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Prediction for the Development of Postoperative Infections in the Operation of Esophageal Cancer Compared with Gastric Surgery

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ABSTRACT

The purpose of this study was to assess the point at which the postoperative infection has occurred in order to decide upon the proper duration of prophylactic antibiotic use. Another goal of this study was to determine whether prediction for the development of postoperative infections in major surgery such as esophagectomy should be the same as that in routine gastroenterological surgery. Twenty-five patients who underwent transthoracic esophagectomy and 127 patients who underwent gastrectomy were studied.

On the third day after gastric surgery, the body temperature of patients who developed an infection was higher than that of the patients who did not develop an infection. The relative changes in peripheral white blood count (WBC), and C-reactive protein (CRP) concentration on the third and fourth days were more predictive of the development of infection than the absolute values. Almost all patients with systemic inflammatory response syndrome (SIRS) on the third day after gastric surgery developed an infection. On the other hand, the incidence of SIRS in patients who did not develop an infection was high on both the third and fourth days after esophageal surgery. It was nearly impossible to predict who would develop an infection in esophageal surgery. The high incidence of postoperative infections, and their significant consequences justify planned successive postoperative antibiotic use in esophageal surgery.

Key words: *Prophylactic antibiotics, Systemic inflammatory response syndrome, Esophageal surgery, Postoperative infection*

One day antibiotic prophylaxis is now commonly employed in North America[1,3,7]. In Japan, however, it was recommended that the preventive administration of the agents be kept for 3 or 4 consecutive days, and, on the sign of infection, that the agents be switched therapeutic remedies[10]. In order to determine whether prophylactic antibiotics can be discontinued or changed to therapeutic antibiotics, the assessment of postoperative infection should be made at that time. The purpose of this study was to determine appropriate assessment of the occurrence of infection on the third or fourth postoperative day.

The concept of the systemic inflammatory response syndrome (SIRS) has been recently introduced[2]. SIRS represents the final common endpoint to overwhelming, persistent infection, massive tissue injury, prolonged tissue oxygen debt, and other insults precipitating global inflammation. In esophageal cancer, the operation itself may cause SIRS for several days[6,8]. Therefore, it is difficult to distinguish SIRS induced by an infection from SIRS induced by surgical insult. Another goal of this study was to determine whether the prediction for development of postoperative infections in major surgery, such as esophagectomy, was the same as in routine gastroenterological surgery.

MATERIALS AND METHODS

Twenty-five patients who underwent transthoracic esophagectomy for esophageal cancer and 127 patients who underwent gastrectomy for gastric cancer between 1991 and 1995, were studied. Cefazoline was administered at a daily dose of 3.0g for prophylaxis until postoperative day 3 in gastric surgery. Cefazoline or cefotiam were administered at a daily dose of 3.0g until postoper-

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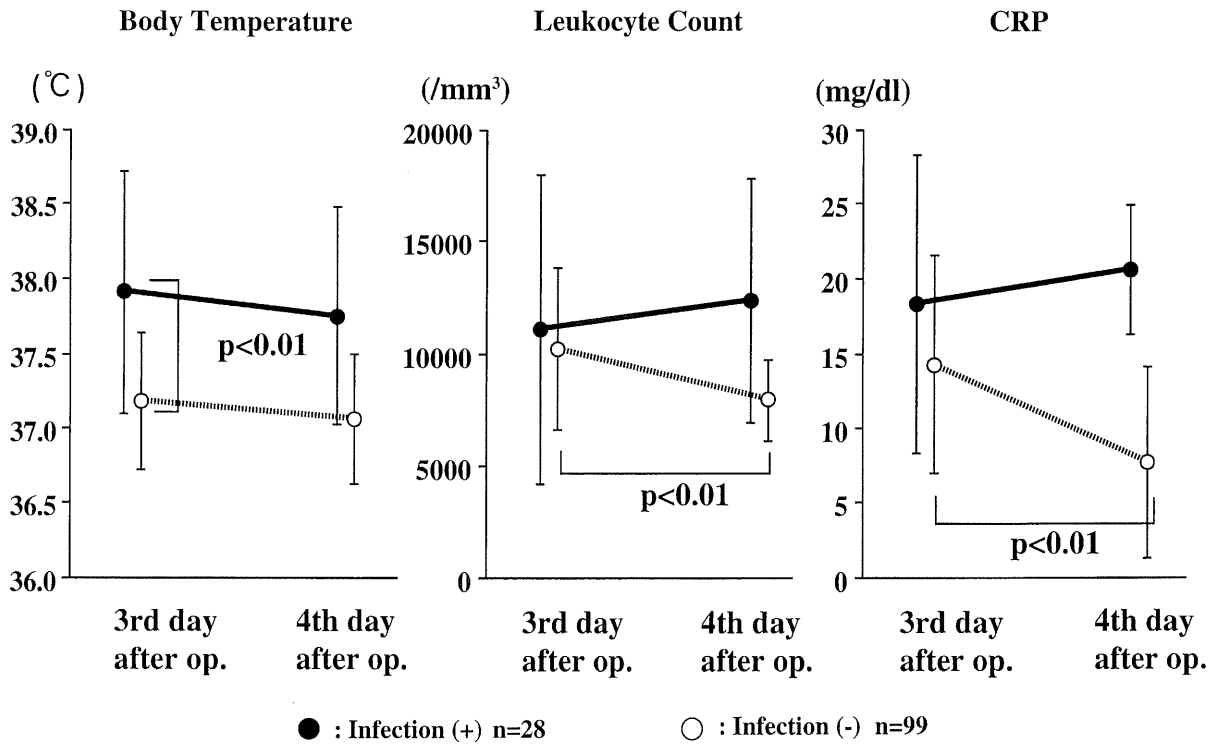

