INTRODUCTION

Esophageal cancer is the sixth leading cause of cancer-related mortality worldwide due to its high malignant potential and poor prognosis (1). The prognosis of this cancer is one of the worst among malignant digestive neoplasms. Its poor survival can be elucidated by its aggressive tumor biology and delayed detection of early esophageal cancer. The survival time in patients with advanced esophageal cancer is, therefore, unsatisfactory despite the development of operative procedures and perioperative managements (2, 3). Esophagectomy is traditionally considered the standard treatment for esophageal cancer. In Japan, the survival rate after esophagectomy has remarkably improved in recent years. Although the overall five-year survival rate exceeds 50%, recurrence still develops within two years after resection in more than 80% of these patients (4). In addition, Kunisaki C et al. reported that more than 50% of tumor recurrences occurred within 12 months of curative esophagectomy (5). According to the type of recurrence, the metachronous lesions are classified as locoregional, distant (including hematogenous metastasis within a solid organ, abdominal paraaortic lymph node metastasis, and peritoneal metastasis), and combined types (5). For such patients, chemotherapy or chemoradiotherapy (CRT) are the main treatments for recurrence (5-8). However, the role of adjuvant treatments, such as chemotherapy and radiotherapy, for esophageal cancer patients after radical esophagectomy remains controversial, although adjuvant therapy for the improvement of prognosis is important.

Therefore, understanding the predictive factors and assessing the pattern and timing of recurrence after curative esophagectomy plays a significant role in ameliorating therapeutic outcomes. These data can also aid in the administration of appropriate treatments according to recurrence pattern and improvement of prognosis after recurrence. With regard to the recurrent treatment of esophageal cancer, Shimada H et al. discussed that the status of serum p53 antibody and serum CRP may predict response and outcome of patients with recurrent esophageal cancer after radical operation (9). Moreover, Kunisaki C et al. have reported a significant difference in survival after recurrence between treatment methods (no treatment vs chemoradiotherapy, p = 0.0063; chemotherapy, p = 0.0247; and radiotherapy, p < 0.0001).

In this study, the recurrence pattern, treatment method, and prognosis of recurrent cases after esophageal cancer surgery were retrospectively examined, and risk factors for recurrence and favorable prognosis factors after recurrence were investigated.

PATIENTS AND METHODS

Patients

This was a single-center retrospective study. Between January 2004 and December 2015, 307 patients with histologically proven squamous cell carcinoma (n = 256: 83.4%), adenocarcinoma (n = 31 : 10.1%), and others (n=20 : 6.5%) were successfully enrolled in the study. The patient population was composed of 267 men and 40 women from ages 39 to 86 years old [mean age ± standard deviation (SD), 66.3 ± 7.9 years]. The patients underwent transthoracic esophagectomy followed by esophagogastric anastomosis or esophagojejunal anastomosis using...
the gastric conduit or jejunal Roux-en-Y at the Department of General Surgical Science, Gunma University Graduate School of Medicine, Japan. Preoperative diagnoses involving endoscopic examination with biopsy, endoscopic ultrasonography, computed tomography (CT), and positron emission tomography (PET) were routinely performed on all patients. Clinical staging and pathological examination for resected specimens were performed in accordance with the Guidelines for Clinical and Pathological Studies on Carcinoma of the Esophagus of the Japanese Society for Esophageal Diseases (10). Furthermore, tumor stage was classified according to the seventh edition of the tumor-node-metastasis classification system developed by the International Union Against Cancer (11). Lymph node metastasis was observed in 179 patients (58.3%). All lymph nodes were defined in accordance with the TNM Classification of Malignant Tumors.

**Surgical procedure**

All patients underwent radical esophagectomy with three-field lymphadenectomy (Mckeown ; 265) or with two-field lymphadenectomy (Ivor-Lewis ; 42). Gastric tubes, the jejunum, and the colon were utilized for the reconstruction of the digestive tract for esophagectomy. Additionally, the anastomotic mode was normally performed using stapling technique anastomosis. Post-mediastinal route was mostly preferred in this study than retrosternal and ante-thoracic routes. Retrosternal route was chosen to avoid interference of the mediastinal tumor recurrence with alimentary tract function. There were no cases of video-assisted thoracoscopic surgery involved in this study. Also, we performed chemoradiotherapy (CRT) for patients with tumors suspected to be T4 or to be associated with extended lymph node metastasis. Adjuvant chemotherapy was performed in 143 (46.6%) patients with pathologically identified lymph node metastasis, had good performance status, and who gave informed consent.

