Surgical complication and postoperative pulmonary function in patients undergoing tumor surgery with thoracic wall resection

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Abstract. Postoperative complications of thoracic wall resection include respiratory complications, skin necrosis and infection. The aim of the present study was to examine postoperative complications in patients who required combined thoracic wall resection during the surgical removal of a tumor. The present study included 68 patients; there were 50 patients with lung tumors and 18 patients with musculoskeletal tumors. The clinical factors associated with complications were compared between the two groups. Preoperative and postoperative pulmonary function tests were performed to examine the residual pulmonary function in 16 patients. Thoracic cage reconstruction was performed in 46 patients. Postoperative complications occurred in 30 (44.1%) patients, and one patient died from postoperative pneumonitis. Compared with the pulmonary function preoperative test results, the postoperative results revealed a decrease in the mean vital capacity percentage and an increase in the mean forced expiratory volume within 1 sec as a percent of the forced vital capacity. In patients with lung tumors, pneumonectomy can result in an increased rate of complications following thoracic wall resection. Residual pulmonary function is affected by impaired thoracic cage expansion and removal of the lung. However, the results of the present study demonstrated that these complications can be somewhat stabilized by thoracic wall reconstruction.

Introduction

Some patients who undergo surgical treatment for soft tissue tumors arising from the thoracic wall and lung tumors invading the thoracic wall require thoracic cage reconstruction. In this procedure, fixation using sutures and mesh, metal implantation, and autologous tissue are used, and a musculocutaneous flap is required if the skin defect is large (1-13). The reconstruction method is preferred with consideration given to the size and site of the defect as well as the patient's health condition and prognosis (14). The purpose of reconstruction is to achieve thoracic cage stability as well as thoracic cavity air and water tightness. Moreover, this procedure is performed for aesthetic purposes (14). At our institution, suture fixation and non- or semi-rigid fixation using a mesh are proactively performed, and have achieved good outcomes.

Complications after thoracic wall resection include respiratory problems, skin necrosis, and infection. When a lung tumor invades the thoracic wall, combined resection of the lung and thoracic wall is required. Therefore, respiratory complications can readily occur. In contrast, in patients with musculoskeletal tumors, the tumor is excised along with surrounding bone and soft tissue, such as muscle and skin, which causes skin and soft tissue defects. To date, there are few studies that have compared patients with lung tumors and those with musculoskeletal tumors (9,15). Furthermore, there is a limited number of studies on the changes in pulmonary function before and after combined thoracic wall resection (16). There is no evidence regarding the effects of reconstruction, non-reconstruction, and type of reconstruction on the functional outcomes after the procedure (9). Therefore, the present study aimed to retrospectively examine patients who required thoracic wall resection at the time of surgery for malignant tumors. The survival rates, disease-free survival period, and incidence of complications were compared between the lung tumor group and the musculoskeletal tumor group to identify the associated risk factors, and the differences between the pre- and postoperative pulmonary functions of the two groups were examined.
Patients and methods

This retrospective study included 68 patients who underwent thoracic reconstruction during surgical treatment of a tumor at our institution or an affiliated institution between 2006 and 2016 (Table I). Because of postoperative complications and respiratory function changes were expected to be different as compared with cases with simple ribs resection and/or sternotomy, patients who underwent diaphragm or vertebral resection were excluded for a simpler analysis. And patients with recurrence were also excluded. Surgical treatment was performed at the Department of Respiratory Surgery or Department of Orthopedic Surgery. During surgery, the patients were under general anesthesia with differential lung ventilation, and postoperative management was performed in the intensive care unit. The criteria for thoracic wall reconstruction using mesh included the following: i) Thoracic wall defect ≥6 cm, ii) costectomy of ≥3 ribs, or iii) suspected thoracic cage instability despite a defect in one or two ribs. In addition, reconstruction was performed by mattress sutures (suture reconstruction). COMPOSIX® Mesh (C.R.BARD) or DUALMESH® (GORE) was used, which was strongly sutured to the ribs and surrounding soft tissues to achieve water tightness. A drainage tube was inserted into the thoracic cavity of all patients. Although the wound could be covered by the skin, when the artificial objects (mesh and sutures) and lung could not be covered by the muscle, reconstruction was performed by a musculocutaneous flap. For the postoperative follow-up, computed tomography scan were performed every 3 months.