Fig. 1. Changes in inflammatory parameters after gastric surgery.
CRP: C-reactive protein concentration, op: operation

ative day 3 of esophageal surgery. Body temperature, peripheral white blood count (WBC), and C-reactive protein (CRP) concentration were measured on the third and fourth days after the surgery. These inflammatory signs were compared in patients with and without postoperative infections in both surgery groups.

SIRS was defined as the presence of two or more of the following: temperature greater than 38°C or less than 36°C; heart rate over 90 beats per minute; tachypnea (>20 respirations per minute, or Carbon dioxide tension (P_{CO_2}) <32 mm Hg); white blood cell count greater than 12 000/mm³ or less than 4000/mm³; more than 10% bands on the peripheral smear. The incidence of SIRS on the third and fourth days after operation was compared between the patients with and without infections in both surgery groups.

Statistical Analysis: a statistical analysis was performed using the Student *t*-test and chi-square. A $p<0.05$ was considered statistically significant. Documented infection was defined as the identification of positive bacterial cultures from normally sterile body fluids and clinical signs of infection.

RESULTS

There was no significant difference in patients with and without infections with respect to age, or underlying disease in either surgery groups. After esophageal surgery, 12 of 25 patients (48.0%) developed an infection within 10 days. After gastric surgery, 28 of 127 patients (22.7%) developed an infection within 10 days. The incidence of surgical site infections (wound infection, intraperitoneal infection, and anastomotic dehiscence) was 44.0% in the esophageal surgery (E) group and 13.4% in the gastric surgery (G) group. The incidence of infections not directly related to the surgical procedure (pulmonary infection, urinary tract infection, catheter sepsis, and enteritis) was 12.0% in the E group and 8.7% in the G group.

In the G group, the body temperature on the third postoperative day in the patients who developed an infection was higher than that in patients without an infection (37.91±0.81°C vs. 37.18±0.46°C, respectively) ($p<0.01$). There were no differences between the infected and non-infected groups with respect to WBC or CRP concentration on the third day. In the non-infected group, the WBC and CRP concentrations on the fourth day were significantly lower than those on the third day (WBC: 7916±1824/mm³ vs. 10224±3608/mm³; CRP: 7.69±6.40mg/dl vs. 14.25±7.30 mg/dl) ($p<0.01$). There were no significant changes in the WBC and CRP concentrations between the third and the fourth days in the infection group (Fig. 1). There was a significant difference in the infection rate between the patients in whom the body temperature on the third postoperative day ranged from 37.7°C to 38.2°C, and those in whom the temperature ranged from 37.1°C to 37.6°C (41.2% vs. 12.2%, respectively) ($p<0.01$) (Fig. 2).

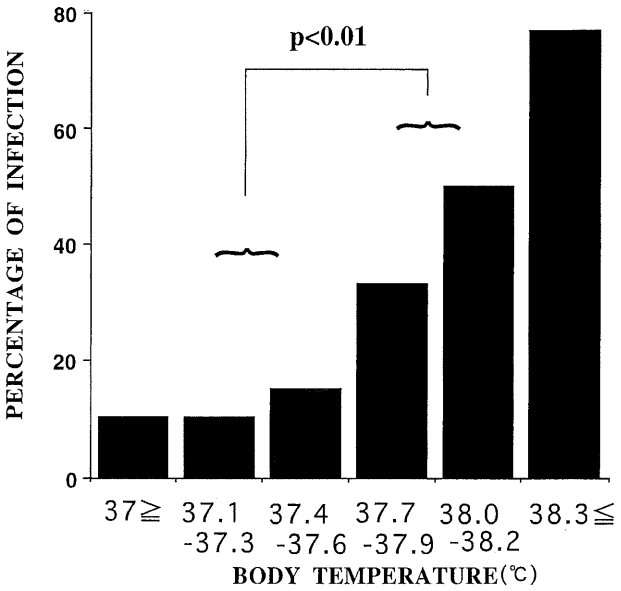

Fig. 2. Relationship between postoperative infection rate and body temperature on the 3rd day after operation.