**Follow-up and Definition of recurrence**

Patients were assessed one month after completing treatment and every three months for the first three years and every 6 months until the fifth year. Additional examinations were made on other timings as necessary. Routinely, CT from the neck to the lower abdomen and FDG-PET/CT were carried out at least twice a year for three years after surgery and then once each year for five years after surgery. Blood sampling, including tumor marker, was performed at the same time as CT and FDG-PET examinations, and X-rays were also performed at appropriate times. Endoscopy was suggested at least every year. The mode of recurrence was classified into three patterns: locoregional, hematogenous, and mixed type (4, 5, 12). Locoregional recurrence was defined as tumors occurring on lymph nodes in the neck; mediastinum, including anastomotic site; or upper abdomen at the site of initial esophagectomy and lymph node dissection. Distant recurrence was described as hematogenous metastasis within the solid organ, abdominal paraaortic lymph nodes, or peritoneal metastasis. Mixed type was defined as recurrence which consisted of locoregional recurrence concomitant with hematogenous recurrence in the same patient, simultaneously. Overall survival (OS) indicated the interval between recurrence and death from any cause, loss to follow-up, or last follow-up. The disease-free survival time was the interval between surgery and first recurrence.

**Statistical Analysis**

We performed all statistical analyses using the JMP Pro Version 14 software (SAS Institute Japan, Tokyo, Japan). We employed the Student’s t-test or the Mann–Whitney U test to assess continuous data and Person’s Chi-squared test, Fisher’s exact test, or the Mann–Whitney U test for categorical data, as appropriate. Univariate and multivariate logistic regression analyses were performed to examine the relationship between several clinical factors and recurrence. P values < 0.05 were considered statistically significant.

**RESULTS**

**Examination of recurrence-related factors**

Recurrence was observed in 110 patients (35.8%) among all patients included in the study. Table 1 demonstrated the relationship between patient characteristics and recurrence. There were significant correlations between depth of invasion (p < 0.001), lymph node metastasis (p < 0.001), distant lymph node metastasis (p < 0.001), lymphatic invasion (p < 0.001), vessel invasion (p < 0.001), and recurrence. Moreover, the recurrence rate was significantly higher in cases where poorly differentiated components were contained in a pathological specimen (p < 0.001). In addition, recurrence was significantly higher in cases with postoperative adjuvant therapies compared with cases who underwent surgery alone (p = 0.001). However, there were no significant difference in other clinicopathological factors. Furthermore, comparison of surgical techniques did not yield any significant difference in the recurrence rate (p = 0.061) or recurrence site (p = 0.101) between two-field and three-field lymphadenectomy.

Table 2 summarizes the univariate and multivariate logistic regression analyses of factors associated with recurrence. The depth of invasion (p = 0.0027), distant lymph node metastasis (p = 0.026), lymphatic invasion (p = 0.0036), and vessel invasion (p = 0.023) were independent recurrence factors after radical esophagectomy.

**Recurrence pattern and Survival**

Table 3 illustrates the recurrence pattern in this study. Locoregional recurrence was observed in 38 cases (35%), and most cases manifested regional lymph node metastases. Distant recurrence was observed in 56 cases (51%), and 67% of distant metastasis were organ metastasis. Furthermore, mixed recurrence was exhibited in 16 (14%) cases. As regards median times until recurrence, locoregional, distant, and mixed were 260 days (38–1549), 198 days (32–2917), and 171 days (range 78–451), respectively. Ninety two percent of all recurrence cases were observed within two years after radical esophagectomy.

