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Palliative brachytherapy and external beam radiotherapy for dysphagia from esophageal cancer: a nationwide survey in Japan

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Abstract

Background: International guidelines recommend brachytherapy for patients with dysphagia from esophageal cancer, whereas brachytherapy is infrequently used to palliate dysphagia in some countries. To clarify the availability of palliative treatment for dysphagia from esophageal cancer and explain why brachytherapy is not routinely performed are unknown, this study investigated the use of brachytherapy and external beam radiotherapy for dysphagia from esophageal cancer.

Methods: Japanese Radiation Oncology Study Group members completed a survey and selected the treatment that they would recommend for hypothetical cases of dysphagia from esophageal cancer.

Results: Of the 136 invited facilities, 61 completed the survey (44.9%). Four (6.6%) facilities performed brachytherapy of the esophagus, whereas brachytherapy represented the first-line treatment at three (4.9%) facilities. Conversely, external beam radiotherapy alone and chemoradiotherapy were first-line treatments at 61 and 58 (95.1%) facilities, respectively. In facilities that performed brachytherapy, the main reason why brachytherapy of the esophagus was not performed was

high invasiveness (30.2%). Definitive-dose chemoradiotherapy with (≥50 Gy) tended to be used in patients with expected long-term survival.

Conclusions: Few facilities routinely considered brachytherapy for the treatment of dysphagia from esophageal cancer in Japan. Conversely, most facilities routinely considered external beam radiotherapy. In the future, it will be necessary to optimize external beam radiotherapy.

Key words: brachytherapy, chemoradiotherapy, dysphagia, Esophageal cancer

Introduction

Esophageal cancer is the eighth most common type of cancer worldwide and the sixth leading cause of cancer-related death (1). Patients with metastatic esophageal cancer have a poor prognosis, including a median survival of 5.5–7.6 months (2, 3). Dysphagia is the predominant symptom in >70% of patients with metastatic esophageal cancer, and it severely affects patient quality of life and necessitates nutritional support (4).

The 2014 Cochrane Database of Systematic Reviews concluded that self-expanding metal stent (SEMS) insertion was a safe, effective and swift treatment for dysphagia palliation compared with other modalities and high-dose intraluminal brachytherapy is a suitable alternative with fewer requirements for re-intervention, additional survival benefits and a better quality of life (5). This strong recommendation was based on two randomized controlled trials (6, 7). However, according to previous surveys, brachytherapy is infrequently used to palliate dysphagia in Europe and the USA (8–11).

Despite the strong evidence supporting brachytherapy, several clinical practices have reported the effect of external beam radiotherapy (EBRT) in patients with dysphagia from esophageal cancer (12–17). Currently, the availability of palliative treatment options for dysphagia from esophageal cancer and the main reasons why brachytherapy is not routinely performed are unknown.

Thus, the current survey investigated palliative treatment focused on brachytherapy and EBRT for dysphagia from esophageal cancer and the current patterns of practice in Japan.

Methods

The Japanese Radiation Oncology Study Group (JROSG) working subgroup on palliative radiotherapy created a survey questionnaire (Table 1). All JROSG members were radiation oncologists. The survey assessed palliative treatment options for dysphagia from esophageal cancer; the total numbers of patients treated with brachytherapy, EBRT alone or chemoradiotherapy in the calendar year 2018; the main reasons why brachytherapy was not routinely performed; and palliative treatments including radiotherapy dose fractionation that they would recommend for three hypothetical cases. Case 1 described a patient with thoracic esophageal cancer and expected long-term survival. Case 2 described a patient with thoracic esophageal cancer, expected limited survival and severe renal failure. Case 3 described a patient with cervical esophageal cancer, expected mid-term survival and mild renal failure.

The survey was sent by email to all JROSG members at 136 facilities on June 7, 2019, and the deadline for replying was 14 July 2019.

Results

In total, 65 radiation oncologists at 61 facilities (44.9% of the JROSG facilities) responded. Of the respondents, 47 (72.3%) worked at university hospitals or cancer centers, and 18 (27.7%) worked at public hospitals. Among the facilities, 43 (70.5%) routinely performed brachytherapy in clinical practice, whereas four (6.6%) performed brachytherapy of the esophagus.

