Preoperative bacterial culture can predict severe pneumonia in patients receiving esophagectomy

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Abstract

Background

Postoperative pneumonia is one of the major complications after esophagectomy. The aim of this study was to determine whether bacterial cultures before esophagectomy could predict occurrence of postoperative pneumonia and help treatment strategies for postoperative pneumonia.

Methods

Sixty-nine patients who underwent subtotal esophagectomy at Fukushima Medical University hospital between January 2017 and May 2021 were included in this study. We collected sputum, oral and/or nasopharyngeal swabs for bacterial culture preoperatively from all patients and from those who were suspected of postoperative pulmonary infections. We compared cultured pathogenic bacteria obtained preoperatively and postoperatively from patients who developed postoperative pneumonia, and investigated their association with incidence of postoperative pneumonia. Fisher's exact test was used to compare categorical variables between groups, and Wilcoxon test was used to compare continuous variables. Risk factors for postoperative pneumonia and severe pneumonia were analyzed using multivariate logistic regression models.

Results

Postoperative pneumonia occurred in 22 (31%) of the 69 patients, and 13 of the 22 patients were classified as with severe pneumonia. Multivariate analysis revealed that longer operative duration (for 30 minutes increase; odds ratio 1.27, 95% confidence interval 1.01–1.51, $p=0.039$) and positivity for preoperative bacterial culture (odds ratio 5.03, 95% confidence interval 1.31–19.2, $p=0.018$) were independent risk factors for severe postoperative pneumonia, but not for all incidence of postoperative pneumonia. Of note, in only 5 out of the 22 patients with pneumonia, the same pathogen species were detected preoperatively and after the onset of pneumonia.

Conclusions

In conclusion, our results implied that preoperative bacterial culture may be useful to predict severe postoperative pneumonia. However, it may not be useful in determining pathogenic bacteria responsible for postoperative pneumonia.

Introduction

Esophagectomy for esophageal cancer is a highly invasive surgery. Even though surgical techniques and perioperative managements have been improved, a number of complications after esophagectomy

remain inevitable [1–3]. Respiratory complication is one of the most common complications after esophagectomy (17.9 – 38.9%) and can lead to prolonged hospital stay and increased mortality [2–6]. Several studies reported that respiratory complications after esophagectomy including pneumonia affected not only short-term outcomes but also patients' survival [4, 7]. Thus, improvement of perioperative management for patients undergoing esophagectomy is required to prevent such complications.

It is generally considered that aspiration of oropharyngeal pathogens is one of the main causes of postoperative pneumonia [8, 9]. Several studies focused on pathogens in oral cavity, dental plaque and tracheal sputum as risk factors for respiratory infections after esophagectomy [10, 11]. When esophagectomy cases develop postoperative pneumonia, it is mandatory to identify the bacteria responsible for the infection and to administer effective antibiotics against them as soon as possible. If pathogens identified preoperatively from sputum or oral cavity are identical to the bacteria responsible for postoperative pneumonia, we can start with appropriate antibiotics immediately. However, clinical usefulness of bacterial culture before esophagectomy remains not fully elucidated.

The aims of this study were whether bacterial cultures before esophagectomy are identical to the responsible bacteria of postoperative pneumonia and can predict the incidence of postoperative pneumonia.

Methods

Patients

This study included patients who underwent subtotal esophagectomy for esophageal or esophagogastric junction cancer at Fukushima Medical University hospital between January 2017 and May 2021, and whose bacterial cultures of sputum and of oral, nasal, and/or pharyngeal swabs were obtained preoperatively. Patients who underwent partial cervical esophagectomy, pharyngo-laryngo-esophagectomy and salvage surgery after definitive chemoradiotherapy were excluded. Written informed consent was obtained from all patients. This study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the institutional review board of Fukushima Medical University (registry number 30169).

Perioperative managements and operative procedure

All patients received respiratory rehabilitation and oral care before surgery. The oral care included oral assessment and extractions of carious teeth by dentists at the Division of the Dentistry and Oral Surgery.

Open thoracic esophagectomy or minimally invasive esophagectomy was performed. Open transthoracic esophagectomy by right thoracotomy was performed with the patient in the left lateral decubitus position. Thoracic manipulation of minimally invasive surgery, including video-assisted thoracic surgery

and robotic assisted thoracoscopic surgery, was performed through the right thorax with the patient in the prone position. In both approaches, esophago-gastrostomy was performed at neck.