In the E group, there were no significant differences in the body temperatures or CRP concentrations in the infected and non-infected groups on either the third or fourth day. Although there were no statistically significant differences, the peripheral WBC in the infected group was lower than in the non-infected group (8309±2718 /mm^3 vs. 11657±6882/mm^3 on the third day, and 7544±2199/mm^3 vs. 9900±4399/mm^3 on the fourth day, respectively) (Fig. 3).

The incidence of SIRS was higher in the E group than in the G group (72.0% vs. 21.3% on the third day, and 64.0% vs. 9.4% on the fourth day, respectively) ($p<0.01$) (Fig. 4). There was no significant difference in the incidence of SIRS in the infected and non-infected groups on the third day after esophageal surgery (69.2% vs. 75.0%). On the fourth day after esophageal surgery, the incidence of SIRS was higher in the infected group (84.6% vs. 41.7%) ($p<0.05$) (Fig. 5).

DISCUSSION

In Japan, 3-day prophylaxis for clean-contaminated surgical procedures is widely accepted[9,10]. Therefore, it is important to assess the development of infections on the 3rd-4th postoperative days, in order to administer therapeutic antibiotics. On the third postoperative day after gastric surgery, the body temperature of the patients who developed infection was higher than that of patients without infection. The patients with a temperature greater than 37.6°C on the third day tended to develop an infection. WBC and CRP concentrations on the third day were not useful in predicting which patients would develop a postoperative infection.

In the patients who did not develop an infection after gastric surgery, the WBC and CRP concentrations on the fourth day were lower than those on the third day. There were no significant changes between the third and the fourth postop-

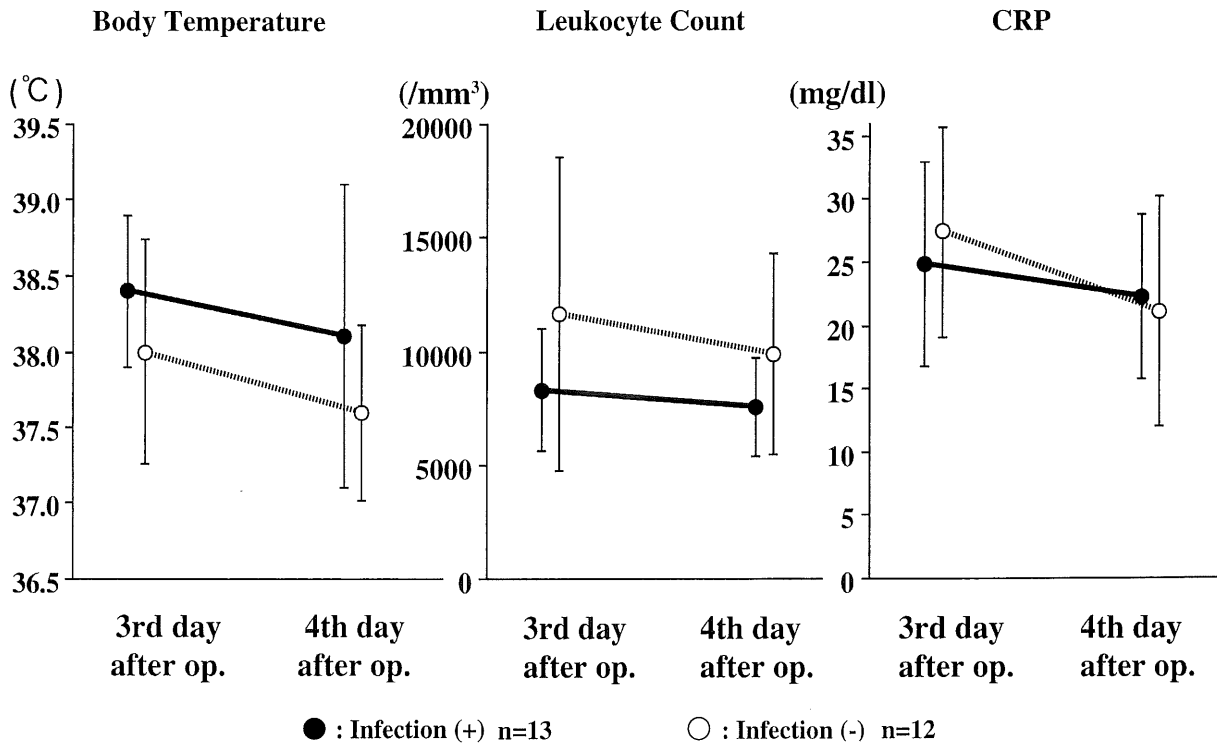

Fig. 3. Changes in inflammatory parameters after esophageal surgery.
CRP: C-reactive protein concentration, op: operation