Figure 1 presents the first- and second-line palliative treatment options for dysphagia from esophageal cancer. Brachytherapy was the first-line treatment at only three (4.9%) facilities, whereas it was a second-line option at four (6.6%) facilities. Conversely, EBRT alone and concurrent chemoradiotherapy were first-line treatments at 61 (100%) and 58 (95.1%) facilities, respectively.

The median numbers of patients with dysphagia treated with brachytherapy, EBRT alone, or concurrent chemoradiotherapy per year at all facilities were 0 (range, 0–1), 2 (0–24), 3 (0–80), respectively. The total numbers of patients treated with brachytherapy, EBRT alone and concurrent chemoradiotherapy per year at all facilities were 2, 209 and 425, respectively.

At facilities that performed brachytherapy, the main reason why brachytherapy of the esophagus was not routinely performed was its high invasiveness (30.2%). Other reported reasons included a lack of experience (23.3%), complexity (18.6%), logistical problems (18.6%), a lack of awareness concerning recommended treatments (2.3%) and others (7%).

Figure 2 presents the first- and second-line palliative treatment options for dysphagia from esophageal cancer for hypothetical cases 1–3. For case 1, 46 of 65 (70.8%) respondents selected concurrent chemoradiotherapy as the first-line treatment, whereas SEMS insertion was the second-line treatment for 25 (32.3%) respondents. For case 2, 58 (89.2%) respondents selected EBRT alone as the first-line therapy, and SEMS was the second-line treatment for 20 (30.8%) respondents. For case 3, 30 (46.2%) respondents each selected concurrent chemoradiotherapy and EBRT alone as the first-line treatment, whereas 25 (38.5%) respondents selected percutaneous endoscopic gastrostomy as the second-line therapy.

Figure 3 presents the dose-fractionation schedules for cases 1–3. In total, 17 different dose schedules were described, ranging from 20 Gy in five fractions to 66 Gy in 33 fractions. In case 1, the most commonly prescribed regimen was 50 Gy in 25 fractions (16/55 [29.1%] respondents). Concurrent chemoradiotherapy with a definitive dose (≥50 Gy) was selected by 33 of 55 (60%) respondents. In case 2, the most commonly prescribed regimen was 30 Gy in 10 fractions (29/58 [50%] respondents). In case 3, the most commonly prescribed regimen was 50 Gy in 25 fractions (14/60 [23.3%] respondents).

Table 2 presents the results of a published survey reporting the palliative treatment of dysphagia from esophageal cancer in Italy (9). Brachytherapy was not considered a treatment option in Italy, similarly as observed in our survey.

Discussion

This survey further clarified the availability of brachytherapy and EBRT for the management of dysphagia associated with

Table 1. Survey questionnaire on the role of palliative therapy for dysphagia from esophageal cancer

