to their enrollment in the study.

Treatment protocol

On day 1, CDDP was administered after docetaxel. Intravenous ondansetron (8 mg) was administered prophylactically and additional antiemetic treatment (prochlorperazine) was given as necessary for a further 5 days after drug administration. Weekly docetaxel was given at a dose of 20 mg/m^2 on days 1, 8, and 15. Docetaxel was discontinued if the neutrophil count was less than 1000/μL or the platelet count was less than 75000/μL on days 8 and 15. Similarly, docetaxel was administered according to the conventional method at a dose of 60 mg/m^2 on day 1. The second cycle of chemotherapy was initiated on day 29 in both groups. Chemotherapy was continued for at least two cycles unless the patient experienced unacceptable toxicity or showed progression of the disease. The following therapy was optional and depended on the investigator's decision. TRT was begun concurrently on day 2 after chemotherapy in all patients. CT-based three-dimensional planning was conducted for treatment planning. Gross tumor volume (GTV) was defined based on the volume of the primary tumor and the involved nodes. The prescribed dose was 60 Gy, administered in 30 fractions over 6 weeks in each patient. Initial anterior-posterior opposed beams included the GTV with margins of 1 – 1.5 cm. The irradiation field was reduced to spare the spinal cord when the accumulated radiation dose to the spinal cord exceeded 40 Gy, and off-cord oblique beams were boosted up to 60 Gy according to the degree of shrinkage of the tumor and lymph nodes as estimated by subsequent CT.

Toxicity and response evaluation

During the study, physical examinations and routine laboratory measurements were performed weekly during the treatment period. If necessary, additional blood count examinations were also performed. Toxicity was evaluated according to the National Cancer Institute Common Toxicity Criteria, version 2.0, and delayed radiation toxicity occurring more than 90 days after the start of chemoradiotherapy was assessed according to the Late Radiation Morbidity Scoring Scheme of the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer. Tumor assessment by chest CT was performed after two cycles of chemotherapy; the tumor response was evaluated according to the World Health Organization criteria. All responses were evaluated carefully and confirmed by independent verification. Progression-free survival and overall survival were calculated from the date of initiation of therapy to the time of detection of disease progression, death, or the date of last follow-up. The

Kaplan-Meier method was used to determine the median and 95% confidence interval (CI) of the time-related parameters.

Results

Patient characteristics

Forty-nine consecutive patients treated between April 1998 and December 2009 were enrolled in this study. The study population consisted of 34 patients in the weekly group and 15 patients in the conventional group. The clinical characteristics of the patients are summarized in Table 1. The patients in the weekly group consisted of 32 men and 2 women with a median age of 61.4 years (range 45 – 75 years), and those in the conventional group consisted of 13 men and 2 women with a median age of 59.8 years (range 42 – 71 years). Four patients in the weekly group and 3 patients in the conventional group had ECOG PS scores of 1, while the others had a PS score of 0. The predominant histological type was adenocarcinoma (n = 19 and n = 9 in the weekly and conventional groups, respectively), followed by squamous cell carcinoma (n = 14 and n = 5, respectively). The numbers of cases of stage IIIA disease in the weekly and conventional groups were 3 and 1, respectively, and those of stage IIIB disease were 31 and 14,

Table 1

	Weekly group		Monthly group	
No.of patients enrolled	34		15	
Sex				
Male	32	94.1%	13	86.7%
Female	2	5.9%	2	13.3%
Age(years)				
Median(range)	61.4	(45-75)	59.8	(42-71)
ECOG performance status				
0	30	88.2%	12	80.0%
1	4	11.8%	3	20.0%
Histologic type				
Aenoccarcinoma	19	55.9%	9	60.0%
Squamous cell carcinoma	14	41.2%	5	33.3%
Large cell carcinoma	1	2.9%	0	0.0%
others		0.0%	1	6.7%
Stage				
III A	3	8.8%	1	6.7%
III B	31	91.2%	14	93.3%

respectively. There were no significant differences in the patient characteristics between the two groups.