Figure 1A demonstrates the OS of each pattern after recurrence. There was no significant difference in terms of survival in each pattern (p = 0.988). However, this data confirmed that there was a small number of long-term survivals in each group after recurrence. Figure 1B shows the OS after recurrence in lymph node (regional lymph node metastasis plus distant lymph node metastasis) and organ recurrence. Cases of lymph node metastasis had significantly longer survival compared with cases of organ metastasis (median survival time, 1.59 year vs 0.69 year, p = 0.0032). Figure 2 describes OS by treatment for recurrence cases. As a result of extensive classification into four categories, there was a significant difference in survival among each treatment (p < 0.0001). Cases who were performed operation (only operation or plus postoperative chemotheraphy) exhibited most better survival among these groups (median survival time, 3.8 year).

**Characteristics of long-term survival cases after recurrence**

Cases that survived more than one year after recurrence treatment were defined as favorable case (n = 13), and other cases were defined was poor cases (n = 97). Table 4 shows the relationship between patient characteristics and prognosis in...
The progression of vessel invasion was significantly a poor prognostic factor for survival over one year after treatment of recurrence (p = 0.015). In addition, local treatment, such as operation or radiotherapy, can significantly lead to the elongation of prognosis (p = 0.037). However, no significant difference was found in other factors, such as age, sex, disease progression, or recurrence type. Table 5 exemplifies a list of favorable cases. It was shown that some patients had long-term survival by excision for cervical lymph node recurrence and CRT for mediastinal lymph node recurrence, although statistical analysis was not possible due to a few numbers of cases in each treatment group.

Table 1. Relationship between patient characteristics and recurrence

|                | Recurrence |          | p-value |
|----------------|------------|----------|---------|
|                | Negative (n=197) | Positive (n=110) |         |
| Age            | 66.8(42-86) | 65.2(39-80) | 0.95    |
| Sex            | Male | 173 | 94 | 0.55 |
|                | Female | 24 | 16 |        |
| Localization   | Upper | 21 | 11 | 0.46 |
|                | Middle | 90 | 43 |        |
|                | Lower | 86 | 56 |        |
| Histological type | SCC | 160 | 96 | 0.36 |
|                | Adeno | 23 | 8 |        |
|                | Others | 14 | 6 |        |
| pT             | 0/Tis | 12 | 1 | <0.001 |
|                | 1 | 101 | 16 |        |
|                | 2 | 29 | 17 |        |
|                | 3 | 51 | 66 |        |
|                | 4 | 4 | 10 |        |
| pN             | 0 | 109 | 19 | <0.001 |
|                | 1 | 58 | 26 |        |
|                | 2 | 24 | 35 |        |
|                | 3 | 6 | 30 |        |
| pM             | 0 | 192 | 92 | <0.001 |
|                | 1 | 5 | 18 |        |
| pStage         | 0 | 11 | 1 | <0.001 |
|                | 1 | 78 | 8 |        |
|                | 2 | 56 | 20 |        |
|                | 3 | 47 | 63 |        |
|                | 4 | 5 | 18 |        |
| Preoperative treatment | Present | 26 | 21 | 0.17 |
|                | None | 171 | 89 |        |
| Adjuvant therapy | Present | 78 | 65 | 0.001 |
|                | None | 119 | 45 |        |
Table 2. Univariate and Multivariate logistic regression analyses of factors associated with recurrence

| Characteristic   | Objective variables | Control | Univariate analysis | Multivariate analysis |
|------------------|---------------------|---------|---------------------|-----------------------|
|                  |                     |         | OR                  | 95% CI                | p-value     | OR   | 95% CI   | p-value |
| Age              | >66                 | ≤65     | 1.3                 | 0.82-2.09             | 0.25        | 2.9  | 1.44-5.96 | 0.0027  |
| Sex              | M                   | F       | 1.2                 | 0.61-2.40             | 0.55        | 1.7  | 0.71-4.34 | 0.22    |
| Pathological T   | T2/3/4              | T0/1    | 7.3                 | 4.17-13.6             | <0.0001     | 2.9  | 1.44-5.96 | 0.0027  |
| Pathological N   | N1/2/3              | N0      | 5.9                 | 3.42-10.7             | <0.0001     | 1.7  | 0.71-4.34 | 0.22    |
| Pathological M   | M1                  | M0      | 7.5                 | 2.89-23.3             | <0.0001     | 3.1  | 1.13-10.3 | 0.026   |
| Pathological Stage| St 2/3/4         | St 0/1  | 9.2                 | 4.64-20.5             | <0.0001     | 1.1  | 0.33-3.85 | 0.86    |
| Por component    | positive            | negative| 2.2                 | 1.37-3.76             | 0.0014      | 1.3  | 0.74-2.43 | 0.32    |
| Lymphatic invasion| ly 1/2/3            | ly 0    | 30.1                | 9.16-186.0            | <0.0001     | 6.9  | 1.78-46.0 | 0.0036  |
| Vessel invasion  | v 1/2/3             | v 0     | 8.8                 | 4.72-17.9             | <0.0001     | 2.3  | 1.11-5.21 | 0.023   |