All questions refer to the common practice in your hospital.
Q1. In your hospital, is brachytherapy routinely performed? (Yes/No)
Q2. Is brachytherapy of the esophagus performed for the treatment of dysphagia? (Yes/No)
Q3. Which of these are available as first-line treatments for dysphagia from esophageal cancer? (Brachytherapy/Self-expanding metal stent/External beam radiotherapy/Concurrent chemoradiotherapy/Chemotherapy/Bypass surgery/Percutaneous endoscopic gastrostomy/Endoscopic dilation/Other)
Q4. Which of these are available as second-line treatments for dysphagia from esophageal cancer once other treatment modalities have failed? (The same options as Q3)
Q5. How many patients with dysphagia from esophageal cancer have you treated with brachytherapy, radiotherapy alone, or concurrent chemoradiotherapy in the calendar year 2018?
Q6. If brachytherapy of the esophagus is not routinely performed, what is the main reason? Which are the other reasons? (Lack of experience/Complexity/Lack of effective response/Strong toxicities/High invasiveness/Lack of awareness of recommended treatment/Logistical problems/Other)
If brachytherapy of the esophagus is not routinely performed, what are the main reasons? (Lack of experience/Complexity/Lack of effective response/Strong toxicities/High invasiveness/Lack of awareness of recommended treatment/Logistical problems/Other)
Q7. Do you have any plans to continue/start utilizing brachytherapy for dysphagia from esophageal cancer? (Yes/No)
Q8. Hypothetical cases
What is your first-line treatment for dysphagia in Cases 1–3? (The same options as Q3) If you selected brachytherapy or EBRT, please indicate the dose fractionation.
What is your second-line treatment for dysphagia in Cases 1–3 once other treatment modalities have failed? (The same options as Q3) If you selected, brachytherapy or EBRT, please indicate the dose fractionation.
Case 1. Patient with expected long-term survival
A 60-year-old man was diagnosed with cT4aN3M1 stage IVB esophageal squamous cell carcinoma (UICC, 8th edition). Gastrointestinal endoscopy revealed stricture of the thoracic esophagus at 24–32 cm from the incisor. Radiologic examinations revealed multiple lung metastases. His dysphasia score is 3 (able to swallow liquids only). His ECOG PS is 1.
Case 2. Patient with expected relatively limited survival and severe loss of kidney function
An 80-year-old man was diagnosed with cT4aN3M1 stage IVB esophageal squamous cell carcinoma. Gastrointestinal endoscopy revealed stricture of the thoracic esophagus at 24–32 cm from the incisor. Radiologic examinations revealed multiple lung metastases. He has severe renal failure with an eGFR of 30 mL/min. His dysphasia score is 3. His ECOG PS is 3.
Case 3. Patient with cervical esophageal cancer, expected middle-term survival and mild loss of kidney function
A 70-year-old man was diagnosed with cT4aN3M1 stage IVB esophageal squamous cell carcinoma. A gastrointestinal endoscopy revealed stricture of the cervical esophagus at 15–23 cm from the incisor. Radiologic examinations revealed multiple lung metastases. He has mild renal failure with an eGFR of 45 mL/min. His dysphasia score is 3. His ECOG PS is 2.
ECOG PS, Eastern Cooperative Oncology Group performance status; eGFR, estimated glomerular filtration rate; EBRT, external beam radiotherapy; UICC, Union for International Cancer Control

Table 2. Published survey reporting the palliative therapy for dysphagia from esophageal cancer

		Italy	Japan
Year		2016	2019
Responding facilities (%)		68/177 (38.4)	61/136 (44.9)
Facilities routinely performed brachytherapy (%)		40/68 (58.8)	43/61 (70.5)
Facilities performed brachytherapy of the esophagus (%)		7/40 (17.5)	4/43 (9.3)
Facilities using brachytherapy as the first-line treatment for dysphagia from esophageal cancer (%)		3/40 (7.5)	3/43 (7)
Facilities using brachytherapy as the second-line treatment for dysphagia from esophageal cancer (%)		4/40 (10)	4/43 (9.3)
Facilities using self-expanding metal stent insertion as the first-line treatment for dysphagia from esophageal cancer line (%)		37/40 (92.5)	31/43 (72.1)
Limitations hindering the use of brachytherapy (%)	Lack of experience	10/40 (25)	10/43 (23.3)
	Complexity	2/40 (5)	8/43 (18.6)
	Logistical problems	1/40 (2.5)	8/43 (18.6)
	Lack of effective response	1/40 (2.5)	0
	High invasiveness	0	13/43 (30.2)
	Lack of awareness of recommended treatment	0	1/43 (2.3)
	Other	16/40 (65)	3/43 (7)

