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# Incidence and Risk Factors for Hospital-acquired Pneumonia After Surgery for Gastric Cancer: Results of Prospective Surveillance

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**Abstract**
*Background* Postoperative hospital-acquired pneumonia (HAP) is recognized as a major risk associated with surgery. Although upper abdominal surgery is known to have the highest incidence of postoperative HAP, little is known about the risk factors that contribute to HAP after gastric cancer surgery. The aim of this study was to determine the incidence and risk factors for HAP after elective surgery for gastric cancer.
*Methods* We conducted prospective surveillance of all elective gastric resections by surgeons in ten affiliated hospitals, including ours, from May 2001 to May 2005. The outcome of interest was postoperative HAP. Univariate and multivariate analyses were performed to determine the predictive significance of variables in gastric cancer surgery.
*Results* A total of 529 patients undergoing elective operations for gastric cancer were admitted to the program. Postoperative HAP was identified in 20 patients (3.6%). Univariate and multivariate analyses showed that male gender and intra- and/or postoperative blood transfusion were independently predictive of postoperative HAP.
*Conclusions* Male gender and intra- and/or postoperative blood transfusion were independent risk factors for the development of HAP after elective resection of gastric cancer. Surgeons should keep these risk factors in mind when managing postoperative patients.

Additional participating investigators are listed at the end of the article.

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## Introduction

Hospital-acquired pneumonia (HAP) is the second most common nosocomial infection and the leading cause of death among patients with hospital-acquired infections, accounting for more than 50% of the deaths related to nosocomial infections [1–3]. In the abdominal surgical population, postoperative HAP occurs in 2–29%, and the associated mortality rate is 19–45%, increasing to 65% in patients who have undergone septic intra-abdominal surgery [4–6].

Patients having upper abdominal surgery are particularly vulnerable to developing HAP [7, 8]. Moreover, HAP has been identified as a measure of quality of care in inpatient populations [9]. Identification of risk factors for postoperative HAP during the perioperative care of patients undergoing gastric cancer surgery might result in a reduction in the incidence of postoperative HAP and might improve postoperative outcome. Despite the significance of HAP, little is known about the risk factors that contribute to HAP after gastric cancer surgery.

We conducted a prospective survey of HAP after elective gastric resection in ten affiliated hospitals, including

ours. The aim of this study was to determine the incidence and risk factors for HAP after elective surgery for gastric cancer.

## Methods

### Data collection

All patients undergoing elective resection of gastric cancer at ten affiliated hospitals, including ours, from May 2001 to May 2005 were included in our survey. Members of the infection control staff in each hospital prospectively collected the survey data, including patient name, age, gender, height, weight, diagnosis, history of diabetes mellitus, preoperative respiratory function, preoperative albumin level, preoperative hemoglobin level, American Society of Anesthesiologists (ASA) score as determined by the anesthesiologist, procedure performed, additional operative procedures including adjacent organ resection (e.g., splenectomy and/or distal pancreatectomy), date of operation, duration of operation, and the need for perioperative blood transfusion. Outcome variables included development and day of onset of postoperative HAP.

### Surgical protocols

All patients were instructed to stop smoking 4 weeks before surgery. All operations were conducted by surgeons specializing in gastrointestinal surgery. All patients received systemic prophylactic antibiotics (first-generation cefem or synthesized penicillin) starting 30 min before incision. All operations were performed under general and epidural anesthesia. A closed drain was placed in the left subphrenic space in total gastrectomy and through Winslow's foramen in subtotal gastrectomy. A nasogastric tube was always placed and left until postoperative day 1.

### Dependent variables

The outcome of interest was a diagnosis of postoperative HAP, as referred to in previous reports [10–13]. The detailed criteria for postoperative HAP are described in Table 1.

### Inclusions and exclusions

We excluded patients who were ventilator dependent before surgery and those who had any infection at admission. All patients undergoing procedures for elective resection of gastric cancer during the survey period were included in the study.

### Independent variables

Eighteen independent clinical variables were analyzed. Characteristics evaluated as categorical variables included patient age (<65 and ≥65 years), body mass index (BMI) in kg/m$^2$ (<25 and ≥25), preoperative serum albumin level (<3.0 and ≥3.1/dl), preoperative hemoglobin level (<1 and ≥11 g/dl), and ASA score (≤2 and ≥3). Duration of anesthesia was evaluated as a continuous and categorical variable (≤5 and >5 h), as was intraoperative blood loss (<300 and ≥300 ml). Blood transfusion was defined as infusion of packed red blood cells or whole blood. Perioperative blood transfusion was evaluated as a single categorical variable. Preoperative blood transfusion was defined as a transfusion in the period from preoperative day 7 to the day before surgery, and postoperative blood transfusion was defined a transfusion in the period from the operative day to one day after surgery. The timing of blood transfusion was divided into two groups: preoperative blood transfusion only and intra- and/or postoperative blood transfusion with or without preoperative blood transfusion. The other variables were all categorical variables and are presented in the Results section.