Table 3. Recurrence pattern in this study

| Pattern                         | Number (%) |
|---------------------------------|------------|
| Local                           | 1(1)       |
| Regional LN                     | 37(34)     |
| Distant LN                      | 19(17)     |
| Distant metastasis other than LN| 37(34)     |
| Mixed                           | 16(14)     |

LN: lymph node metastasis

A. Survival comparison among each recurrence pattern
Median survival times (years) of locoregional, distant, and mixed patterns were 1.59, 1.06, and 0.71 years, respectively.

B. Survival comparison between lymph node metastasis and distant metastasis cases
Median survival times (years) of cases of lymph node metastasis and cases of distant metastasis were 1.59 and 0.69 years, respectively.

Figure 1. Overall survival after recurrence
Figure 2. Overall survival by treatment for recurrent cases
Median survival times (years) of operation, radiation, and chemotherapy groups and BSC were 3.8, 1.59, 0.92, and 0.13 years, respectively.

Table 4. Relationship between patient characteristics and prognosis in recurrence cases

|                        | Prognosis |                | p-value |
|------------------------|-----------|----------------|---------|
|                        | Poor (n=97) | Favourable (n=13) |         |
| Age                    | 65.2(39-86) | 65.2(57-74) | 0.98    |
| Sex                    | Male | 84 | 10 | 0.38 |
|                        | Female | 13 | 3 |     |
| Time to recurrence     | 218 (38 - 1549) | 309 (42 - 2917) | 0.63   |
| (day, median)          |         |                |         |
| Localization           | Upper | 10 | 1 | 0.51 |
|                        | Middle | 36 | 7 |     |
|                        | Lower | 51 | 5 |     |
| Histological type      | SCC | 83 | 13 | 0.34 |
|                        | Adeno | 8 | 0 |     |
|                        | Others | 6 | 0 |     |
| por component          | + | 45 | 5 | 0.84 |
|                        | - | 57 | 8 |     |
| ly                     | + | 94 | 13 | 0.47 |
|                        | - | 2 | 0 |     |
| v                      | + | 88 | 9 | 0.015 |
|                        | - | 8 | 4 |     |
| pT                     | 0/Tis | 1 | 0 | 0.15 |
|                        | 1 | 12 | 4 |     |
|                        | 2 | 13 | 4 |     |
|                        | 3 | 62 | 4 |     |
|                        | 4 | 9 | 1 |     |
| pN                     | 0 | 17 | 2 | 0.55 |
|                        | 1 | 21 | 5 |     |
|                        | 2 | 31 | 4 |     |
|                        | 3 | 28 | 2 |     |
| pM                     | 0 | 81 | 11 | 0.91 |
|                        | 1 | 16 | 2 |     |
| pStage                 | 0 | 1 | 0 | 0.73 |
|                        | 1 | 6 | 2 |     |
|                        | 2 | 17 | 3 |     |
|                        | 3 | 57 | 6 |     |
|                        | 4 | 16 | 2 |     |
| recurrence lesion      | locoregional | 33 | 5 | 0.93 |
|                        | distant | 50 | 6 |     |
|                        | mixed | 14 | 2 |     |
| Preoperative treatment | Present | 20 | 1 | 0.22 |
|                        | None | 77 | 12 |     |
| Adjuvant therapy       | Present | 57 | 8 | 0.84 |
|                        | None | 40 | 5 |     |
| Treatment              | OpeaCT | 8 | 3 | 0.037 |
|                        | RT±CT | 38 | 8 |     |
|                        | CT | 40 | 2 |     |
|                        | BSC | 11 | 0 |     |