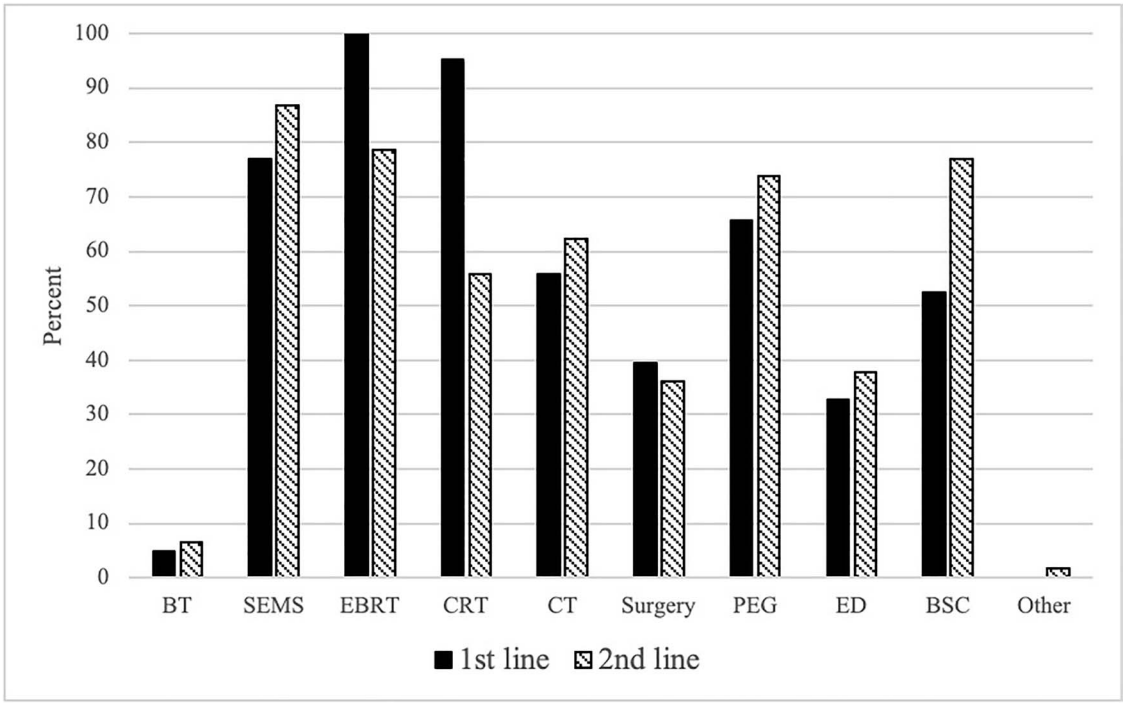

Figure 1. Palliative treatment options for dysphagia from esophageal cancer. BT, brachytherapy; EBRT, external beam radiotherapy; CRT, chemoradiotherapy; CT, chemotherapy; PEG, Percutaneous endoscopic gastrostomy; ED, endoscopic dilation; BSC, best supportive care.

