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Original Research

Surgical and long-term outcomes following oesophagectomy in oesophageal cancer patients with comorbidity

Hiroshi Ichikawa [a], Shin-ichi Kosugi [b, *], Tatsuo Kanda [c], Kazuhito Yajima [d], Takashi Ishikawa [a], Takaaki Hanyu [a], Yusuke Muneoka [a], Takahiro Otani [a], Masayuki Nagahashi [a], Jun Sakata [a], Takashi Kobayashi [a], Hitoshi Kameyama [a], Toshifumi Wakai [a]

[a] Division of Digestive and General Surgery, Niigata University, Graduate School of Medical and Dental Sciences, 1-757 Asahimachi-dori, Chuo-ku, Niigata 951-8510, Japan
[b] Department of Digestive and General Surgery, Uonuma Institute of Community Medicine, Niigata University, Medical and Dental Hospital, Niigata 949-7320, Japan
[c] Department of Surgery, Sanjo General Hospital, 5-1-62 Tsukanome, Sanjo-shi, Niigata 955-0055, Japan
[d] Department of Surgery, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, 3-18-22 Honkomagome, Bunkyo-ku, Tokyo 113-8677, Japan

HIGHLIGHTS

- Oesophagectomy in oesophageal cancer patients with comorbidity is feasible.
- Less-invasive treatment modification is needed to minimize morbidity and mortality.
- The overall survival after oesophagectomy in patients with comorbidity was unfavorable.
- The incidence of death from other diseases, especially pneumonia, is very high.

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ABSTRACT

Introduction: The elucidation of the clinical impact of comorbidities is important to optimize the treatment and follow-up strategy in oesophageal cancer. We aimed to clarify the surgical and long-term outcomes following oesophagectomy in oesophageal cancer patients with comorbidity.
Methods: A total of 658 consecutive patients who underwent oesophagectomy for oesophageal cancer between 1985 and 2008 at our institution were enrolled. Based on the criteria of comorbidity as we defined it, we retrospectively reviewed and compared the surgical outcomes and survival between the comorbid (n = 251) and non-comorbid group (n = 407).
Results: Postoperative morbidity and mortality were not significantly different between the two groups. The 5-year overall survival rate of the comorbid group was significantly lower (39.3% vs. 45.2%, adjusted HR = 1.31, 95% CI: 1.07–1.62) but the 5-year disease-specific survival rate was not significantly different between the comorbid and non-comorbid groups (53.9% vs. 53.1%, adjusted HR = 1.11, 95% CI: 0.86–1.42). The 5-year incidence rate of death from other diseases in the comorbid group was significantly higher than that in the non-comorbid group (26.7% vs. 14.8%, P < 0.01). The leading cause of death from other diseases was pneumonia.
Conclusions: Oesophagectomy in oesophageal cancer patients with comorbidity can be safely performed. However, the overall survival after oesophagectomy in these patients was unfavorable because of the high incidence of death from other diseases, especially pneumonia.

1. Introduction

Oesophageal cancer is the eighth most common cancer and the sixth most common cause of cancer death worldwide [1].

* Corresponding author. Department of Digestive and General Surgery, Uonuma Institute of Community Medicine, Niigata University, Medical and Dental Hospital, 4132 Urasa, Minamiuonuma-shi, Niigata 949-7320, Japan
E-mail address: sugishin@med.niigata-u.ac.jp (S.-i. Kosugi).

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Oesophagectomy with lymphadenectomy is one of the major curative treatment options for this disease [2]. Recent advances in operative techniques, preoperative therapies and perioperative management have improved survival after oesophagectomy for locally advanced oesophageal cancer, and the 5-year overall survival rate has reached about 50% [3–7]. Oesophagectomy with lymphadenectomy is still accompanied by high morbidity and mortality, however [8]. Careful preoperative assessments of the surgical risk and the selection of appropriate candidates for oesophagectomy are thus important to further improve the clinical outcome of oesophageal cancer [9].

Tobacco use, alcohol consumption, obesity and increased age are well-known risk factors for oesophageal cancer [2]. These are also the risk factors for chronic diseases such as chronic obstructive pulmonary disease, cardiovascular disease, cerebral stroke, chronic kidney disease and diabetes mellitus [10,11]. It was reported that 68.1% of patients with oesophageal cancer had some comorbidities, and a poor general condition due to one or more severe comorbidities is one of the reasons to avoid surgery [12]. Even if a patient has a performance status that is adequate for oesophagectomy, the presence of comorbidity is reported as one of the risk factors for morbidity and mortality after oesophagectomy [13–16]. Regarding long-term outcome too, the presence of comorbidity is known to be an unfavorable prognostic factor in patients with malignant tumors [17,18]. However, especially in oesophageal cancer patients, the significance of comorbidities for long-term outcome after oesophagectomy is not fully understood. The elucidation of the clinical impact of comorbidities is important to optimize the treatment and follow-up strategy in oesophageal cancer.