We administered cefazolin as a prophylactic antibiotic during esophagectomy every 3 hours during the operation. We placed a jejunostomy tube in all cases and gave enteral nutrition through the tube on the next day after surgery. Oral intake was started after confirmation of the absence of anastomotic leakage by radiography on the 7th postoperative day.

Bacterial cultures

We routinely collected sputum, oral, nasal and/or pharyngeal swabs within 7 days before esophagectomy. The samples were cultured, and identification of normal flora and pathogens was performed in our microbiology laboratory. Postoperative sputum culture was not carried out routinely, but only in cases of suspicious of pulmonary infections. Patients were defined as positive if pathogenic bacteria were detected, and those with normal flora or non-pathogenic bacteria were defined as negative.

Postoperative pneumonia

We defined postoperative pneumonia as development of new infiltrations on chest radiography and/or computed tomography (CT), and the presence of at least one of the following two clinical features as previously reported: increase in body temperature to 38°C or higher; or increase in white blood cell count to 9,000/mm³ or higher [12, 13]. Severe pneumonia was defined as grade IIIa or higher according to Clavien-Dindo classification including acute respiratory distress syndrome (ARDS) [14].

Statistics

The software package STATA15 (STATA Corp., College Station, TX, USA) was used for statistical analysis. Fisher's exact test was used to compare categorical variables between groups, and Wilcoxon test was used to compare continuous variables. Risk factors for postoperative pneumonia and severe pneumonia were analyzed using multivariate logistic regression models. *P*-values less than 0.05 were considered significant.

Results

Patient characteristics and postoperative pneumonia

Sixty-nine patients were included in this study. Among them, pathogenic bacteria were detected from at least any one of the cultures of sputum, oral swab, nasal swab, and/or pharyngeal swab obtained preoperatively in 20 (28%) patients. The remaining 49 patients were defined as negative.

Clinical characteristics and surgical outcomes of these two groups are summarized in Table 1. Although the Brinkman index of the positive group was marginally higher than that of the negative group ($p=0.058$), the background data did not differ among the two groups.

Table 1
Patients' characteristics and surgical outcomes

	Preoperative bacterial culture		
	Negative (n = 49)	Positive (n = 20)	<i>p</i> -value
Age [†] (years)	68 ± 8.3	69 ± 6.6	0.63
Gender (male/female)	37/12	19/1	0.09
Brinkman index [†]	500 ± 443	727 ± 446	0.058
Comorbidity			
COPD	8	3	0.60
Diabetes mellitus	8	3	0.60
Location of tumor			0.86
Ut	9	3	
Mt	24	8	
Lt	10	6	
Ae	6	3	
Histological type			0.90
Squamous cell carcinoma	38	7	
Adenocarcinoma	6	10	
Others	5	3	
Neoadjuvant therapy			0.17
None	21	7	
Neoadjuvant chemotherapy	13	10	
Neoadjuvant chemoradiotherapy	15	3	
Thoracic surgical approach			1.0

[†] Plus-minus values are means ± standard deviation.

*Statistically significant

COPD chronic obstructive pulmonary disease, *Ut* upper thoracic esophagus, *Mt* middle thoracic esophagus, *Lt* lower thoracic esophagus, *Ae* abdominal esophagus, *MIS* minimally invasive surgery

	Preoperative bacterial culture		
Open	13	5	
MIS	36	15	
Operative duration (minutes) [†]	529 ± 96	571 ± 103	0.11
Blood loss (g) [†]	283 ± 417	390 ± 545	0.67
3-field lymphadenectomy	33	12	0.58
pStage			0.86
0, I	16	4	
II	15	8	
III	13	5	
IV	5	3	
Recurrent laryngeal nerve palsy	12	6	0.76
Postoperative pneumonia	12	10	0.05*
Severe postoperative pneumonia (≥IIIa)	5	8	0.007*
[†] Plus-minus values are means ± standard deviation.			
*Statistically significant			
<i>COPD</i> chronic obstructive pulmonary disease, <i>Ut</i> upper thoracic esophagus, <i>Mt</i> middle thoracic esophagus, <i>Lt</i> lower thoracic esophagus, <i>Ae</i> abdominal esophagus, <i>MIS</i> minimally invasive surgery			

Postoperative pneumonia occurred in 22 (31%) of the all 69 patients, and 13 of the 22 patients were classified as with severe pneumonia (including 1 ARDS). Postoperative pneumonia was more frequently observed in the positive group than the negative group ($p=0.05$), and the incidence of severe pneumonia was also higher in the positive group than the negative group ($p=0.007$). No significant differences were observed in age, preoperative comorbidity, location of the tumor, neoadjuvant therapy, thoracic surgical approach, range of lymphadenectomy or recurrent laryngeal nerve palsy, between the two groups.