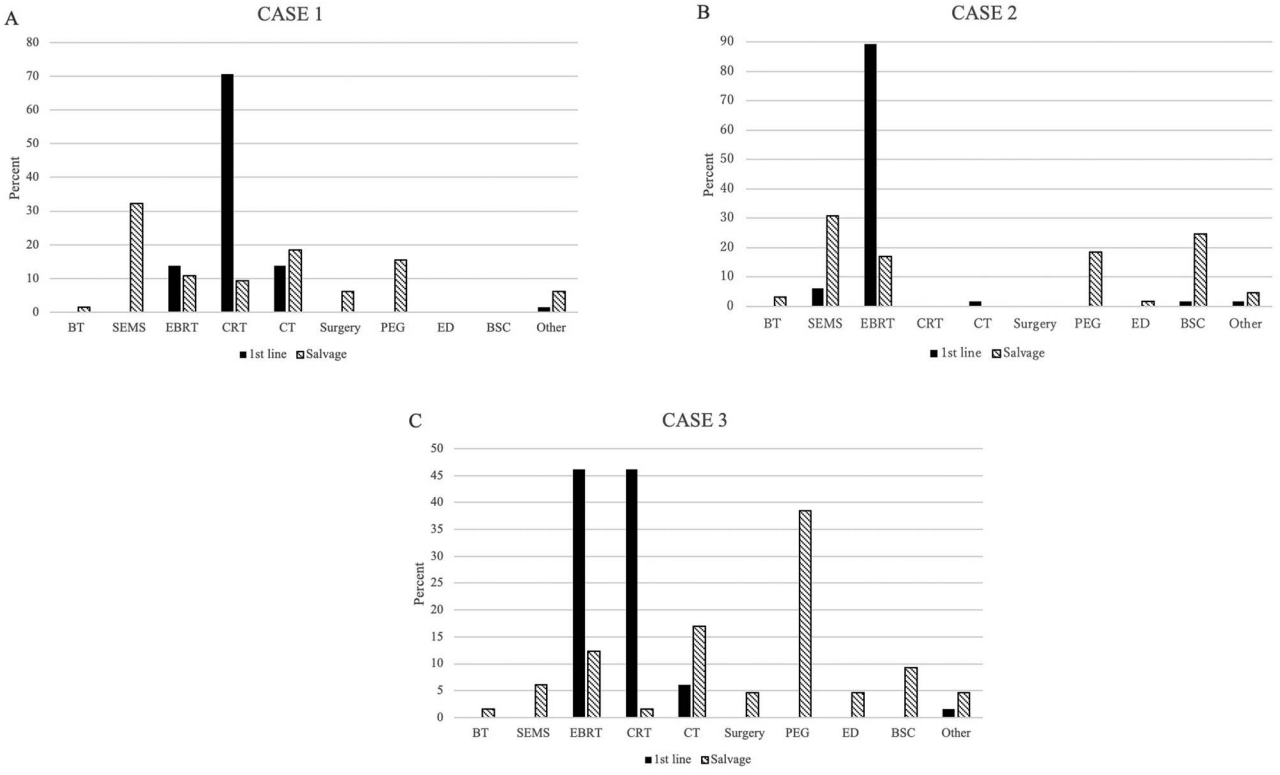

Figure 2. Palliative treatment options for dysphagia from esophageal cancer for hypothetical case (A) 1, (B) 2 and (C) 3. BT, brachytherapy; EBRT, external beam radiotherapy; CRT, chemoradiotherapy; CT, chemotherapy; PEG, Percutaneous endoscopic gastrostomy; ED, endoscopic dilation; BSC, best supportive care.

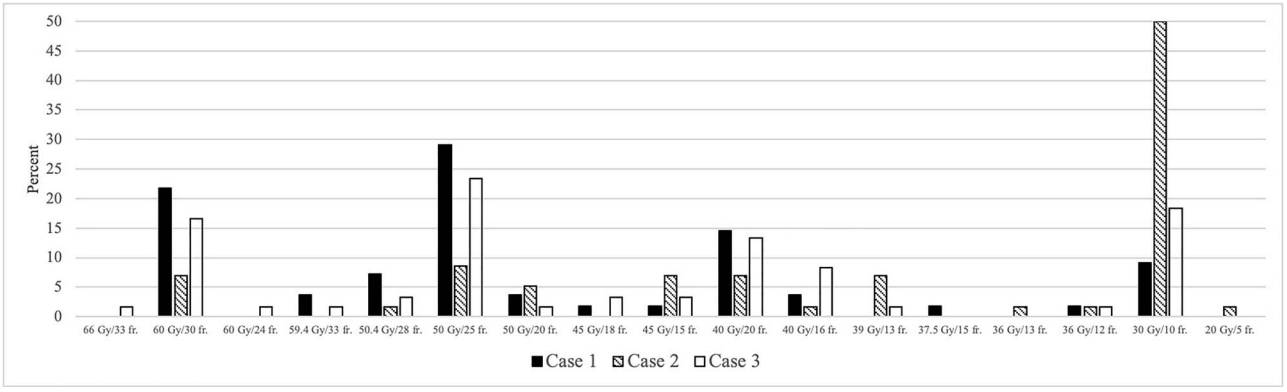

Figure 3. Dose-fractionation schedules for palliative radiotherapy of esophageal cancer.

esophageal cancer. The findings revealed that only a few facilities routinely considered brachytherapy for the treatment of dysphagia from esophageal cancer mainly because of its high invasiveness. Conversely, almost all facilities routinely considered EBRT.