In the lung tumor group, the overall survival and disease-free survival period were classified by lymph node metastasis (N factor) and free margin (R factor) and examined. In the musculoskeletal tumor group, the overall survival and disease-free survival period were classified by the R factor and examined.

The present study was approved by the ethics review board of Aichi Cancer Center Hospital (approval no. 2017-285). The requirement for written informed consent was waived due to the retrospective nature of the study.

Complications. The incidence of complications observed within 90 days after surgery was examined. Potential predictors (age, sex, operative duration, estimated volume of intraoperative blood loss, number of resected ribs, reconstruction method, histological type, and history of resection and musculocutaneous flap reconstruction) of severe complications (grade ≥3) were analyzed using the Common Terminology Criteria for Adverse Effects (CTCAE) version 4.03 (17).

Pre- and postoperative pulmonary functions were compared among 16 patients (Table II) who consented to undergo the testing, which was performed within 2 years postoperatively.

Statistical analysis. For statistical analysis on patient background, Fisher's exact test was used for sex, Mann-Whitney U test was used for age at surgery, follow-up period, blood loss, and operation time. Fisher's exact test was used to analyze the relationship between the number of resected ribs and the reconstruction method. The survival rate and disease-free survival period (in months) of the lung tumor and musculoskeletal tumor groups were compared. The overall survival rate and disease-free survival period were calculated using the Kaplan-Meier method and compared using the log-rank test. The risk factors associated with the complications, including age, sex, operative duration, estimated volume of intraoperative blood loss, number of resected ribs, reconstruction method, presence or absence of musculocutaneous flap reconstruction, histological type (lung tumor vs. musculoskeletal tumor), and the presence or absence of combined lung resection, were examined via univariate analysis. The following statistical tests were used: Mann-Whitney U test, Fisher's exact test, and t-test. Pre- and postoperative pulmonary function were compared in terms of percent vital capacity (%VC) and forced expiratory volume within 1 sec (FEV1.0%) using a paired t-test.

All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of the R commander designed to add statistical functions frequently used in biostatistics (18).

Results

The study sample included 50 patients with lung tumors and 18 patients with musculoskeletal tumors (Table I). The patients were mostly male (58, 85.3%), with a mean age of 61.9 (range, 13-79) years at the time of surgery. Compared with the musculoskeletal tumor group, the lung tumor group mostly consisted of male patients (P=0.02) who were older at the time of surgery (P<0.01). The mean observation period was 42.4 (range, 1-164) months. No significant differences were observed in the estimated blood loss. The operation time was significantly longer in the musculoskeletal tumor group than in the lung tumor group.

Squamous cell lung cancer was the most common tumor histological type (20 patients, 29.4%), followed by pulmonary adenocarcinoma (nine patients), and large cell lung cancer (eight patients; Table III). In the musculoskeletal tumor group, chondrosarcoma was most common (three patients, 4.4%). Metastatic tumors were observed in patients with pulmonary metastasis. Two patients presented with colorectal cancer, and one patient presented with pharyngeal cancer. Regarding to the extent of resection, one, two, three, and four ribs were resected in 14, 21, 24, and four patients, respectively, and five patients underwent costectomy and sternum resection (Fig. 1). Thoracic cage reconstruction was performed in 50 (73.5%) patients. When there was only one rib resection, the reconstruction rate was significantly lower than ≥2 ribs or sternum resection. All patients with ≥4 resected ribs and those who also underwent sternum resection underwent thoracic cage reconstruction. In total, 52 (76.5%) patients also underwent resection of the lungs, and all patients in the lung tumor group also underwent lung resection. Musculocutaneous flap reconstruction was performed in 11 patients, all of whom were in the musculoskeletal tumor group. Free margins were observed in 57 (83.8%) patients (R0), microscopically positive margins (R1) were observed in 11 (16.2%) patients, and no R2 margin was observed. In the lung tumor group, the R0 margin was observed in 41 (82.0%) patients, and R1 was observed in nine (18.0%) patients. In the musculoskeletal tumor group, the R0 margin was observed in 16 (88.9%) patients, and R1 was observed in two (11.1%) patients.
In the lung tumor group, excluding patients with metastatic tumors, 35 (74.5%) patients were N0, eight (17.0%) patients were N1, and four (8.5%) patients were N2.