Toxicity

The numbers of patients at the highest grade level of toxicity during the therapy are shown in Table 2. The hematological toxicity was generally mild in the weekly group, but leukopenia/ neutropenia were observed at a high frequency in the monthly group (Table 2a). The rates of over grade 3 leukopenia and neutropenia in the weekly and conventional groups were 11.3/23.5 and 73.3/80 %, respectirely. Thus, the rates of grade 3/4 leukopenia and neutropenia were significantly higher in the conventional group than in the weekly group. However, none of the patients developed febrile neutropenia in either group. In the conventional group, the second course of chemotherapy had to be postponed in 4 patients and radiotherapy

Table 2

toxicity	Weekly group grade					Precent grade3/4	Monthly group grade					Precent grade3/4	P
	0	1	2	3	4	(%)	0	1	2	3	4	(%)	
A.Hematologic													
Leukopenia	2	15	13	3	1	11.8	0	1	3	5	6	73.3	<0.001
Neutropenia	1	14	11	7	1	23.5	1	0	2	4	8	80.0	<0.001
Anemia	24	5	2	3	0	8.8	11	1	1	2	0	13.3	0.975
Thrrombocytopenia	27	2	2	1	2	8.8	14	1	0	0	0	0.0	0.589
B.Non-hematologic													
Nausea/vomiting	18	14	2	0	0	0.0	3	7	5	0	0	0.0	-
Anorexia	3	16	12	3	0	8.8	2	4	9	0	0	0.0	0.589
Hepatotoxicity	31	2	1	0	0	0.0	15	0	0	0	0	0.0	-
Nephrotoxicity	32	2	0	0	0	0.0	14	1	0	0	0	0.0	-
Esophagitis	7	9	12	5	1	17.6	7	0	8	0	0	0.0	0.206
Pneumonitis	15	11	4	4	0	11.8	12	3	0	0	0	0.0	0.412
Colitis	33	0	1	0	0	0.0	15	0	0	0	0	0.0	-
Hyponatremia	32	1	1	0	0	0.0	13	0	0	2	0	13.3	0.164
Dermatitis	32	0	0	2	0	5.9	11	1	3	0	0	0.0	0.860

had to be interrupted in 1 patient for 10 days due to neutropenia. Grade 3/4 thrombocytopenia was detected in 3 patients (8.8%) in the weekly group and docetaxel administration on day 15 was skipped in these patients. Day 15 docetaxel had to be cancelled in both the first and second courses of treatment in one of these patients, and only in the second course of treatment in the remaining two cases. None of the patients in the conventional group developed grade 3/4 thrombocytopenia. Grade1/2 nausea, vomiting, and anorexia were recorded in many cases, but they were well tolerated in both groups (Table 2b). One patient in the weekly group developed ischemic colitis during the first course of chemotherapy and subsequent chemotherapy was discontinued. Hepatorenal toxicity was mild in both groups. Grade 1 nephrotoxicity was recorded in 1 patient in the conventional group, and the second course of CDDP was exchanged with carboplatin in this case. In only the conventional group, 2 patients developed grade 3 hyponatremia, but they improved without specific treatment. Esophagitis more severe than grade 3 was observed in 17.6% of the patients in the weekly group. Radiotherapy had to be interrupted in 1 patient for 1 week because of esophagitis, but this patient eventually received the entire radiation dose of 60 Gy. One patient developed a bronchoesophageal fistula 3 months after chemoradiotherapy. None of the patients in the conventional group developed grade 3/4 esophagitis. Grade 1/2 radiation pneumonitis occurred in 44.1% of cases in the weekly group and in 20.0% of those in the monthly group. However, radiation pneumonitis over grade 3/4 occurred in 4 patients (11.8%) only in the weekly group.

Chemoradiotherapy could be completed in 29 subjects (85.3%) in the weekly group and in 9 subjects (60.0%) in the conventional group without any modifications to the therapeutic regimen; this difference was significant ($P < 0.05$).

