

Retrospective analysis of head and neck cancer cases from the database of the Niigata Prefecture Head and Neck Malignant Tumor Registration Committee and Niigata University

Katsuro Sato

Department of Speech, Language and Hearing Sciences, Niigata University of Health and Welfare, Niigata, Japan

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Abstract

Head and neck cancers includes oral, nasal and paranasal, nasopharyngeal, mesopharyngeal, hypopharyngeal, laryngeal, and salivary gland cancers, as well as cancers that involve the thyroid gland, ear, trachea, face, and neck. Epidemiological analysis of head and neck cancer cases in a single institution during a short period is extremely difficult because of its low incidence. We here assessed the epidemiology of head and neck cancer throughout Niigata Prefecture, and included changes in clinical features and treatment results from a single institution (Niigata University). A total of 8,572 cases were registered in the Niigata Prefecture Head and Neck Malignant Tumor Registration Committee database over 25 years, and the most common sites were larynx, followed by the oral cavity and thyroid gland. A tendency of an increasing number of cases and advanced patient ages was observed in head and neck cancer cases. In the Department of Otolaryngology, Niigata University School of Medicine, 1,288 cases of head and neck cancer were treated over a 20-year period. Data of Niigata University showed a predominance of hypopharyngeal, nasal and paranasal, mesopharyngeal, and ear cancer cases.

The 5-year survival rates of tongue, oral floor, nasopharyngeal, hypopharyngeal cancer cases that underwent pharyngolaryngectomy and pharyngolaryngoesophagectomy, and stage IV laryngeal, and ear cancer cases that underwent surgery were excellent (73.8%, 58.9%, 71.2%, 58.5%, 67.2%, and 82.4%, respectively). Further analysis of the data of Niigata Prefecture and Niigata University is required to keep abreast of advances in head and neck cancer treatment.

Introduction

‘Head and neck’ cancers are malignancies that occur above the shoulder with the exception of the intracranial and orbital regions. According to the “General Rules for Clinical Studies on Head and Neck Cancer” formulated by the Japan Society for Head and Neck Cancer, head and neck cancers occur in 7 regions: (1)the lips and oral cavity, (2)nasal cavity and paranasal sinuses, (3) nasopharynx, (4)mesopharynx, (5)hypopharynx, (6)larynx, and (7)salivary glands [1]. However, other malignancies that occur in the thyroid gland, ear, trachea, face, and neck are also recognized as head and neck cancers.

Clinical features of head and neck cancer include the following: (1)According to the scarce

Corresponding author: Katsuro Sato

Department of Speech, Language and Hearing Sciences, Niigata University of Health and Welfare, 1398 Shimami-cho, Kita-ku, Niigata City, Niigata, 950-3198, Japan

TEL/FAX: +81-25-257-4412, E-mail: katsuro-sato@nuhw.ac.jp

compared to malignancy of the other sites, advanced cases are common due to late diagnosis, because of patients lacked the knowledge on head and neck cancer; (2) a high percentage of metastatic lymph nodes in the neck; (3) involvement of fatal functional disorders such as respiration and swallowing; and (4) involvement of communication disorders such as speech and hearing [2]. In addition, tobacco smoking and chronic alcohol consumption are risk factors for head and neck cancer, and complications from other malignancies (e.g., cancers of the esophagus and lung as well as other malignancies involving the head and neck) occurs in a high percentage of head and neck cancer cases [3-5]. Furthermore, treatment standardization is difficult because of the rarity of head and neck cancer cases, and the subsequent lack of study participants outside a large cancer center.

We here assessed the epidemiological data of head and neck cancer cases from the database of the Niigata Prefecture Head and Neck Malignant Tumors Registration Committee, Niigata Prefecture, Japan in a retrospective multiple-center study. Secondly, the incidence of specific diseases and results of head and neck cancer cases

treated at Niigata University, as a single medical institution in the prefecture, is discussed.

