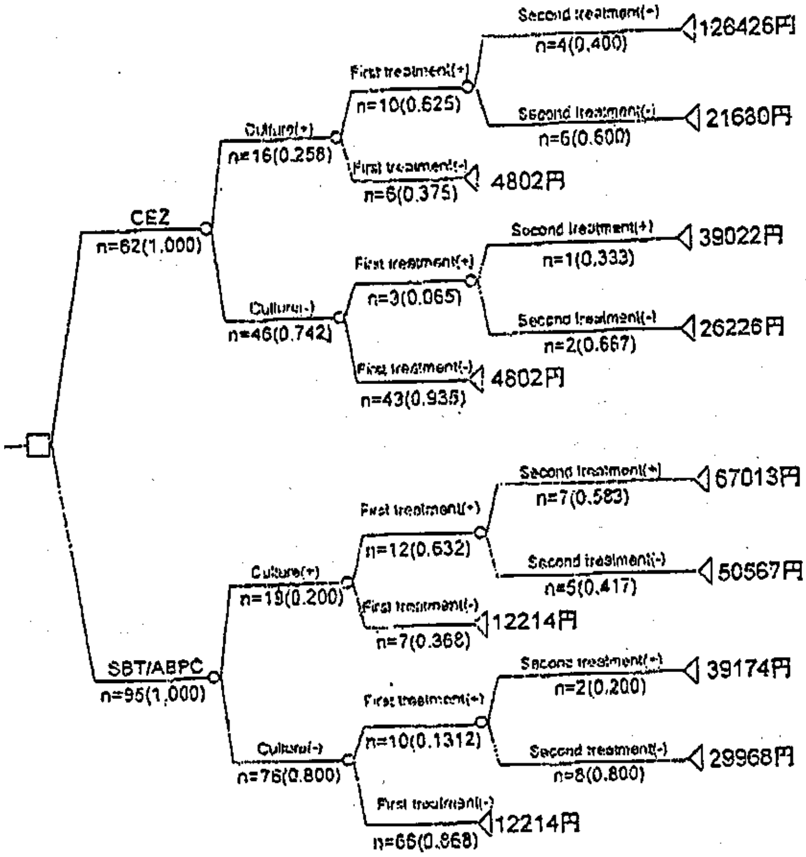

Fig. 2. Decision Analysis Model of Antibiotic Therapy of Postoperative Infection in Gastrectomy Patients

めたグラム陽性菌に強い抗菌活性を示すことが報告されている.[8,9] 逆に *Klebsiella* 株などのグラム陰性菌に関しては CEZ の方が SBT/ABPC と比較して高い抗菌活性を示すことが報告されており,[10] この抗菌活性の差が今回の実験結果に反映している可能性が考えられる. また, 今回の細菌検査は術後感染発症阻止薬の投与終了までに施行されているため, 本研究における細菌検出率に感染治療薬の投与は影響していないものと考えられる.

CEZ 投与群と SBT/ABPC 投与群の患者1人当たりの期待抗菌薬の合計を比較すると, CEZ 投与群が 15556 円, SBT/ABPC 投与群が 20402 円であり, SBT/ABPC 投与群の方が高コストであった. また, 費用対効果比は CEZ 投与群では 22545, SBT/ABPC 投与群では 29355 であり, 術後に CEZ を投与した方が抗菌薬費用対効果はよいことが示唆された. しかしながら, 細菌培養が陽性であり, 2回目以降の治療が行われたシナリオにおいて, SBT/ABPC 投与群は約 67013 円であったが, CEZ 投与群が約 126426 円と倍近く抗菌薬費用がかかっていることを考えると, 感染症が特に重篤となると予想される症例には術後感染発症阻止薬として SBT/ABPC を投与した方がよい可能性が考えられる. われわれは, 胃癌術後感染症の発症には加齢, 手術時間, 術中出血量の増加及び性別（男性の方が発症割合が高い）が重要な役割を果たしていることを報告しており（医療薬学投稿中）, このような因子を多く有する（又は有すると予測される）患者には SBT/ABPC 使用の判断を十分に検討する必要があると考える. また, 治療抗菌薬は医師の裁量により投与されたものでなく, 抗菌薬使用のガイドライン[12]に従ったものであるため, 感染の治療効果に医師の裁量の差は影響していないものと考える.

なお, 本分析を行うに当たり抗菌薬以外の治療費（治療に費やした輸液等の薬剤費）や感染症が生じた場合の入院日数の影響を含める必要があると考えられるが, 両群ともに Table 1 に示す薬物療法スケジュールにほぼ従っており, たとえ感染症を起こしていても両群で異なるのはほとんど抗菌薬費用のみだったこと, 本研究を行うに際しては患者のレセプ

トを閲覧することができなかったことから，本研究では抗菌薬費用のみの分析とした．しかし，今後はこれら抗菌薬以外の影響も含めて分析をしなければいけないと考える．また，今回の分析は当院一病院のデータであり，この研究結果を他の病院に適応することは難しいかもしれない．しかし，このような研究は病院の薬剤師が自ら実践できるものであり，院内の感染予防対策や CP における抗菌薬の選択に用いられるならば，それなりの説得力があると考える．このような費用対効果分析を行う際，海外のメタアナリシスや添付文書等のデータを用いて分析を行った方が研究の信頼性，妥当性は得られると考えたが，このようにして当院以外のデータを用いて解析を行っても，当院医師の信頼は全く得られず，説得力がない．そのため本研究は当院のデータを用いて術後感染発症阻止効果並びに費用対効果の検討を行った．

近年，医療費の高騰が大きな社会問題として認識されており，医療従事者は患者に対して最良の医療を限られたコスト内で提供することが求められてきている．この課題を同時に評価するために，費用対効果分析は非常に有用なツールになると思われる．アメリカでは，治療法を代替する際の薬剤選択に，また，類似医薬品の中から採用医薬品を決定する際にこの手法が用いられている．さらに，実際に薬剤師が現場での薬物療法を薬剤経済学的に評価し，医療スタッフに情報を提供することで，薬剤師の医療チーム内での信頼度の向上につながり，その結果として患者の Quality of Life（QOL）が向上すると思われる．また，DPC が導入されている現在，臨床における費用対効果分析は病院経営的な側面からみても非常に有用であると考えられる．このように薬物療法を薬剤経済学的に評価することは，今後病院薬剤師の重要な業務の1つになると思われる．[13]

以上の結果より，胃切除 CP 患者における術後感染発症阻止薬の選択に当たっては費用対効果のより高い CEZ を投与する方が適切である可能性が示唆された．しかしながら，術後感染症が重篤化する可能性の高い症例には SBT/ABPC 使用の判断を十分に検討する必要があると考える．

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