Efficacy

One case showed a complete response and 29 cases showed a partial response, with an overall objective response rate of 61.2 %; those in the weekly group and the conventional group were 61.8% and 60.0%, respectively. The overall survival curve in all cases is shown in Figure 1. The MST was 26.0 months (95% CI, 11.4 – 42.8), and the 1-, 2-, and 3-year survival rates were 78.5%, 52.5%, and 41.2%, respectively. In the weekly group, the MST was 26.4 months (95% CI, 4.6 – 39.2) and the 1-, 2- and 3-year survival rates were 76.0%, 51.7%, and 48.6%, respectively. In the conventional group, MST could not be reached. The 1-, 2-, and 3-year survival rates were 91.7%, 76.4%, and 61.1%,

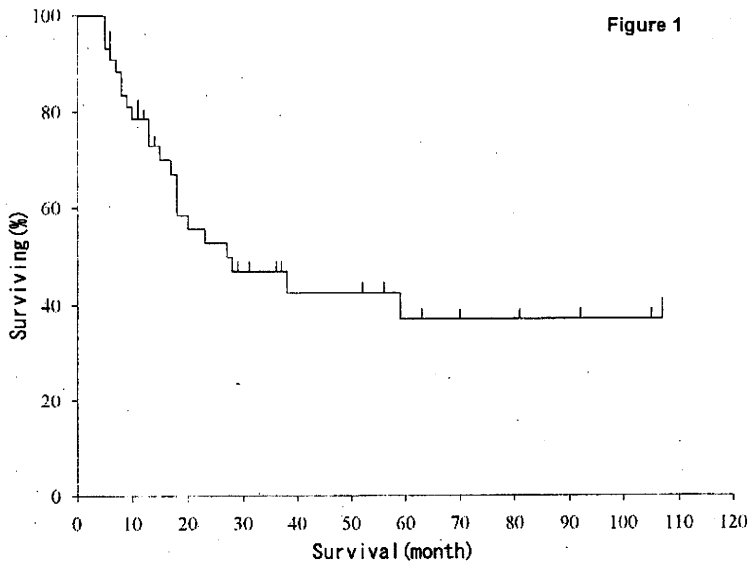

Figure 1: Overall survival of the 49 patients with locally advanced non-small cell lung cancer treated by CDDP + docetaxel chemotherapy with concurrent radiotherapy.

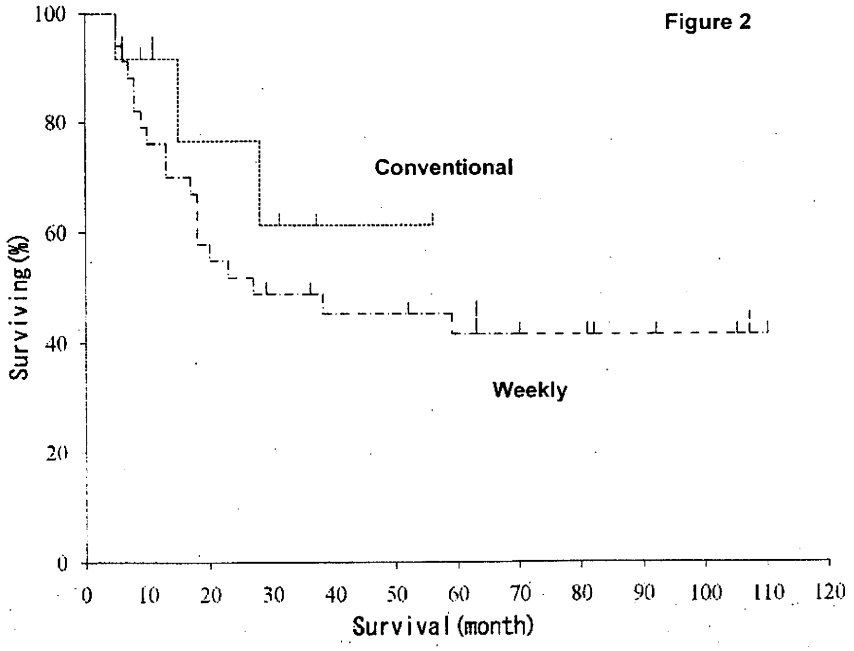

Figure 2: Overall survival of locally advanced non-small cell lung cancer treated by CDDP + weekly or conventional docetaxel chemotherapy with concurrent radiotherapy.

respectively. There were no significant differences in survival between the two groups **(Figure 2).**

Discussion

The present study was performed to compare the efficacy and toxicities of CDDP combined with weekly and conventional docetaxel along with concurrent TRT in our institute. We found that weekly use of docetaxel was a feasible combined-modality treatment with moderate toxicity, especially hematotoxicity, which resulted in a high scheduled chemoradiotherapy completion rate. However, significantly higher frequencies of esophageal and pulmonary toxicity were observed in the weekly docetaxel group compared with the group given conventional administration of docetaxel. Responses to both therapeutic regimens were observed in 61.2% of the patients, with an MST of 26.0 months and survival rates of 76.5% at 1 year and 41.2% at 3 years, with no significant differences between weekly and conventional docetaxel administration groups.