Part I: The basic data on head and neck cancer in Niigata Prefecture, Japan

In 1986, the Niigata Prefecture Head and Neck Malignant Tumor Registration Committee was founded by the Departments of Otolaryngology of 23 hospitals. It began to survey the epidemiology of head and neck cancer throughout Niigata Prefecture [6]. Disease surveillance was conducted for 25 years until 2010, and then commenced again. Head office of the Niigata Prefecture Head and Neck Malignant Tumor Registration Committee has been set up in the Department of Head and Neck Surgery, Niigata Cancer Hospital, and annual meeting has been held once a year to confirm data validation of registered cases. Between 1986 and 2010, a total 8,572 head and neck cancer cases were identified, and the most common cancers in descending order were laryngeal (2,394 cases; 27.9%), thyroid (1,488 cases; 17.4%) and oral (1,112 cases; 13.0%) (Figure 1). The rate of laryngeal cancer was similar to that in a report of 14-year surveillance conducted by the Niigata Prefecture

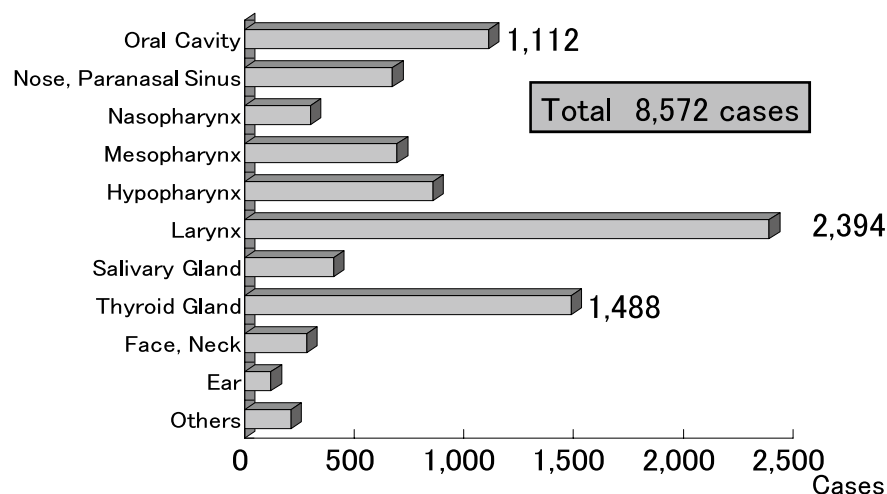


Figure 1. Head and neck cancer cases registered in the Niigata Prefecture Head and Neck Malignant Tumor Registration Committee over a 25-year period (1986-2010).

Head and Neck Malignant Tumor Registration Committee between 1986 and 1999 [3]. However, patients with thyroid and oral cancers (the second and third most common diseases) were treated in departments other than otolaryngology; therefore, construction of an inclusive database is necessary to completely elucidate the epidemiology of thyroid and oral cancers.

Part II: Incidence of head and neck cancer cases treated at Niigata University

The incidence of head and neck cancer cases treated at the Department of Otolaryngology, Niigata University School of Medicine over a 20-year period (1991-2010) was retrospectively analyzed using medical records and incidence feature was discussed by comparing with the database of the Niigata Prefecture Head and Neck Malignant Tumor Registration Committee. Clinical data of the registered cases has been presented to the department members annually and data validation has been discussed. During this period, a total of 1,288 head and neck cancer cases were treated, of which the most common in the descending order were laryngeal (277 cases;

21.5%) oral (201 cases; 15.6%), and hypopharyngeal (159 cases; 12.3%) (Figure 2). The number of laryngeal and thyroid cancer cases reported by Niigata University was relatively lower than that reported by the Niigata Prefecture Head and Neck Malignant Tumor Registration Committee, whereas the number of hypopharyngeal, nasal and paranasal, mesopharyngeal, and ear cancer cases reported by Niigata University was relatively higher. The number of consultations to laryngeal and thyroid cancer patients at Niigata University was fewer since the majority patients with these 2 diseases were treated at local hospitals. At Niigata University, hypopharyngeal and ear cancer patients are supposed to be consulted frequently, because there is a wide range of treatments available for these 2 diseases. The total number of head and neck cancer cases doubled during the 20-year period from 1991 to 2010, and the number of individual types tended to increase with the largest surge in hypopharyngeal cancer, which dominated the surge in laryngeal cancer, the most common head and neck cancer, during the 3-year period from 2008 to 2010 (Figure 3). The increase in total hypopharyngeal cancer cases