Perioperative bacterial culture

Table 2 shows the detection rate of pathogenic bacteria in preoperative cultures from each site. The positive rate was 22% in sputum culture, 18% in nasal swab culture, 5% in oral swab culture, and 11% in pharyngeal swab culture. Fig. 1 shows the number of pathogenic bacterial species detected in pre- and postoperative cultures. In preoperative cultures, methicillin-susceptible *Staphylococcus aureus* (MSSA)

was detected most frequently, followed by Klebsiella pneumoniae. Twenty-three bacteria were identified in postoperative cultures of sputum from the 22 patients with postoperative pneumonia.

Table 2 Detection rate of pathogenic bacteria in preoperative cultures	
	Positive rate
Sputum	10/45 (22%)
Nasal swab	11/58 (18%)
Oral swab	3/56 (5%)
Pharyngeal swab	1/9 (11%)

Eleven out of the 22 postoperative pneumonia patients were positive for postoperative sputum culture, and in 5 out of the 11 cases, pathogenic bacteria in postoperative sputum culture were identical to those in preoperative culture.

Risk factors associated with postoperative pneumonia

Table 3 shows the risk factors associated with postoperative pneumonia. According to the univariate analysis, postoperative pneumonia was associated with longer operative duration ($p=0.023$), extensive blood loss ($p=0.024$), and positivity for preoperative bacterial culture test ($p=0.043$). However, the multivariate analysis showed no significant impact of the risk factors on postoperative pneumonia development.

Table 3
Logistic regression analysis for postoperative pneumonia

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (for 10-year increase)	0.93 (0.49–1.79)	0.84		
Male	7.20 (0.87–59.4)	0.067		
Brinkman index (for 100 increase)	1.04 (0.93–1.16)	0.48		
Comorbidity				
COPD	1.26 (0.32–4.89)	0.72		
Diabetes mellitus	0.17 (0.02–1.47)	0.10		
Neoadjuvant therapy (vs surgery alone)	2.34 (0.78–7.04)	0.12		
Neoadjuvant chemotherapy (vs surgery alone)	2.82 (0.83–9.57)	0.096		
Neoadjuvant chemoradiotherapy (vs surgery alone)	1.83 (0.48–6.94)	0.37		
Thoracic surgical approach Open (vs MIS)	2.92 (0.95–8.94)	0.06		
Operative duration (for 30 minutes increase)	1.20 (1.02–1.41)	0.023*	1.03 (0.97–1.09)	0.29
Blood loss (for 50 g increase)	1.10 (1.01–1.20)	0.024*	1.08 (0.98–1.18)	0.094
3-field lymphadenectomy (vs 2-field)	0.90 (0.31–2.60)	0.85		
Recurrent laryngeal nerve palsy	1.48 (0.57–3.84)	0.41		
Preoperative bacterial culture test Positive (vs negative)	3.08 (1.03–9.18)	0.043*	2.65 (0.81–8.69)	0.10
*Statistically significant				
OR odds ratio, CI confidence interval, COPD chronic obstructive pulmonary disease, MIS minimally invasive surgery				

Table 4 shows the multivariate logistic regression analysis for the risk factors of severe postoperative pneumonia. Of note, longer operative duration (for 30 minutes increase; odds ratio 1.27, 95% confidence interval 1.01–1.51, $p=0.039$) and positivity for preoperative bacterial test (odds ratio 5.03, 95% confidence interval 1.31–19.2, $p=0.018$) were significant independent risk factors for developing severe postoperative pneumonia.