The overall 5-year survival rate of the patients was 57.4% (Fig. 2). The 5-year survival rates were 53.4% [95% confidence interval (CI), 37.3-67.1] in the lung tumor group and was significantly lower than the rate of 77.0% (95% CI, 43.9-92.0) in the musculoskeletal tumor group (P=0.02; Fig. 3A). There was no statistically significant difference in the disease-free survival between the two groups (P=0.41; Fig. 3B). Localized recurrence
was observed in 14 patients (20.6%) [lung tumor group: 10 (20.0%) patients; musculoskeletal tumor group: four (22.2%) patients], and postoperative distal metastasis was observed in 17 (25.0%) patients [lung tumor group: 12 (25.5%) patients; musculoskeletal tumor group: five (27.8%) patients]. The outcomes at the time of the final observation were continuous disease-free in 33 patients, alive with disease in eight patients, dead from disease in 26 patients, and dead from other diseases in one patient (Table I). No statistically significant differences were observed in the postoperative survival according to the reconstruction method or number of resected ribs.

The overall survival and disease-free survival rates by R stage and N stage are shown in Figs. 4 and 5, respectively. In our study, there were no significant differences between the overall survival and the disease-free survival rates for R and N stage.

Complications were observed in 30 (44.1%) patients, including air leak in 10 patients and atelectasis in eight patients; and other complications are presented in Table IV. The incidence of complications was 52.0% (26 patients) in the lung tumor group and 22.2% (four patients) in the musculoskeletal tumor group. Respiratory complications, such as air leak and atelectasis, were common in the lung tumor group. In the musculoskeletal tumor group, skin necrosis was the most common complication, affecting three patients. Only one patient died from postoperative pneumonitis. Thus, the perioperative mortality rate was 1.5%. The significant risk factors

### Table III. Histopathologic distribution.

| Lung tumor                          | Total n (n=50) | Bone and soft tissue tumor | Total n (n=18) |
|-------------------------------------|----------------|----------------------------|----------------|
| Squamous cell carcinoma            | 20             | Chondrosarcoma             | 3              |
| Adenocarcinoma                     | 9              | Ewing sarcoma              | 2              |
| Large cell carcinoma               | 8              | Myxofibro sarcoma          | 2              |
| Neuroendocrine carcinoma           | 4              | Solitary fibrous tumor     | 1              |
| Adenosquamous carcinoma            | 2              | Osteosarcoma               | 1              |
| Small cell carcinoma               | 1              | Angiosarcoma               | 1              |
| Non-small cell lung cancer         | 1              | Synovial sarcoma           | 1              |
| Sarcomatoid carcinoma              | 1              | Chondroid syringoma        | 1              |
| Pleomorphic carcinoma              | 1              | WDLS                       | 1              |
| Metastatic carcinoma               | 3              | UPS                        | 1              |
|                                    |                | Malignant phyllodes tumor  | 1              |
|                                    |                | Fibrosarcoma               | 1              |
|                                    |                | Inflammatory pseudo tumor  | 1              |
|                                    |                | Myofibroblastic sarcoma    | 1              |

WDLS, well-differentiated liposarcoma; UPS, undifferentiated pleomorphic sarcoma.

### Table IV. Postoperative complications.

| Complication           | Total, n (%) | Lung tumor, n | Bone and soft tissue tumor, n |
|------------------------|--------------|---------------|-------------------------------|
| Total no. of patients  | 68           | 50            | 18                            |
| Air leak               | 10 (14.7)    | 10            | -                             |
| Atelectasis            | 8 (11.8)     | 6             | 2                             |
| Bronchial obstruction  | 5 (7.4)      | 5             | -                             |
| Pain                   | 5 (7.4)      | 5             | -                             |
| Pneumothorax           | 4 (5.9)      | 4             | -                             |
| Brachial neuralgia     | 3 (4.4)      | 3             | -                             |
| Skin necrosis          | 3 (4.4)      | -             | 3                             |
| Surgical site infection| 3 (4.4)      | 2             | 1                             |
| Arrhythmia             | 2 (2.9)      | 2             | -                             |
| Aerodermectasia        | 2 (2.9)      | 2             | -                             |
| Postoperative pneumonia| 2 (2.9)     | 2             | -                             |
| Bleeding               | 2 (2.9)      | 1             | 1                             |
| Pleural effusions      | 1 (1.5)      | 1             | -                             |
| Chylothorax            | 1 (1.5)      | 1             | -                             |
| Total with duplicate, n (%) | 30 (44.1) | 26 (52.0)     | 4 (22.2)                      |
Figure 3. Overall survival and disease-free survival. (A) The Kaplan-Meier method was used to compare the overall survival according to histopathological type. The musculoskeletal tumor group exhibited significantly good prognosis ($P=0.02$). (B) The Kaplan-Meier method was used to compare disease-free survival according to histopathological type.