BSC: best supportive care
CT: chemotherapy
RT: radiotherapy
After radical surgery, cancer progression is characterized as either a locoregional recurrence or a distant metastasis, and sometimes it includes both. In this study, we reported the current status and treatment of recurrent cases after esophagectomy. Surgical resection has constituted the main treatment option in esophageal cancer management. In Japan, cervical lymph node dissection, in addition to conventional thoraco-abdominal lymph node dissection, a three-field lymph node dissection, has been advocated for the improvement of surgical outcomes at many institutions (13). However, the use of surgery alone still results in high rates of locoregional recurrence and distant metastasis (14, 15). Despite advances in surgical methodologies, long-term survival after surgery for advanced esophageal cancer has remained poor. High rates of locoregional and distant recurrence resulted in the death of resected esophageal cancer patients and have led to intense exploration on the application of multidisciplinary approaches in esophageal cancer treatment. The implementation of perioperative chemotherapy has improved survival rates. The standard chemotherapy and treatment regimen of perioperative chemotherapy has improved survival outcomes. We hope that the accumulated data on esophageal cancer surgery. We hope that the accumulated data on esophageal cancer surgery.

Kuwano H et al. revealed the depth of invasion, tumor length, and intramural metastasis as independent prognostic factors in multivariate analysis (17). Mariette et al. (18) also reported that a multivariate analysis identified the depth of tumor invasion as a predictive recurrence factor. Thus, patients harboring these pathological risk factors should be monitored closely for any signs of recurrence. In this study, our data described that the depth of invasion, tumor length, and intramural metastasis were independent recurrence factors after radical esophagectomy. This result is consistent with previous studies, and it is necessary to consider more powerful chemotherapy in order to suppress recurrence, as much as possible, in cases possessing these recurrence factors. However, it is necessary to consider the recovery state after surgery and the advantages and disadvantages.

Moreover, in this study, distant recurrence was observed in 56 cases (51%), and 67% of distant metastases were organ metastasis. Results indicated that the efficacy of adjuvant chemotherapy is not sufficient enough to reduce organ metastases after esophageal cancer surgery. We hope that the accumulated data on the use of triple-drug chemotherapy (19) and the introduction of nivolumab (20) will show improved outcomes after esophagectomy.

In favorable cases of this study, it was illustrated that some patients had long-term survival by excision for cervical lymph node recurrence and CRT for mediastinal lymph node recurrence. With regard to patients with isolated tumor recurrence, salvage therapeutic options include systemic chemotherapy, irradiation, surgical resection, or a combination of the above. Due to poor prognosis, only a few retrospective studies with small series of selected patients and several case reports showing results of surgical treatment exist. Therefore, the benefit of surgical resection as part of multimodality treatment for patients with isolated distant recurrence in solid organs is controversial. However, it is true that there are cases where long-term prognosis is obtained by local treatment among recurrent cases, and it is important to establish a method for selecting recurrent cases that are cured by such local treatment.