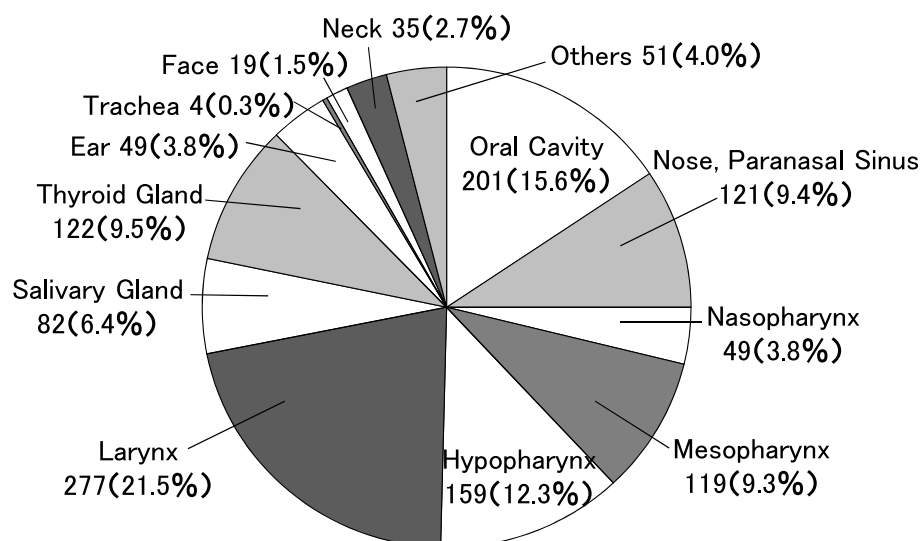


Figure 2. Head and neck cancer cases treated at the Department of Otolaryngology, Niigata University School of Medicine, over a 20-year period (1991-2010).

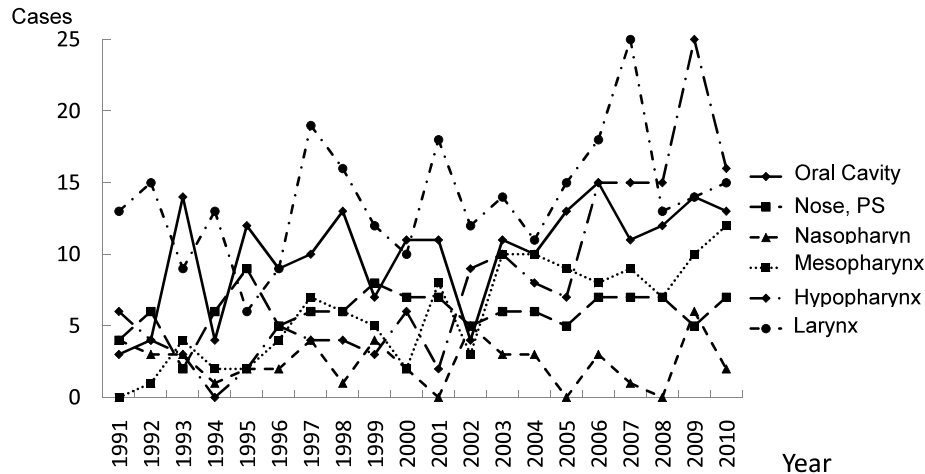


Figure 3. Treatment course of patients with any of the 6 main cancers (oral, nasal and paranasal sinus, nasopharyngeal, mesopharyngeal, hypopharyngeal, and laryngeal cancer) over a 20-year period (1991-2010). PS: paranasal sinus.

may have been due to the increased number of consultations performed at Niigata University, which has a large otolaryngology department staff. Furthermore, the 6-major cancers (oral, nasal and paranasal, nasopharyngeal, mesopharyngeal, hypopharyngeal, and laryngeal) have clinical features similar to those of head and neck cancer and were also evaluated because they were defined as “squamous cell carcinomas in the luminal organs”. The mean patient age in these 6-major cancers has been increasing (59.6 years in 1991 to 68.7 years in 2010), demonstrating an obvious tendency of late onset in head and neck cancer cases. During this 20-year period, surgery has been the primary treatment for oral cancer, and the number of surgeries performed for hypopharyngeal and laryngeal cancers has decreased. Most surgeries for oral cancer cases were performed for early diagnosis and resection, since the frequency of multiple cancers within the oral cavity is high, and lower number of hypopharyngeal and laryngeal cancer surgeries is likely a result of the increased use of chemoradiotherapy and endoscopic resection for organ preservation.