Other modified dosing schedules of CDDP + docetaxel with concomitant TRT in patients with unresectable stage III NSCLC have been reported (12 – 16). Yamamoto *et al.* (12) conducted a dose escalation study of weekly CDDP + docetaxel with concurrent TRT for NSCLC and recommended administration of CDDP at 25 mg/m^2 and docetaxel at 20 mg/m^2 on days 1, 8, and 15, with cycles repeated every 4 weeks. Wu *et al.* (13) also conducted a trial using the same schedule of chemotherapy (20 mg/m^2 of CDDP, 20 mg/m^2 of docetaxel, each week for 6 weeks). In addition, Kiura *et al.* (15) examined the effects of biweekly administration of both docetaxel + CDDP with concurrent TRT and reported a recommended dose of 40 mg/m^2 for both docetaxel and cisplatin.

High incidence rates of esophageal and pulmonary toxicity have been reported with concurrent chemoradiotherapy (3,4). For the CDDP + docetaxel regimen, severe esophageal toxicity was reported to occur at an incidence rate of 8% – 25% (12,15,16). In our experience, rates of severe esophageal and pulmonary toxicity were significantly higher in the weekly docetaxel group. However, the incidence was identical to other reports. Severe pulmonary toxicity was also more frequent in the weekly group (11.8%) than that in the conventional group in the present study. The frequency of severe pulmonary toxicity in the weekly group was also comparable to those reported for other chemotherapeutic agent combinations (8% – 20%) (3,17,18), but higher than those reported for modified CDDP + docetaxel regimens (0% – 4.8%)(12 – 16) and in the conventional group in the present study. Onishi *et al.* (10)

suggested an increased risk of radiation pneumonitis associated with weekly docetaxel combined with TRT for stage III NSCLC, because they observed pneumonitis greater than grade 3 in severity in 47% of cases. Thus, the precise risk of radiation pneumonitis associated with divided-dose docetaxel administration remains unresolved, and further detailed studies are required to reach definitive conclusions.

In the present study, the overall response rate to the combined-modality therapy (61.2%) was slightly disappointing. However, the 1-, 2-, and 3-year survival rates were 78.5%, 52.5%, and 41.2%, respectively. Kiura *et al.* (15) reported that biweekly administration of both docetaxel + CDDP with concurrent TRT showed an MST of 23.4 months, with an overall survival rate of 76% at 1 year and 54% at 2 years; these results were comparable to those of the present study. The trial was also well-tolerated. Survival in all trials must be balanced against toxicity and compliance (19). The present trial provided satisfactory prolongation of survival rate, and this may have been due to the reduced toxicity and enhanced compliance with the treatment schedule. In addition, in recently published studies of concurrent chemoradiotherapy, the MST obtained with chemotherapy was 23 months (vinorelbine/CDDP, both administered in divided doses on days 1 and 8 every 3 weeks)(20) or 27 months (biweekly docetaxel/carboplatin)(21). These findings, along with those of the present study, suggest that the efficacies of modified and divided-dose schedules of chemotherapeutic agent administration are similar to those of conventional administration schedules [3,4,6] in combined modality therapy, *e.g.*, platinum-containing chemotherapy and concurrent TRT. However, the optimum chemotherapeutic regimen using newer chemotherapeutic agents for combination with radiotherapy has not yet been established and there are no data available from phase III studies. Among the newly developed agents, weekly administration of docetaxel should be considered for locally advanced stage III NSCLC.

In summary, our results indicated that docetaxel plus cisplatin with concurrent thoracic irradiation is a potentially feasible combined-modality treatment with moderate toxicity. Although various administration methods (weekly, biweekly, or conventional) of docetaxel were studied, it is still unclear which of these shows optimal efficacy. However, the CDDP plus docetaxel

treatment regimen is promising and merits further evaluation in patients with stage III NSCLC.