Our study has several limitations. This is a single-center

**DISCUSSION**

| Table 5. List of favorable cases after recurrence treatment. |
|---|---|---|---|---|---|---|---|---|
| Case | Age | Sex | Location | pT | pN | pM | pStage | Prognostic factor | Adjuvant therapy | Time to recurrence | recurrence organ | recurrence treatment | Survival after recurrence |
| 1 | 73 | M | MI | 1a | 0 | 0 | IA | - | Khor Lewis | 673 | cervical LN | lymphadenectomy + ONF | 2946 |
| 2 | 57 | M | LR | 1a | 1 | 0 | IB | - | Michiura | 154 | long cervical LN | partial resection lymphadenectomy + IP | 3073 |
| 3 | 64 | M | MI | 2 | 2 | 1 | IV | - | Michiura | 120 | cervical LN | lymphadenectomy + OF | 2011 |
| 4 | 64 | F | L1 | 4 | 1 | 0 | IIC | CRT | Michiura | 42 | lung, 16 | CDDP + T | 2729 |
| 5 | 57 | M | MI | 1b | 1 | 0 | IB | - | Khor Lewis | 2917 | Ba, 9 | heavy or to Ba | 923 |
| 6 | 67 | F | ML | 1b | 3 | 1 | IV | - | Michiura | 1573 | - | DC/P-RT | 1935 |
| 7 | 68 | M | MI | 3 | 2 | 0 | IB | - | Michiura | 1300 | 10ps | DC/P-RT | 1901 |
| 8 | 56 | M | LR | 3 | 2 | 0 | IB | - | Michiura | 371 | mediastinal LN | DC/P-RT + IP | 1979 |
| 9 | 64 | M | LT | 2 | 0 | 0 | IB | - | Michiura | 371 | mediastinal LN | DC/P-RT + IP | 1979 |
| 10 | 73 | F | MI | 2 | 2 | 0 | IV | - | Michiura | 457 | mediastinal LN | DC/P-RT | 1901 |
| 11 | 62 | M | MI | 2 | 2 | 0 | IB | - | Michiura | 140 | chest wall | DC/P-RT + OF | 1836 |
| 12 | 74 | M | MI | 3 | 0 | 0 | IV | - | Michiura | 371 | multiple liver | OF | 1979 |
| 13 | 72 | M | L1 | 3 | 3 | 0 | HC | - | Michiura | 118 | 112, 16 | OF | 1296 |

DCF: docetaxel, cisplatin, fluorouracil
DNF: docetaxel, nedaplatin, fluorouracil
FP: fluorouracil, cisplatin
LFT: ligation or crush
TNT: docetaxel
CDDP: cisplatin
retrospective study, and results may, therefore, have been influenced by selection and statistical bias. Patients who did not receive treatment had a poor performance status, were older, or gave no informed consent were excluded from the study. Moreover, chemotherapy was frequently performed in patients with distant metastasis, whereas chemoradiotherapy was mainly employed in patients with locoregional recurrence. As the selection criteria for treatment were controlled by the physician, future work should focus on a randomized controlled trial conducted in patients who do and do not receive treatment. Due to the lack of strict guidelines on the therapeutic approach in each recurrence site, well-organized prospective multicenter studies may offer a possibility to draw firmer conclusions.

In conclusion, most esophageal cancer recurrences develop within two years after esophagectomy, and strict follow-up within two years after esophagectomy is important to establish a method for selecting recurrent cases that are cured by such local treatment.

CONFLICT OF INTEREST

The authors have no financial conflicts of interest to disclose concerning the study.