Figure 4. Overall survival rate by R and N factors. The Kaplan-Meier method was used to compare overall survival according to the R and N factors. The N factor was statistically analyzed with N0 as negative, and N1 and 2 as positive. There are no statistically significant differences between the factors.

Figure 5. Disease-free survival rate by R and N factors. The Kaplan-Meier method was used to compare disease-free survival according to the R and N factors. There are no statistically significant differences between the factors.
associated with severe complications (grade ≥3) included a large volume of estimated blood loss (p=0.01), lung cancer as the histological type (p=0.01), and also undergoing lung resection (p=0.03; Table V).
The patient who compared pre- and postoperative pulmonary function, details are shown in Table VI. Postoperative pulmonary function testing was performed at a mean of 12.0 (range, 3-24) months after surgery. Of the 16 patients, 13 (81.3%) presented with lung tumor and three (18.8%) with musculoskeletal tumor, of which 13 (81.3%) were male and three (18.8%) were female, with a mean age of 66.1 (range, 43-78) years (Table II). No reconstruction was performed for two patients (12.5%), reconstruction by suture fixation was performed for 10 (62.5%) patients, and mesh reconstruction was performed for four (25.0%) patients. In total, one, two, three, and four ribs were resected in three (19.0%), five (31.3%), five (31.3%), and two (12.5%) patients, respectively, and sternum resection was performed in one (6.3%) patient. Twelve (75.0%) patients were upper rib resection and three (18.8%) were lower rib resection. Lung resection was performed in 13 patients, all of which were in the lung tumor group. Single lobectomy was performed in nine patients (56.3%), wedge resection, segmental resection, segmental resection with lobectomy and double lobectomy were performed in one patient respectively (Table VI).

Compared with preoperative pulmonary function testing, postoperative pulmonary function testing revealed that the mean %VC decreased from 92.4 to 67.8% (paired t-test, P<0.01) and the mean FEV1.0% increased from 74.9 to 81.2%. %VC, vital capacity (%); FEV1.0%, forced expiratory volume within 1 sec (%).

Figure 6. Comparison of pulmonary function test. Compared with the preoperative pulmonary function test results, the postoperative pulmonary function test results revealed that the mean %VC decreased from 92.4 to 67.8% (paired t-test, P<0.01) and the mean FEV1.0% increased from 74.9 to 81.2%. %VC, vital capacity (%); FEV1.0%, forced expiratory volume within 1 sec (%).

Figure 7. Pulmonary function test compared by histopathological type. The %VC of the lung tumor group was significantly decreased post-surgery (paired t-test). *P<0.01, as indicated. %VC, vital capacity (%); FEV1.0%, forced expiratory volume within 1 sec (%); OP, operation.

Compared with preoperative pulmonary function testing, postoperative pulmonary function testing revealed that the mean %VC decreased from 92.7 to 73.8% (paired t-test, P<0.01) and the mean FEV1.0% increased from 74.3 to 77.5% (paired t-test, P=0.07; Fig. 6). Therefore, a restrictive
ventilator impairment-like change was observed postoperatively compared with the preoperative status. Comparison of the patients with lung and musculoskeletal tumors showed that the mean %VC significantly decreased from 93.9% preoperatively to 69.8% postoperatively in lung tumor patients (paired t-test, P<0.01) and increased from 87.1 to 91.0% in musculoskeletal tumor patients, but the difference was not significant (paired t-test, P=0.44; Fig. 7). The average postoperative FEV1.0% increased from 74.3 to 78.2% in lung tumor patients and from 74.7 to 74.8% in musculoskeletal tumor patients, but differences were not significant in either patient group (paired t-test, P=0.44 and 0.99, respectively). Compared with the number of resected ribs, the mean %VC decreased in all patients after the operation (Fig. 8). Additionally, the mean postoperative FEV1.0% increased in the patients other than those who underwent sternum resection. Compared with the reconstruction method, we observed a statistically significant decrease in the mean postoperative %VC and an increase in the mean postoperative FEV1.0% only in suture reconstruction (paired t-test, P=0.002 and 0.03, respectively) (Fig. 9). However, all patients who underwent pulmonary function testing did not experience problems in activities of daily living due to changes in pulmonary function.