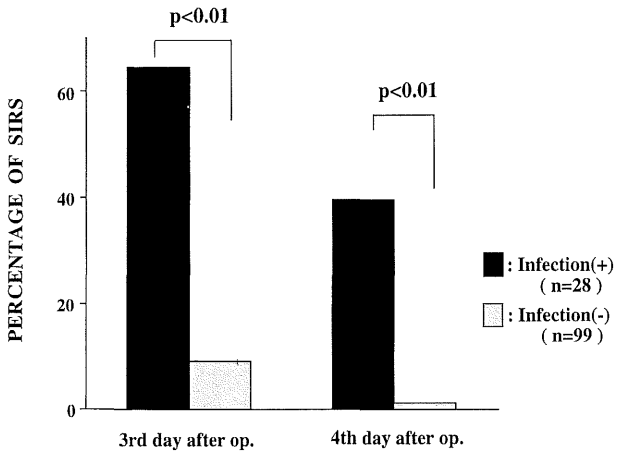

Fig. 4. Incidence of systemic inflammatory response syndrome (SIRS) after operation for gastric cancer.
op: operation

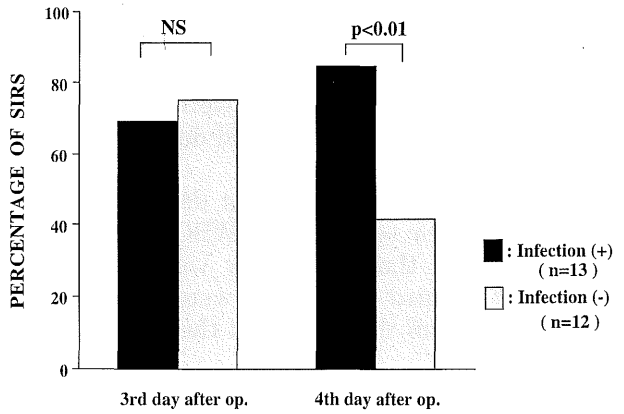

Fig. 5. Incidence of systemic inflammatory response syndrome (SIRS) after operation for esophageal cancer.
op: operation

erative days in the infected patients. We thus concluded that the relative changes in WBC and CRP concentrations on the third and the fourth days were more predictive of the development of infection than the absolute values. In our practice, in the patients with a body temperature greater than 37.6°C on the third day after surgery, the WBC and CRP concentrations are measured. These are compared with the values obtained on the fourth day. In the patients in whom an infection is deemed likely to occur, therapeutic antibiotics are administered. In the remaining patients, the prophylactic antibiotics are discontinued.

Yokoyama et al[11] have demonstrated that CRP concentrations reach a peak on the third day after an operation in patients without infection. Imamura[4] has reported that the maximal increase in WBC is observed within 24 hours after operation. Hence, the most significant changes in the WBC may take place before the third postoperative day. However, prediction of postoperative infections would be difficult using WBC alone.

Due to prolonged high fevers and the high incidence of postoperative infections after surgery for esophageal cancer, antibiotic administration tends to continue for more than 3 days. Furthermore, more advanced-generation cephalosporins are often used. In our study, there were no significant differences in the body temperature, peripheral WBC or CRP concentration in the infected and non-infected groups on the third and fourth days. The incidence of SIRS in the patients undergoing esophageal surgery was higher than in the patients undergoing gastric surgery on the third and fourth days. Almost all patients with SIRS after gastric surgery developed an infection. On the other hand, the incidence of SIRS in the patients who did not develop an infection was high on both the third and fourth days after esophageal surgery. This suggests that the influence of surgical insult after an esophageal operation lasts longer than that after gastric surgery.

After esophageal operations, higher serum cytokine levels have been reported than after gastric procedures[6,8]. Because it is difficult to distinguish infection-induced SIRS from that induced by esophageal surgery, it is nearly impossible to predict who will develop an infection. Therefore, it is difficult to determine when the prophylactic antibiotics should be discontinued in esophageal surgery. The high incidence of postoperative infections, and their significant consequences justify planned successive postoperative antibiotic use in esophageal surgery. Broad spectrum antibiotics are recommended until resolutioin of the inflammatory signs after 3 days of prophylaxis with first- or second-generation cephalosporins.

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