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Recording of morbidity

Validation of the Total Dysphagia Risk Score (TDRS) as a predictive measure for acute swallowing dysfunction induced by chemoradiotherapy for head and neck cancers

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ABSTRACT

Background and purpose: Methods for predicting acute swallowing dysfunction in patients with head and neck cancers undergoing definitive chemoradiotherapy have not been established. We investigated the validity of the Total Dysphagia Risk Score (TDRS) as a predictive measure for this morbidity.

Materials and methods: Forty-seven patients with head and neck cancers who underwent definitive chemoradiotherapy between December 1998 and March 2006 were reviewed retrospectively. Median age was 63 years (range, 16–81). Almost all patients underwent platinum-based concomitant chemoradiotherapy. Factors of the TDRS were as follows: T-classification, neck irradiation, weight loss, primary tumour site and treatment modality. Patients were classified into three risk groups according to the TDRS.

Results: Swallowing dysfunction was observed in 27 patients (57%) as RTOG grade 2 or higher acute morbidity. This classification was significantly associated with grade 2 or higher acute swallowing dysfunction ($P < 0.001$). In ROC (receiver operator characteristic) analysis, the cut-off value of TDRS was set at 18 (sensitivity = 0.81; specificity = 0.85). Prediction of severe (grade $\geqslant 3$) acute swallowing dysfunction was similarly obtained.

Conclusion: The TDRS is a useful tool to predict acute swallowing dysfunction induced by chemoradiotherapy for head and neck cancers.

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Definitive chemoradiotherapy is now a widely accepted treatment option for patients with head and neck cancers. In recent years, it has been revealed that addition of concomitant chemotherapy to radiotherapy not only improves the outcome but also increases toxicity of the treatment. Rosenthal et al. reported that 40–70% of patients undergoing concomitant chemoradiotherapy for head and neck cancers experienced severe mucositis and 50–80% required feeding tube placement during the course of therapy [1]. Severe swallowing dysfunction arising during the course of therapy reduces the patient's quality of life and adversely affects their physical condition. Prediction of this morbidity may facilitate prophylactic intervention and prevention of these adverse effects [2], but accurate predictive methods have not been established.

Recently, Langendijk et al. advocated a simple measure designated as the Total Dysphagia Risk Score (TDRS) to predict swallowing dysfunction after curative radiotherapy for head and neck cancers [3]. They also reported that this predictive model could also be adapted for acute morbidity. Here, a retrospective review of patients with head and neck cancers who underwent definitive chemoradiotherapy in our facility was performed to investigate the validity of the TDRS as a predictive measure for acute swallowing dysfunction in these patients.

Materials and methods

Between December 1998 and March 2006, 47 patients with head and neck cancers underwent definitive chemoradiotherapy at our facility. The patients' characteristics are shown in Table 1. In our facility, definitive chemoradiotherapy is usually performed in patients with good performance status, with no distant metastasis and 75 years old or less.

All except two patients underwent platinum-based concomitant chemoradiotherapy; the two exceptions were treated by radiotherapy and docetaxel-alone chemotherapy, respectively. Various chemotherapy regimens were adopted (Table 2). As we had been searching for the optimal chemotherapy regimen for several years and the method of therapy had consequently changed over that time, the chemotherapeutic agents used in the cases included in the present study were heterogeneous. The cumulative dose of *cis*-diamminedichloroplatinum (cisplatin) ranged from 80 mg/m^2 to 300 mg/m^2 (median, 100 mg/m^2). 5-Fluorouracil (5-FU) was administered to 43 patients. The cumulative dose of

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Table 1
Patient characteristics.

Characteristics		Number of patients
Gender	Male	41
	Female	6
Age		16–81 (median: 63)
Performance status	0	44
	⩾1	3
T-classification	T2	24
	T3–T4	23
Stage	II	20
	III	6
	IV	21
Primary site	Larynx	18
	Oropharynx	11
	Nasopharynx	7
	Hypopharynx	7
	Nasal cavity	2
	Oral cavity	2
Histology	Squamous cell carcinoma	47
Chemotherapy	Platinum-based	45
	Docetaxel alone	2
Radiation schedule	Conventional fractionation	41
	Hyperfractionation	6
Neck irradiation	Local or unilateral	20
	Bilateral	27
Weight loss (baseline)	No weight loss	36
	1–10%	10
	>10%	1

Table 2
Chemotherapy regimens.