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REFERENCES

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D: Global cancer statistics. CA Cancer J Clin 61: 69-90, 2014
2. Isono K, Ochiai T, Okuyama K, Onoda S: The treatment of lymph node metastasis esophageal cancer by extensive lymphadenectomy. Jpn J Surg 20: 151-157, 1990
3. Baba M, Aikou T, Yoshinaka H, Natsugoe S, Fukumoto T, Shimazu H, Akazawa K: Long-term results of subtotal esophagectomy with three-field lymphadenectomy for carcinoma of the thoracic esophagus. Ann Surg 219: 310-316, 1994
4. Sugiyama M, Morita M, Yoshida R, Ando K, Egashira A, Ogba T, Saeki H, Oki E, Kakeji Y, Sakaguchi Y, Maehara Y: Patterns and time of recurrence after complete resection of esophageal cancer. Surg Today 42: 752-758, 2012
5. Kunisaki C, Makino H, Takagawa R, Yamamoto N, Nagano Y, Fujii T, Otsuka T, Ohno S, Furusawa M, Sugimachi K: Characteristics and sequence of the recurrent patterns after curative esophagectomy for squamous cell carcinoma. Surgery 116: 1-7, 1994
6. Fujita H, Sueyoshi S, Tanaka T, Shirouzu K: Three-field dissection for squamous cell carcinoma in the thoracic esophagus. Ann Thorac Cardiovasc Surg 8: 328-335, 2002
7. Nakagawa S, Kanda T, Kosugi S, Ohashi M, Suzuki T, Hatakeyama K: Recurrence pattern of squamous cell carcinoma of the thoracic esophagus after radical esophagectomy with three-field lymphadenectomy. Am Coll Surg 198(2): 205-11, 2004
8. Bhansali MS, Fujita H, Kakegawa T, Yamana H, Ono T, Hikita S, Toh Y, Fujii T, Tou S, Shirouzu K: Pattern of recurrence after extended radical esophagectomy with three-field lymph node dissection for squamous cell carcinoma in the thoracic esophagus. World J Surg 21: 275-281, 1997
9. Kanda M, Koike M, Shimizu D, Tanaka C, Hattori N, Hayashi M, Yamada S, Omae K, Kodera Y: Characteristics Associated With Nodal and Distant Recurrence After Radical Esophagectomy for Squamous Cell Carcinoma of the Thoracic Esophagus. Ann Surg Oncol, 2020
10. Kuwano H, Watanabe M, Sadanaga N, Kamakura T, Nozoe T, Yasuda M, Mimori K, Mori M, Sugimachi K: Univariate and multivariate analyses of the prognostic significance of discontinuous intramural metastasis in patients with esophageal cancer. J Surg Oncol 57: 17-21, 1994
11. Mariette C, Balon JM, Pissens G, Fabre S, Van Deuningen I, Triboulet JP: Pattern of recurrence following complete resection of esophageal carcinoma and factors predictive of recurrent disease. Cancer 97: 1616-23, 2003
12. Miyazaki T, Ojima H, Fukuchi M, Sakai M, Suhda M, Tanaka N, Suzuki S, Ieta K, Saito K, Sano A, Yokobori T, Hara Y, Kudo T, Hironaka S, Hara H, Kudo T, Yasui T, Ohno S, Furusawa M, Sugimachi K: Therapeutic strategy for the treatment of postoperative recurrence of esophageal squamous cell carcinoma: Clinical efficacy of radiotherapy. Dis Esophagus 24: 166-71, 2011
13. Onodera K, Yamada S: Long-term results of radiochemotherapy for solitary lymph node metastasis after curative resection of esophageal cancer. Int J Radiat Oncol Biol Phys 83: 172-7, 2012
14. Bhansali MS, Fujita H, Kakegawa T, Yamana H, Ono T, Hikita S, Toh Y, Fujii T, Tou S, Shirouzu K: Pattern of recurrence after extended radical esophagectomy with three-field lymphadenectomy. Am Coll Surg 198(2): 205-11, 2004
15. Kuwano H, Watanabe M, Sadanaga N, Kamakura T, Nozoe T, Yasuda M, Mimori K, Mori M, Sugimachi K: Univariate and multivariate analyses of the prognostic significance of discontinuous intramural metastasis in patients with esophageal cancer. J Surg Oncol 57: 17-21, 1994
16. Mariette C, Balon JM, Pissens G, Fabre S, Van Deuningen I, Triboulet JP: Pattern of recurrence following complete resection of esophageal carcinoma and factors predictive of recurrent disease. Cancer 97: 1616-23, 2003
17. Miyazaki T, Ojima H, Fukuchi M, Sakai M, Suhda M, Tanaka N, Suzuki S, Ieta K, Saito K, Sano A, Yokobori T, Inose T, Nakajima M, Kato H, Kuwano H: Phase II Study of Docetaxel, Nedaplatin, and 5-Fluorouracil Combined Chemotherapy for Advanced Esophageal Cancer. Ann Surg Oncol 22: 3653-3658, 2015
18. Kato K, Doki Y, Ura T, Hamamoto Y, Kojima T, Tsushima T, Hironaka S, Haru H, Kudo T, Iwasa S, Muro K, Yasui H, Minashi K, Yamauchi K, Ohtsu A, Kitagawa Y: Long-term Efficacy and Predictive Correlates of Response to Nivolumab in Japanese Patients With Esophageal Cancer. Cancer Sci 111: 1676-1684, 2020