### Statistical analysis

The univariate relationship between each independent variable and clinical postoperative HAP was evaluated using a logistic model for continuous variables and Pearson's $\chi^2$ test for categorical variables. Independent variables with $p < 0.10$ in the univariate analysis were entered into a multivariate logistic regression model with a likelihood ratio of $p < 0.05$.

## Results

A total of 571 elective operations for gastric cancer were performed during our surveillance program. After excluding 24 patients who underwent procedures without resections and 18 patients who had infections before surgery, 529 were eligible for the study. The mean age was 68 years (range = 22–91 years) and 359 (68%) were men. Total gastrectomy was performed in 177 patients (33%) and proximal or distal gastrectomy was performed in 352 (67%). Postoperative HAP was identified in 20 patients (3.8%). Although three patients needed respiratory care, none died from HAP. Three patients who had not developed postoperative HAP died of disease progression as inpatients.

**Table 1** Definition of postoperative HAP

| Patient met one of the following two criteria after surgery: |
|---|
| 1. Rales or dullness to percussion on physical examination of chest and any of the following: |
| New onset of purulent sputum or change in character of sputum |
| Isolation of organism from blood culture |
| Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy |
| 2. Chest radiography showing new or progressive infiltrate, consolidation, cavitation or pleural effusion, and any of the following: |
| New onset of purulent sputum or change in character of sputum |
| Isolation of organism from blood culture |
| Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy |
| Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy |
| Isolation of virus or detection of viral antigen in respiratory secretions |
| Diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for pathogen |
| Histopathologic evidence of pneumonia |

### Univariate analysis

Among the examined variables relating to patient characteristics, male gender was the only factor that was statistically associated with development of postoperative HAP (Table 2). Postoperative HAP tended to develop in patients older than 65 years and with advanced disease stage.

Table 3 shows the association between surgical characteristics and postoperative HAP. Intra- and/or postoperative blood transfusion was the only factor that was statistically associated with a higher incidence of postoperative HAP. Postoperative HAP tended to develop in patients with noncurative resection.

### Multivariate analysis

After univariate analysis, variables with $p < 0.1$ were selected for multivariate analysis using a stepwise logistic regression model. Table 4 summarizes the results of the multivariate analysis. Male gender and intra- and/or postoperative blood transfusion were independent risk factors for developing clinical postoperative HAP.

## Discussion

This study demonstrated that male gender and intra- and/or postoperative blood transfusion were independent risk factors for postoperative HAP after an elective operation for gastric cancer. Our postoperative HAP rate of 3.4% was within the published range of 1.5–17.5% [7, 14]. There were no deaths associated with postoperative HAP in our series, which might be a reflection of the study population in which 41% had early-stage disease.

Postoperative HAP ranks as the third most common postoperative infection, after urinary tract and wound infections [15]. Upper abdominal surgery, especially gastrectomy, has the highest incidence of postoperative HAP [8, 16]. A better understanding of patients who are at a higher risk of developing postoperative HAP after gastric cancer surgery is important for surgeons. To our knowledge this is the first multicenter prospective study to evaluate the incidence of HAP in the gastric cancer surgery population.

Previous studies of risk factors have used various definitions of postoperative pulmonary complications. Atelectasis, postoperative pneumonia, acute respiratory distress syndrome, and postoperative respiratory failure have been included [5, 17–19]. Although the clinical significance of each of these complications varies greatly, they were grouped together as a single outcome in previous studies [19]. This heterogeneity of data within each study explains why there is a wide discrepancy in postoperative pulmonary complication rates and risk factors among the studies. A more consistent definition of postoperative HAP may lead to better homogeneity of data. Identification of risk factors may result in a reduction in the rate of postoperative HAP.

The single most important independent variable associated with the development of postoperative HAP was intra- and/or postoperative blood transfusion. Allogeneic blood transfusion induces immunosuppression and predisposes to postoperative infection [20–23]. An increased incidence of postoperative infection has been observed in recipients of allogeneic transfusions in retrospective and prospective studies [15, 20–28]. The present results indicate that the transfusion effect is stronger in intra- and/or postoperative blood transfusion than in preoperative transfusion, which is consistent with previous findings [28].

Recent large studies [16, 29] of general surgery did not include detailed operative events as independent variables in the analysis of risk factors for postoperative HAP. These studies focused mainly on preoperative factors. In our study, we examined both preoperative and intraoperative variables that contribute to postoperative HAP. We clearly defined the period of postoperative blood transfusion as being from the operative day to one day after surgery. Using this definition, we discovered that intra- and/or postoperative blood transfusion is an additional risk factor. We think that stratifying blood transfusion according to its timing should be considered when identifying risk factors in future studies.