Chemotherapy agents	Number of patients
Cisplatin (10 mg/m^2 on days 36–40, 43–47) + 5-FU (400 mg/m^2 on days 36–40, 43–47)	26
Cisplatin (50 mg/m^2 on days 6–7, 41–42, 71–72) + 5-FU (800 mg/m^2 on days 1–5, 36–40, 43–47)	9
Cisplatin (80 mg/m^2 on day 29) + 5-FU (400 mg/m^2 on days 29–33)	5
Others	7

5-FU ranged from 2000 mg/m^2 to 12,000 mg/m^2 (median 4000 mg/m^2).

In radiation therapy, casts for immobilisation and a photon beam of 4 MV were used in all patients. The fraction size was 1.5–2.0 Gy. The total dose of radiation therapy ranged from 50–70 Gy, and the median dose was 70 Gy. As various treatment protocols with different fraction sizes and total doses had been used in our facility, we also calculated the biologically effective dose (BED) in a linear-quadratic model [4]. BED was defined as $nd(1 + d/\alpha/\beta)$, with units of Gy, where n is the fractionation number, d is the daily dose and α/β was assumed to be 10 for tumours and acute toxicity. The BED ranged from 60 to 84 Gy (median 84 Gy). Forty-one patients received a once-daily fractionation schedule and six patients were treated with a partially accelerated hyperfractionation schedule. In this schedule, patients initially received 40 Gy in once-daily fractionation with a fraction size of 2 Gy. Subsequently, radiation field size was reduced to avoid the spinal cord and 30 Gy was added in twice-daily fractionation with a fraction size of 1.5 Gy. Lateral opposing portals alone or lateral opposing and anterior portals (3-field approach) were used according to the individual tumour spread. Stage II disease was usually treated by locally confined portals. The whole (bilateral) neck was usually included in the treatment of stage III–IV disease initially. The spinal cord was usually avoided by cone-down field reduction after administration of 40 Gy. CT images for radiation dose distribution were attained in 14 patients. None of the patients underwent intensity-modulated radiation therapy. Overall treatment time ranged from 31 to 109 days (median, 50 days).

Morbidity was retrospectively assessed using medical records, and scored by the Radiation Therapy Oncology Group (RTOG) Acute Radiation Morbidity Scoring Criteria [5]. In these criteria, grade 2 swallowing dysfunction is defined as moderate dysphagia and/or odynophagia, which may require narcotic analgesics and/or pureed or liquid diet. Grade 3 is defined as severe dysphagia or odynophagia with dehydration or weight loss requiring naso-gastric feeding tube, intravenous fluids or hyperalimentation. The TDRS is a summation of the following risk points: T-classification (T3 = 4 points; T4 = 4 points), neck irradiation (bilateral neck irradiation = 9 points), weight loss (1–10% = 5 points; >10% = 7 points), primary tumour site (oropharynx = 7 points; nasopharynx = 9 points) and treatment modality (accelerated radiotherapy = 6 points; concomitant chemotherapy = 5 points). The definition used in this study was identical to that of Langendijk et al. [3]. In the present study, patients who underwent partially accelerated radiation therapy were not allocated to 6 points. Accordingly, the risk points of treatment modality were set at 5 in all patients. The patients were divided into a low risk group (TDRS = 0–9), intermediate risk group (TDRS = 10–18) and high risk group (TDRS > 18).

Statistical analyses were performed using the χ^2 test, and $P < 0.05$ was taken to indicate statistical significance. ROC (receiver operator characteristic) curves were also plotted to evaluate the predictive capability of TDRS for grade 2 or higher acute swallowing dysfunction.

These analyses were performed using the statistical software JMP version 5.1.1 (SAS Institute Inc., Cary, NC, USA).

Results

Grade 2 or higher swallowing dysfunction was observed in 27 patients (57%) as an acute morbidity. Of those, severe (grade ⩾ 3) dysfunction occurred in 22 patients (81%). The results of classification into three risk groups according to TDRS and the relationship between the risk groups and RTOG grade are shown in Table 3. This classification was significantly associated with both grade ⩾ 2 and grade ⩾ 3 acute swallowing function. The ROC curve was plotted to evaluate the prediction capability of TDRS for grade ⩾ 2 acute swallowing dysfunction (Fig. 1). The cut-off value was set at 18 (sensitivity = 0.81; specificity = 0.85), which was consistent with the borderline between the intermediate and high risk groups. Accuracy for prediction was moderate (area under the curve = 0.80). Almost the same accuracy was obtained when grade ⩾ 3 acute swallowing dysfunction was defined as positive (area under the curve = 0.83). The cut-off value was also set at 18 (sensitivity = 0.86; specificity = 0.76).