Discussion

Thoracic cage reconstruction maintains anatomical and structural stability, protects vital organs, and helps sustain the respiratory mechanism. The procedure is required in 40-60% of individuals who have undergone thoracotomy (1,9,11).
Reconstruction is required for individuals with ≥3 resected ribs and defects that are ≥5 cm in diameter or even for patients with smaller defects and cases of suspected thoracic cage instability (9-11,13,19). Furthermore, because anterior and anterolateral movements are greater than posterior movements, thoracic cage reconstruction is often required (19). Rigid reconstruction has found wide use because it is effective for stabilizing the thorax and preventing postoperative respiratory complications, but it can be costly and also induce severe complications, including deep infections and postoperative pain, plate exposure, screw loosening (4,13). To minimize the development of postoperative complications, our group selected a simpler suture or mesh method rather than rigid reconstruction (4,20). In the present study, thoracic cage reconstruction was performed in 73.5% of the patients who underwent thoracic wall resection. To achieve thoracic cage stability, the reconstruction was performed using simple methods rather than those used in previous studies, and stable postoperative outcomes were observed.

With regard to the postoperative overall survival rate, the 5-year survival rates were 53.4% in the lung tumor group and 77.0% in the musculoskeletal tumor group. With regard to the postoperative outcomes of individuals with lung cancer who presented with thoracic wall invasion, positive margin (R1,2) and lymph node metastasis (N1,2) have been reported as poor prognostic factors (1,9,10). The number of resected ribs and thoracic wall invasion reportedly did not affect prognosis (1). Furthermore, regarding primary thoracic wall tumors, Bagheri et al (5) reported that the presence of distal metastasis significantly worsened prognosis, and any significant effect on survival was regardless of whether reconstruction was performed. According to previous studies, the 5-year survival rates are 21-61% in patients with lung cancer who present with thoracic wall invasion (1,9) and 73.9-88.5% in those with tumors arising from the soft tissues of the thoracic wall (10,19), results that are comparable to those of our study. However, in our study, neither the R factor nor the N factor caused statistically significant differences in prognosis. Since the N factor shows a tendency to worsen prognosis, it is possible that a significant difference may be obtained by accumulating a greater number of cases. Our study had a similar number of patients as in the report by Scarnecchia et al (9). The conclusion was different despite the fact that the ratios of R factor and N factor were equivalent. This can be explained by the fact that in our study, the 5-year survival rate was approximately 60%, but their study it was 44%, the thoracic reconstruction methods and reconstruction rate were different, and the average observation period was 10 months shorter in our study. Further studies are needed to clarify whether these differences affect prognosis.

Postoperative complications were observed in 44.1% of the patients. The incidence of complication was 52.0% in the lung tumor group and 22.1% in the musculoskeletal tumor group. Previously reported complications included pneumonitis, acute respiratory distress syndrome, tissue necrosis, and infection (4). Among these complications, respiratory complications are commonly associated with perioperative death, and therefore, postoperative pain and respiratory management that prevent complications are thought to be important. However, studies on the risk factors associated with the onset of complications are limited. We therefore compared the risk factors associated with severe complications in both the lung tumor and musculoskeletal tumor groups. As a result, a large volume of estimated intraoperative blood loss, a high number of resected ribs, lung tumor, and undergoing lung resection were considered to be significant risk factors. In contrast, no significant difference was observed in the incidence of severe complications in terms of whether musculocutaneous flap and thoracic wall reconstructions were performed. This result suggested that good clinical outcomes can be obtained by performing soft tissue reconstruction even in the event of extensive soft tissue defect.