**Table 2** Patient characteristics and postoperative HAP

| Variables | *n* | Pneumomia (%) | *p* value |
|---|---|---|---|
| Gender | | | |
| Female | 170 | 1.2 | |
| Male | 359 | 5.0 | 0.0292 |
| Age (years) | | | |
| ≤65 | 194 | 1.5 | |
| >65 | 335 | 5.1 | 0.0560 |
| Body mass index (kg/m$^2$) | | | |
| <25 | 469 | 3.6 | |
| ≥25 | 60 | 5.3 | 0.4864 |
| History of smoking | | | |
| Yes | 140 | 4.3 | |
| No | 389 | 3.6 | 0.7963 |
| Diabetes mellitus | | | |
| Yes | 41 | 2.4 | |
| No | 488 | 3.9 | >0.9999 |
| COPD | | | |
| Yes | 17 | 11.8 | |
| No | 512 | 3.5 | 0.1315 |
| Body weight loss of more than 10% | | | |
| Yes | 126 | 6.3 | |
| No | 403 | 3.0 | 0.1056 |
| Albumin (g/dl) | | | |
| ≥3.0 | 493 | 3.0 | |
| <3.0 | 36 | 8.3 | 0.1165 |
| Anemia | | | |
| No | 444 | 3.2 | |
| Yes | 85 | 4.7 | 0.5097 |
| ASA score | | | |
| ≤2 | 497 | 3.8 | |
| ≥3 | 32 | 3.1 | >0.9999 |
| TNM stage | | | |
| Early (0,IA,IB) | 218 | 1.8 | |
| Advanced (IIIA,IIIB,IV) | 311 | 5.1 | 0.0630 |

**Table 3** Surgical characteristics and postoperative HAP

| Variables | *n* | Pneumonia (%) | *p* value |
|---|---|---|---|
| Operation | | | |
| Subtotal gastrectomy (distal or proximal) | 352 | 2.8 | |
| Total gastrectomy | 177 | 5.7 | 0.1454 |
| Adjacent organ resection (pancreas, spleen, colon) | | | |
| No | 479 | 4.0 | |
| Yes | 50 | 2.0 | 0.7100 |
| Duration of anesthesia (min) | | | |
| <300 | 256 | 2.7 | |
| ≥300 | 273 | 4.8 | 0.2590 |
| Blood loss (ml) | | | |
| <300 | 291 | 2.4 | |
| ≥300 | 238 | 5.5 | 0.1065 |
| Blood transfusion timing | | | |
| No transfusion | 455 | 2.6 | |
| Preoperative | 32 | 6.3 | 0.0977 |
| Intra- or postoperative | 42 | 14.3 | 0.0033 |
| Lymph node dissection | | | |
| <D2 | 208 | 3.9 | |
| ≥D2 | 321 | 3.7 | >0.9999 |
| Curability | | | |
| Curative (R0) | 464 | 3.2 | |
| Noncurative (R1,2) | 65 | 8.3 | 0.0857 |

**Table 4** Multivariate analysis

| Variables | Odds ratio | 95% CI | *p* value |
|---|---|---|---|
| Male gender | 5.153 | 1.158–22.921 | 0.0313 |
| Intra- and/or postoperative blood transfusion | 6.781 | 2.357–19.514 | 0.0004 |
| Preoperative blood transfusion | 3.180 | 0.662–15.282 | 0.1458 |

We found that male patients were five times more likely than female patients to develop postoperative HAP. There are only two published studies that identify gender as a risk factor for postoperative HAP. Konard et al. [30] found that males were more likely than females to develop HAP in the ICU setting. On the other hand, Thompson et al. [16] found that females were more likely than males to develop postoperative HAP. Given these findings, further research is needed to better understand the influence of gender on postoperative HAP and whether the greater incidence in males is caused by an increased incidence of frailty in males, or by disease specifics.

Of those risk factors for postoperative HAP frequently identified in other multivariate analyses, age, duration of anesthesia, history of chronic obstructive pulmonary disease, smoking history, and increased BMI were not identified as significant in this study. The reason these risk factors did not remain significant in the multivariate analysis is related to the limited study population.

Several important limitations of this study should be emphasized. First, this was a retrospective analysis of prospectively collected data and not a randomized controlled study to examine the significance of specific risk factors for postoperative HAP. Statistical correlations between the risk factors and postoperative HAP do not determine any "cause-and-effect" relationship between them. Thus, it is important to carefully examine the results of the analysis to avoid misinterpretation. Second, there are

other known risk factors that were not evaluated but could predispose a patient to postoperative HAP, including weight loss [29], alcohol use [29], cerebral vascular accident [31], long-term steroid use [32], and the use of $H_2$ receptor antagonists [33]. Finally, the low incidence of HAP (3.6%) in the current study would be difficult to adjust for the various confounding factors in the multivariate model.

In the present study, all variables to be recorded were determined from the start of our survey program, and all the data were collected prospectively. The addition of retrospective research by reviewing medical records was discouraged because the accumulation of incorrect or missing data could have degraded the quality of the data. Despite these limitations, we think that this study reflects actual postoperative HAP rates as well as risk factors in this patient population and data set.

In summary, male gender and intra- and/or postoperative blood transfusion were independent risk factors for the development of postoperative HAP after elective resection of gastric cancer. Surgeons should keep these risk factors in mind when managing postoperative patients.

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