The median duration of severe (grade ⩾ 3) swallowing dysfunction was 53 days (range, 21–142 days). To manage the severe swallowing dysfunction, total parenteral nutrition was usually adopted at our facility. Enteral feeding was not usually adopted. Seventeen

Table 3
Relationships between the three risk groups and grading of swallowing dysfunction in RTOG Acute Radiation Morbidity Scoring Criteria.

Risk groups	Total	RTOG grade		
		0–1	⩾2	⩾3
Low	16	13 (81%)	3 (19%)	1 (6%)
Intermediate	9	4 (44%)	5 (56%)	4 (44%)
High	22	3 (14%)	19 (86%)	17 (77%)
Total	47	20 (43%)	27 (57%)	22 (47%)

The differences were statistically significant ($P < 0.001$; degrees of freedom = 2) in both grade ⩾ 2 and grade ⩾ 3 acute swallowing dysfunction.

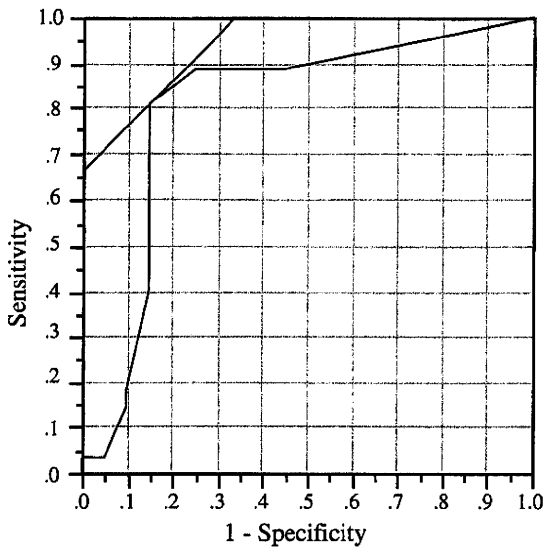

Fig. 1. ROC (receiver operator characteristic) curve to evaluate the prediction capability of the TDRS for grade 2 or higher acute swallowing dysfunction.

patients required total parenteral nutrition. No patients in the low risk group and three patients (33%) in the intermediate risk group required this procedure. In contrast, 14 patients (64%) in the high risk group required this procedure. Median duration of hospitalization after termination of treatment in the low, intermediate, and high risk group was 15 days (range, 1–31), 26 days (range, 7–117) and 41 days (range, 17–77), respectively.

Discussion

Cisplatin-based chemoradiotherapy for locally advanced head and neck cancers is now widely recognised as a standard form of therapy for patients with locally advanced disease, although considerable clinical problems remain to be resolved. This can be a rather toxic form of therapy despite using non-surgical modalities [6]. Swallowing dysfunction caused by the therapy sometimes becomes severe, and this is one of the largest obstacles in conducting concomitant chemoradiotherapy for head and neck cancers. Few previous studies have addressed this issue [7], but some reports mentioned that more than half of the cases required enteral feeding temporarily [8], and about 20% required long-term enteral feeding [1]. Nguyen et al. reported that aspiration was frequently observed during the course of therapy, sometimes leading to fatal aspiration pneumonia [9,10]. Swallowing dysfunction leads to malnutrition, which causes body weight loss during the course of therapy. This results in not only physical damage for the patients, but also worsening of the clinical outcome [11]. Body weight loss also causes dosimetric problems. The risk of delivering an inadequate radiation dose to the target volume and critical structures may arise if coordinated replanning is not performed during the course of the therapy, especially when using highly conformal methods [12].

As mentioned above, care must be taken regarding swallowing dysfunction during concomitant chemoradiotherapy for head and neck cancers and appropriate measures should be taken to alleviate secondary averse effects, such as aspiration or body weight loss. Nutritional support is a high priority issue in the management of these patients. Enteral feeding is generally the preferred method [13]. However, total parenteral nutrition was usually adopted in our facility. This might be due to preference of the attending physicians who were also in charge of the management of chemoradiotherapy for oesophageal cancers. Another part of the reason might be that healthcare system in our district has not strictly regulated this procedure.