Among the patients who also underwent lung resection (n=52), one patient died due to postoperative pneumonitis (1.9%). Previous studies have indicated that the perioperative mortality rate of individuals who underwent thoracic wall resection along with pneumonectomy was relatively high at 6%, which is three-fold higher than the rate for those who underwent simple lobectomy (1). Thoracic wall reconstruction was performed more often in our study than in previous studies. Although rigid reconstruction was not performed and our reconstruction method was used, the perioperative mortality rate did not increase.

Leuzzi et al (15) reported that postoperative respiratory function of patients with chest wall resection decreased %VC from 94.1 to 82.0 and FEV1.0% from 87.1 to 82.3, but reported no significant difference. And they also said that the location of chest wall defect (antero-lateral) and lung resection are significant as a risk factor for FEV1.0% decline. In the present study, postoperative pulmonary function testing showed a reduced %VC but increased FEV1.0%, and a tendency of restrictive impairment was observed. Since the detail of cases in which respiratory function tests were conducted in the report of Leuzzi et al (15) has not been clarified, the cause of the difference from our study results is not clear. In contrast, although sternotomy was described, Nishida et al (16) have reported that no significant difference in postoperative changes in FEV1.0% was observed in patients who underwent non-rigid or semi-rigid fixation, but %VC significantly decreased, and restrictive impairment was more likely to occur. This phenomenon might be attributed to reduced lung expansion resulting from thoracotomy and pneumonectomy. Among the 16 patients who underwent pulmonary function testing, 13 presented with lung tumor and underwent combined lung resection. Regarding pulmonary function after lobectomy, it has been reported that %VC decreased to 97.4% and FEV1.0% was 83 to 94% of the preoperative value 12 months after surgery (21,22). In our study, %VC decreased significantly in the lung tumor group but did not differ between before and after surgery in the musculoskeletal tumor group. In the lung tumor group, 11 of 13 patients resected the lungs as extensively as single lobectomy. Therefore, in this study, the decrease in vital capacity observed after resection of the chest wall mainly reflects the pulmonary resection, and it seems that the expansion capability of the thoracic cage is preserved.

In lung resection, reconstruction prevents the decline in pulmonary function to the extent of inhibiting activities of daily living, and this is comparable with the results of the
present study. Regarding the relationship between postoperative respiratory complications (RPCs) and postoperative pulmonary function, Haragushi et al. (23) reported in a study of elderly individuals that when the predicted postoperative (ppo) %VC and/or ppoFEV1.0% was <55%, the rate of RPCs increased. The early period showed a ppo%VC and/or ppoFEV1.0% of <55%, which is considered to be the most significant risk factor in elderly patients (23). In the present study, pulmonary function did not deteriorate to that extent, and with regard to the risk of complications, the results were permissible for our reconstruction method. The evaluation of pulmonary function according to thoracic wall resection must be validated in future studies.

The present study had several limitations. This was a retrospective study with a small sample size. Not all participants who were included in this study underwent pulmonary function testing. Moreover, the postoperative pulmonary function evaluation period slightly varied among the patients, and the effects of rigid reconstruction were not compared. However, studies that examined the postoperative vital capacity in individuals with both musculoskeletal and lung tumors are extremely limited. We consider it to be of value that the present study compared the vital capacities of individuals with both musculoskeletal and lung tumors.

In conclusion, compared with individuals with primary lung cancers, individuals with musculoskeletal tumors arising from the thoracic wall had a better prognosis and were more likely to require musculocutaneous flap reconstruction. Even in the event of extensive soft tissue defect, good clinical outcomes were obtained by performing thoracic wall and musculocutaneous flap reconstructions. When combined thoracic wall and lung resection was performed, a high rate of postoperative complications was observed. However, problems with activities of daily living due to complications were not observed in any patient. In this present study, the pulmonary function of patients who underwent thoracic wall resection alone was not thoroughly evaluated and therefore should be further examined in the future.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors’ contributions

TH analyzed the patient data and wrote the manuscript. NS, DI, EK and MY acquired the data. YS and HY were involved in the planning of the research plan, provided guidance throughout the research, and gave final approval of the version to be published. ST performed data analysis and interpretation. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the ethics review board of Aichi Cancer Center Hospital (approval no. 2017-285). The requirement for written informed consent was waived due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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