Part III: Details of Head and Neck Cancer in Niigata University

1. Oral cancer [7]

A total of 118 oral cancer cases involving 135 sites, which were treated at the Department of Otolaryngology, Niigata University School of Medicine during a 15-year period between 1991 and 2005 were clinically analyzed. The most dominant subsite was the tongue, followed by the oral floor, cheek mucosa, gingiva, lip, and hard palate. The mean patient age was 63 years, and the ratio of male to female was 1.9:1. Stage I, II, III, and IV cases accounted for 16.3, 20.7, 22.2, and 40.7% of all oral cancer cases treated at Niigata University. The distribution of subsites and stages demonstrated that communication between the faculties of the Department of Medicine and Dentistry of Niigata University is important, as the number of multiple malignancies in oral cancer cases was re-confirmed by the high-frequency multiple malignancies throughout the body and within the oral cavity. Our policy of surgery-oriented therapeutic strategy revealed an excellent 5-years survival rates of 73.8% in tongue cancer

cases and 58.9% in oral floor cancer cases (Figure 4). Since the prognosis of cases receiving radiotherapy without surgery was poor, the treatment strategy for patients who refuse surgery involves oral cancer education and frequent clinical visit to clinics, especially in cases at inoperable stages.

2. Nasopharyngeal cancer [8,9]

A total of 41 nasopharyngeal cancer cases were treated at the Department of Otolaryngology, Niigata University School of Medicine during a 17-year period between 1991 and 2007. The mean patient age was 53 year, and the ratio of male-to-female was 3.7:1. As a characteristic distribution of age, 6 cases involved patients aged under 30 years. The most common complaint was ear symptoms due to Eustachian tube obstruction in the nasopharynx, followed by neck swelling due to neck lymph node metastasis, neurological symptoms due to cranial base invasion, and nasal symptoms due to choana occlusion. The most common histopathological finding was squamous cell carcinoma followed by undifferentiated carcinoma, adenocarcinoma, spindle cell carcinoma, and malignant melanoma. For squamous cell carcinoma cases, concurrent chemoradiotherapy using platinum agents with

fluorouracil followed by adjuvant chemotherapy was most often administrated. The disease-specific 5-year survival rate was excellent at 71.2%. The differences between stage I+II and III+IV and stage I+II+III and IV were not statistically significant by using Kaplan-Meier method (Figure 5). The recurrence rate was 24.4%, and distant metastasis was more frequent compared to local recurrence. In advanced cases, it is important to make a diagnosis based on various symptoms, and chemoradiotherapy using platinum agents followed by adjuvant chemotherapy is recommended for squamous cell carcinoma cases.

3. Pharyngolaryngectomy and pharyngolaryngoesophagectomy for hypopharyngeal cancer [10]

A total of 37 hypopharyngeal cancer cases were treated by pharyngolaryngectomy and pharyngolaryngoesophagectomy at the Department of Otolaryngology, Niigata University School of Medicine during an 18-year period between 1991 and 2008. The 37 cases comprised 31.4% of the total number of hypopharyngeal cancer cases during the study period. The mean patient age was 65 years (range 39-83 years), and the proportion of males was 94.6%. Histopathological analysis revealed that

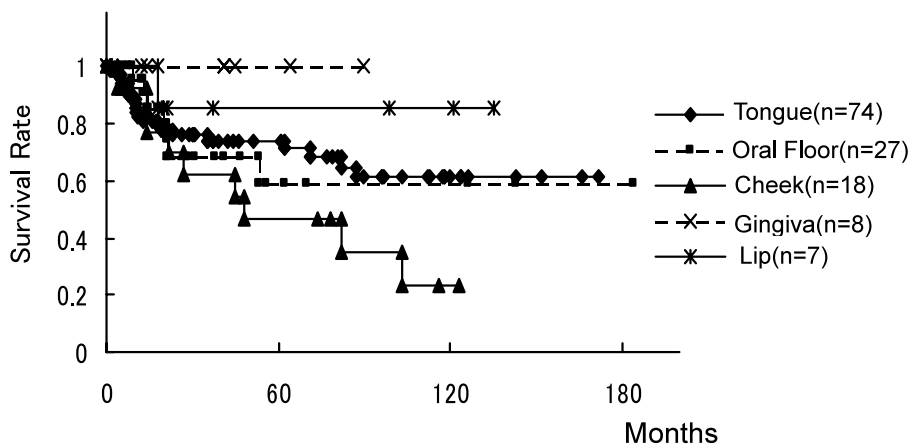


Figure 4. Prognosis of oral cancer according to the subsites.