The aims of this study were to clarify the surgical outcomes and assess the long-term outcome following oesophagectomy in oesophageal cancer patients with comorbidity.

2. Materials and methods

2.1. Study population and comorbidity

A total of 658 consecutive patients who underwent an oesophagectomy with curative intent for thoracic oesophageal cancer between January 1985 and December 2008 at Niigata University Medical and Dental Hospital were enrolled in this study. This study was approved by the Ethical Committee of the Niigata University Medical and Dental Hospital, and designed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [19]. The blood gas analysis, spirometry, measurement of the 24-hour creatinine clearance, electrocardiogram and echocardiography were performed to determine each patient's ability to tolerate the planned treatments. The patients' comorbidities were assessed on the basis of their medical history, current presentation, and findings on the above-mentioned examinations. We classified the comorbidities into six categories as follows: (1) diseases of the cardiovascular system, (2) diseases of the respiratory system, (3) liver dysfunction; (4) renal insufficiency; (5) diseases of the nervous system, and (6) diseases of the endocrine system and collagen disease. We defined the diagnostic criteria of the comorbidities as shown in Table 1.

We compared the clinicopathological characteristics, surgical outcomes and survival between the two groups: patients with at least one of these comorbidities (comorbid group, n = 251) and those without comorbidity (non-comorbid group, n = 407). The clinicopathological characteristics of the two groups are shown in Table 2. The median age of the comorbid group was significantly higher than that of the non-comorbid group (67.0 years vs. 62.0 years, $P < 0.01$). The tumor status was not significantly different between the two groups.

2.2. Surgical procedure

Transthoracic oesophagectomy with three-field lymphadenectomy (3FL) including systemic bilateral cervical, mediastinal and abdominal node dissection was a standard surgical procedure in our institute, as described [20]. In the patients who could not tolerate optimum treatments because of comorbidity, less-invasive modifications for treatments were applied according to the clinicians' discretion, as shown in Table 2. Transhiatal oesophagectomy and 2FL were performed significantly more frequently in the comorbid group than in the non-comorbid group ($P = 0.04$ and $P < 0.01$, respectively). The number of dissected nodes was significantly lower in the comorbid group compared to the non-comorbid group ($P < 0.01$). Preoperative treatments tended to more frequently performed in the comorbid group ($P = 0.05$), and postoperative therapies were significantly less frequently performed in the comorbid group ($P < 0.01$).

2.3. Surgical outcomes and histopathological examination

For the assessment of the patients' surgical outcomes, we determined the operative times, blood loss, number of dissected nodes, morbidity, mortality and hospital stays. We evaluated postoperative complications during the hospital stay according to the Clavien-Dindo classification system [21]. Overall morbidity was defined as any complication, and major morbidity was defined as a complication of grade III or higher. Thirty-day mortality was defined as in-hospital death within 30 days after oesophagectomy. Operative mortality included all of the in-hospital deaths after oesophagectomy, regardless of the length of hospital stay. Surgically resected specimens were histopathologically examined, and the tumor status was evaluated according to the tumor-node-metastasis (TNM) classification defined by the Union for International Cancer Control (UICC) [22].

2.4. Statistical analysis

We used the Wilcoxon test to compare the continuous variables, and used the chi-square or Fisher's exact test to compare categorical variables between the two groups. Overall survival (OS) and disease-specific survival (DSS) was defined as the time from oesophagectomy to death from any cause and to death from oesophageal cancer, respectively. The median follow-up period in the patients who were alive at the time of the last follow-up was 116 months (range 5–237 months). In the survival analysis, patients were stratified using the clinicopathological factors. Continuous variables were dichotomized by median values of entire population. Cumulative survival rates were estimated by using the Kaplan-Meier method, and differences were evaluated by the log-rank test for the univariate analysis. A multivariate analysis was performed using the Cox proportional hazard model to examine the independent prognostic impact of comorbidity by calculating hazard ratios (HRs) with 95% confidence intervals (CIs) adjusted for significant confounding factors in the univariate analysis. We estimated the cumulative incidence rate of death from other diseases by using the Kaplan-Meier method and censoring patients who had died from oesophageal cancer or were alive at the last follow-up. All statistical analyses were performed using the SPSS 17.0J software package (SPSS Japan, Tokyo). A P-value less than 0.05 (two-tailed) was considered significant.

3. Results

3.1. Surgical outcomes

The details of the patients' surgical outcomes are given in