As a measure for enteral feeding, percutaneous endoscopic gastrostomy (PEG) tube placement is one of the most effective interventions. Prophylactic PEG tube placement has been recognised as a beneficial approach for ameliorating the nutritional status of these patients [2]. Although a relatively safe procedure, PEG placement is invasive and this may leads to critical complications [14]. Therefore, it is not reasonable to place a PEG tube in all patients, and a selection index to identify patients requiring prophylactic PEG tube placement is urgently needed [2]. Several studies have addressed risk factors for severe swallowing dysfunction in radiotherapy for head and neck cancers. Manger et al. argued that clinical stage, general condition and history of smoking may be risk factors for severe dysphagia in chemoradiotherapy for head and neck cancers [8]. Poulsen et al. suggested that irradiated volume of the pharyngeal mucosa and musculature are strongly related to the swallowing toxicity in radiotherapy alone for head and neck cancers [15]. Other factors such as primary site or combined modality were also described as risk factors [2], but there is no comprehensive index in the literature. The Total Dysphagia Risk Score (TDRS) proposed by Langendijk et al. is a predictive model for swallowing dysfunction after curative treatment for head and neck cancers [3]. As this model was derived from data regarding late radiation morbidity, it is intended for prediction of late swallowing dysfunction. However, this simple model may also be useful for predicting acute morbidity, as suggested by Langendijk et al. The results of the present study indicated that TDRS is a valid measure for predicting acute swallowing dysfunction in patients with head and neck cancers undergoing definitive chemoradiotherapy. The TDRS was applicable despite the differences in patient characters and method of therapy. Thus, the TDRS may become an international index to predict swallowing dysfunction. Initially, validity of the TDRS for predicting grade 2 or higher acute swallowing dysfunction was set as the endpoint of the present study. This was due to the fact that the TDRS was defined as a measure to predict RTOG grade 2 or higher swallowing dysfunction. However, more than 80% of the morbidity in patients with experienced grade 2 or higher swallowing dysfunction was severe (grade $\geqslant 3$) in the present study. Then, we set validity of the TDRS for predicting severe acute swallowing dysfunction as another endpoint of this study. ROC analysis in our study suggested that severe acute swallowing dysfunction may be similarly predictive. These observations suggest that the TDRS could be a predictive tool for severe swallowing dysfunction. Thus, the TDRS would allow selection of the patients most likely to benefit from prophylactic PEG placement. Our previous study indicated that radiation portal size is a risk factor for severe swallowing dysfunction in chemoradiotherapy for head and neck cancers [16]. Of the five factors included in the TDRS, T-classification, neck irradiation and primary tumour site are related to radiation portal size.

The annual number of the patients included in this study was relatively low (5–6 patients per year). This was the actual number of patients which we treated during this period. In our facility, definitive chemoradiotherapy has been strictly confined to patients with quite good condition. This might lead to scarcity of the number of patients.

It is obvious that radiotherapy plays a major role in the occurrence of swallowing dysfunction. Broader mucous membranes and more anatomical parts important for swallowing would be affected to a greater degree by larger radiation portals, and these would be amplified by chemotherapy. Therefore, improving radiotherapy may allow reduction of this complication. Intensity-modulated radiotherapy (IMRT) has been widely used for head and neck cancers [17]. Using this advanced technique, complications

can now be reduced without compromising therapeutic outcome [18].

Determining whether a patient actually requires concomitant chemotherapy also must be considered [19]. Recently, use of biologically targeted therapy has been shown to improve the outcome without increasing the common toxic effects of radiotherapy plus chemotherapy [20]. These promising approaches combined with robust nutritional support may yield further improvement in the management of non-surgical therapy for head and neck cancers.

Conclusions

The TDRS has the potential to become a useful measure for predicting acute swallowing dysfunction induced by chemoradiotherapy for head and neck cancers. This measure may serve as an index to enable selection of appropriate candidates for prophylactic PEG placement.

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Conflict of interest statement

The authors report no actual or potential conflicts of interest.

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