all cases were squamous cell carcinomas and the most common disease stage was IVA, followed by III, II, and IVB. Of the surgical procedures, 62.2% were pharyngolaryngectomies and 37.8% pharyngolaryngoesophagectomies. Postoperative radiotherapy was administrated in 62.2% of the cases and chemotherapy in 40.5%. Although the recurrence rate was 37.8%, the disease-specific 5-year survival rate of all cases was fair (58.5%). The prognosis of postoperative radiotherapy, which had been histopathologically indicated for high-risk cases, was not worse than that for non-postoperative radiotherapy cases, suggesting that

usefulness of postoperative radiotherapy for high-risk cases. Local and cervical recurrence rates in the cases that underwent chemotherapy were significantly ($p=0.046$) lower than those in the cases treated without chemotherapy (Figure 6), which suggests the importance of a multi-faceted treatment strategy including chemotherapy.

4. Stage IV laryngeal cancer [11]

A total of 44 stage IV laryngeal cancer cases were treated at the Department of Otolaryngology, Niigata University School of Medicine during a 19-year period between 1991

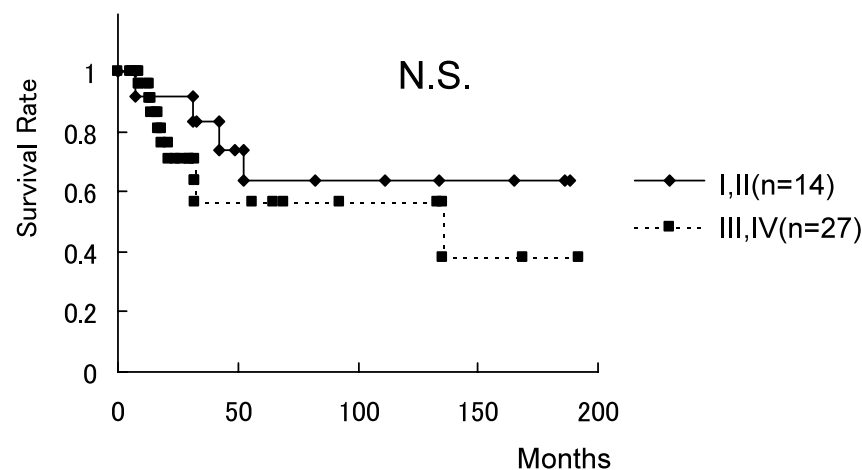


Figure 5. Prognosis of nasopharyngeal cancer according to the stage. N.S.: not significant.

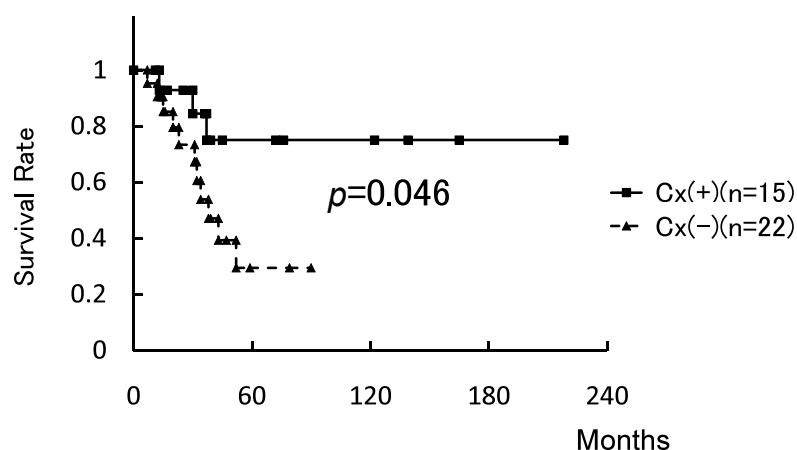


Figure 6. Prognosis of hypopharyngeal cancer cases that underwent pharyngolaryngectomy and pharyngolaryngoesophagectomy with and without chemotherapy. Cx: chemotherapy.