Table 4
Logistic regression analysis for severe postoperative pneumonia

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
Age (for 10-year increase)	1.51 (0.65–3.54)	0.33		
Male	3.27 (0.38–27.7)	0.27		
Brinkman index (for 100 increase)	1.07 (0.93–1.22)	0.31		
Comorbidity				
COPD	0.94 (0.17–5.02)	0.95		
Diabetes mellitus	0.38 (0.04–3.29)	0.38		
Neoadjuvant therapy (vs surgery alone)	1.11 (0.32–3.84)	0.86		
Neoadjuvant chemotherapy (vs surgery alone)	1.27 (0.31–5.10)	0.72		
Neoadjuvant chemoradiotherapy (vs surgery alone)	0.92 (0.19–4.43)	0.91		
Thoracic surgical approach Open (vs MIS)	3.14 (0.88–11.1)	0.076		
Operative duration (for 30 minutes increase)	1.26 (1.04–1.52)	0.015*	1.27 (1.01 – 1.51)	0.039*
Blood loss (for 50 g increase)	1.06 (1.00–1.13)	0.045*		
3-field lymphadenectomy (vs 2-field)	0.82 (0.23–2.85)	0.75		
Recurrent laryngeal nerve palsy	1.08 (0.34–3.43)	0.88		
Preoperative bacterial culture test Positive (vs negative)	5.86 (1.61–21.2)	0.007*	5.03 (1.31 – 19.2)	0.018*
*Statistically significant				
OR odds ratio, CI confidence interval, COPD chronic obstructive pulmonary disease, MIS minimally invasive surgery				

Discussion

It has been generally considered that bacteria in the oral cavity could cause postoperative pneumonia in theory. However, there are only a few studies that investigated the relationship between oral cavity bacteria and postoperative pneumonia, and the clinical significance of preoperative bacterial culture is not well established. This study revealed that the presence of pathogenic bacteria in the oropharyngeal cavity and sputum before esophagectomy was a predictive factor for the development of severe postoperative pneumonia, but not for all incidence of pneumonia. Moreover, the concordance rate in the bacterial species between preoperative screening culture and postoperative diagnostic culture for pneumonia was very low.

Several previous studies reported that relationship between the presence of pathogenic bacteria detected in perioperative routine cultures and postoperative pneumonia was controversial [8, 13, 15]. Jimbo et al reported that preoperative various bacterial culture could predict neither the occurrence of postoperative pneumonia nor its causative bacteria [13]. However, Matsunaga et al reported that the presence of *Pseudomonas aeruginosa* in preoperative bacterial culture was associated with pneumonia after esophagectomy [8]. Yuda et al reported that preoperative presence of allopatric bacteria, especially antibiotic-resistant bacteria, in the oropharyngeal microflora two days before esophagectomy was a predictive factor for postoperative pneumonia [16]. In the present study with a multivariate analysis, it is likely that positivity for preoperative bacterial culture can independently predict severe postoperative pneumonia, but not all incidence of pneumonia. Therefore, detection of positive bacterial culture preoperatively can prompt us to take care the patient as having a risk for developing severe pneumonia after esophagectomy.

Of note, pathogenic bacteria species cultured from sputum of patients with postoperative pneumonia did not match to those in preoperative cultures in the present study. In only 5 out of the 22 (22%) patients with pneumonia, pathogens detected preoperatively were identical to pathogenic bacteria responsible for postoperative pneumonia. It is reported that the concordance rate between bacteria detected before and after esophagectomy was relatively low (7 – 40%) [8, 13, 17]. Sok et al reported that pathogens in sputum in the early postoperative period which had caused postoperative infective complications were different from those in the preoperative bacterial culture [18]. These findings in the present study and previous studies suggest that preoperative bacterial culture is not able to determine causative pathogenic bacteria, and seems not to be useful to select appropriate antibiotics immediately after onset of postoperative pneumonia.

This study has some limitations. First, this study was a retrospective design with a small population in a single institute. Second, in contrast with preoperative culture test, we did not routinely collect sputum culture after esophagectomy except when the patients showed any signs of postoperative pneumonia. Therefore, the timing of postoperative sputum culture varied among the patients, which might have affected the detection rate and concordance of pathogenic bacteria.

Conclusions

Our results implied that preoperative bacterial culture may be useful to predict severe postoperative pneumonia. However, it may not be useful in determining pathogenic bacteria responsible for postoperative pneumonia.

Abbreviations

CT: Computed tomography

ARDS: Acute respiratory distress syndrome

MSSA: Methicillin-susceptible *Staphylococcus aureus*

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki, and the study protocol was approved by the institutional review board of Fukushima Medical University (registry number 30169). Written informed consent was obtained from all patients.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to privacy of patients but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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None.

Authors' contributions

AK and KK designed the study. TS, HN, TM and TT collected clinical data. AK, YW, HH and SH performed statistical analysis. AK prepared the manuscript, ZS and KK reviewed and revised. All authors read and approved the final manuscript.

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Figures

Figure 1

Number of pathogenic bacterial species detected in pre- and postoperative bacterial cultures. BLNAR β -lactamase negative ampicillin resistant, MRSA methicillin-resistant *Staphylococcus aureus*, MSSA methicillin-susceptible *Staphylococcus aureus*