and 2009. Stage IV cases was 16.8% of total laryngeal cancer cases and 77.3% of stage IV cases was supraglottic types. The disease-specific 5-year survival rate of all stage IV cases was excellent at 67.2%. Since the differences between tumor stages below T3 and T4, and lymph node stages below N1 and above N2 were not statistically significant, positive treatment was useful even with advanced stage in both the larynx and neck. Laryngeal surgery resulted in no significant differences in prognosis, suggesting that the treatment choice was appropriate according to the stage of the larynx. The prognosis of cases that underwent neck dissection was significantly ($p=0.032$) better than that of those without neck dissection (Figure 7), indicating that neck with neck dissection was especially useful in cases with neck lymph nodes metastasis. Administration of radiotherapy and chemotherapy in histopathologically indicated high-risk cases had no statistical significance on prognosis, which suggested the usefulness of additional treatments in high-risk cases.

5. Ear cancer [12]

A total of 36 ear cancer cases were treated at the Department of Otolaryngology, Niigata University School of Medicine during a 17-year period between 1991 and 2007. The ear cancer

cases represented 3.5% of the 1,032 total cases of head and neck cancer during the study period. The most common primary site was the external auditory canal (66.7%), followed by the middle ear (19.4%) and auricle (13.9%). The mean patient age was 65 years (range 29-84 years) and the ratio of male to female was 1.57. The most common complaint in external auditory canal and middle ear cancer cases was otorrhea (48.4%), followed by aural itching (29.0%) and otalgia (12.9%). A past history of ear surgery was reported in 25.8% of the cases and a habit of ear picking was observed in 35.5% of cases with external auditory canal and middle ear cancers. Under our treatment policy for indication of surgery as the first-line treatment followed by postoperative radiotherapy for cases with insufficient safety surgical margins, surgery was performed in 61.8% of all cases, and primary radiotherapy was administrated in 38.2%. Post operative radiotherapy was administrated in 66.7% of the surgery cases. The 5-year survival rate of external auditory canal cancer was the highest at 73.6%, followed by auricular cancer at 66.7%, and middle ear cancer at 34.3%. The surgery cases had an excellent 5-year survival rate at 82.4%, which was significantly ($p=0.004$) better than that of inoperable cases (28.6%) (Figure 8). However, no statistical significance

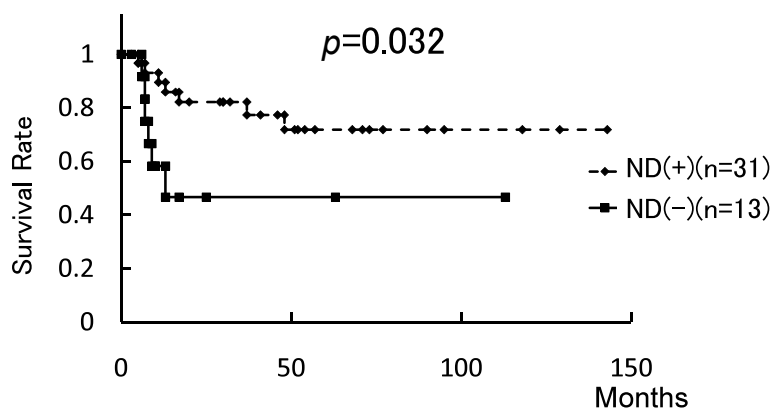


Figure 7. Prognosis of stage IV laryngeal cancer cases with and without neck dissection. ND: neck dissection.

was found between cases with and without postoperative radiotherapy in the surgical group. For ear cancer treatment, the high rate of surgery and the low number of cases refusing surgery was considered an important factor in the overall survival rate. Furthermore, postoperative radiotherapy seemed appropriate as a secondary treatment strategy.

6. Neck dissection [13]

Of a total of 131 neck cancer cases, 210 neck dissections were performed at the Department of Otolaryngology, Niigata University School of Medicine. The importance of neck dissection has been established in oral, mesopharyngeal, and

hypopharyngeal cancer cases. Recurrence in the neck after neck dissection was observed in 8.4% of cases and mortality due to neck metastasis was relatively low (19.0%). The most common disease associated with neck recurrence was oral cancer; therefore, the area of neck dissection and additional postoperative treatment should be carefully evaluated in oral cancer cases. There was a statistically significant ($p=0.0001$) difference in pathological N stage scores, although there was none in preoperative N stage scores in cases treated with or without postoperative radiotherapy (Figure 9), suggesting the importance of indicating postoperative radiotherapy. The prognosis of metastatic cases

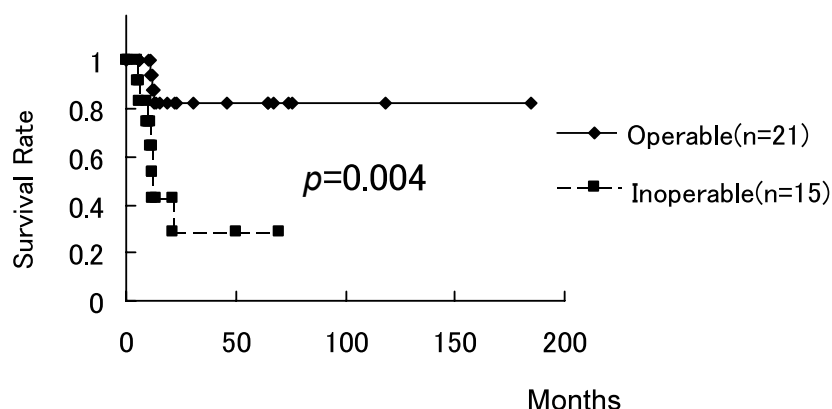


Figure 8. Prognosis of operable and inoperable ear cancer cases.

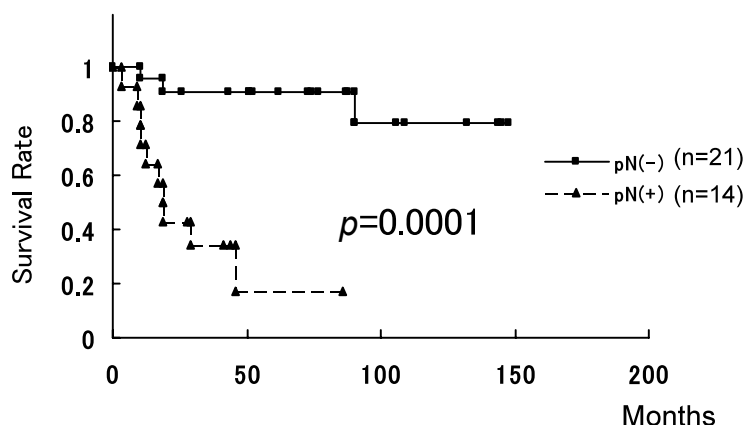


Figure 9. Prognosis of neck dissection according to positive and negative pathological node metastasis without postoperative radiotherapy. pN: pathological node metastasis.

with involvement of more than 2 lymph nodes was significantly poorer than cases with fewer than single metastatic lymph node; therefore, postoperative treatment is recommended for cases with more than 2 metastatic lymph nodes.

Conclusion

Since the incidence of head and neck cancer is low, its diagnosis tends to be late because of the lack of knowledge of head and neck cancer in patients. Wide resection surgery is often required for advanced-stage head and neck cancer; therefore, the selection of a reconstruction procedure is important. The choice of a treatment modality is difficult in neck cancer and local lesion because of the high incidence of neck lymph node metastasis [14] and the occurrence of functional complications in respiration, swallowing, and sensation. Therefore, a novel treatment strategy should be considered for the preservation of quality of life without diminishing the prognosis. Furthermore, since head and neck cancer patients have a higher incidence of multiple malignancies [3-5], treatment strategies and follow-up regarding early diagnosis of multiple malignancies are essential. Lastly, further analyses of the Niigata Prefecture Head and Neck Malignant Tumor Registration Committee and Niigata University database concerning for better cooperation of the hospitals based on the clinical character of each hospitals in Niigata Prefecture are necessary to keep abreast of advances in head and neck cancer treatment in Niigata Prefecture, Japan.

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