The reason for the reported high invasiveness of brachytherapy in this study might be the assumption that the procedure, including the setup, applicator insertion, image review and irradiation, would be performed without sedation. In a previous study, all patients were sedated with midazolam during treatment (6). However, using sedation routinely has been linked to complexity. It may be difficult to sedate patients in poor general health conditions, making the requirement of another physician, such as an anesthesiologist, necessary for sedation. Moreover, a matched comparison of brachytherapy versus EBRT had recently described significant improvements in pain after treatment with EBRT (18). These findings may reflect that brachytherapy has a lower acceptance rate than EBRT.

The lack of experience also appeared to deter the popularization of brachytherapy for the treatment of dysphagia from esophageal cancer. In fact, in facilities that routinely performed brachytherapy for patients with dysphagia from esophageal cancer, the number of cases treated per year was low, in line with the results of the Italian survey (9). Palliative chemoradiotherapy also has a risk of high invasiveness, whereas the lack of experience with brachytherapy might be linked to its high invasiveness compared with routinely performed definitive chemoradiotherapy for locally advanced esophageal cancer. The 2017 Japanese guidelines for esophageal cancer stated that brachytherapy is an uncommon treatment for dysphagia, whereas EBRT was weakly recommended (19). This could be linked to the underuse of brachytherapy.

The lack of awareness regarding recommended treatments was not the main reason for the underuse of brachytherapy. Before this survey, we believed that a lack of awareness might explain the underuse of brachytherapy, which might have necessitated a public awareness campaign. Contrary to our expectation, it was not the main cause. In general, patients with dysphagia from esophageal cancer are primarily diagnosed by oncologists, gastroenterologists or surgeons. Case discussion may not be routinely performed for dysphagia from esophageal cancer after definitive treatment is excluded and palliative treatment is proposed. In the current survey, it was unclear whether oncologists, gastroenterologists and surgeons lacked awareness of the recommended treatments for dysphagia from esophageal cancer. In this regard, each facility should have case discussion to support the adoption of a fully multidisciplinary approach to the management of patients with dysphagia from esophageal cancer involving oncologists, gastroenterologists, surgeons and radiation oncologists.

In our survey, chemoradiotherapy with a definitive dose (≥50 Gy) was commonly selected for the case with expected long-term survival. Recent studies found that local therapies such as radiotherapy may control primary lesions and prolong the survival of some patients with metastatic disease (20, 21). A study using the National Cancer Database found that definitive-dose chemoradiotherapy to primary sites of distant metastatic esophageal cancer can result in excellent local control, favorable outcomes and long-term survival for some patients (22). However, it remains unclear whether definitive-dose chemoradiotherapy is suitable for palliative purposes. A previous phase III study found that palliative chemoradiotherapy consisting of 30–35 Gy in 10–15 fractions resulted in a modest, but not statistically significant, increase in dysphagia relief and minimal improvement in dysphagia-related progression-free survival compared with the effects of radiotherapy alone (30–35 Gy in 10–15 fractions) (23). Conversely, other retrospective studies reported that a higher radiation dose schedule provided improvements in nutrition-support-free survival and a longer time to the second intervention (14, 17). To establish a new treatment option, a clinical trial assessing definitive-dose chemoradiotherapy in patients with dysphagia from esophageal cancer is needed.

Our survey had several limitations. Our results might not accurately represent the practice of radiation oncologists because of the relatively low response rate (44.1%) and small absolute sample size ($n = 61$). Moreover, recommendations for hypothetical cases might not accurately reflect clinical management. However, it is extremely important to understand the practice patterns, and the findings will be considered in future next clinical trials.

In conclusion, brachytherapy is infrequently considered a treatment option for dysphagia from esophageal cancer in Japan mainly because of its high invasiveness, whereas EBRT is routinely recommended. Our survey clarified the reasons for the discrepancy between the best available evidence and common practices. The results of this survey indicated scope for considering the irradiation dose for EBRT, thereby warranting a clinical study to optimize EBRT use in future trials.

Conflict of interest statement

Dr. Harada received grants from Japan Agency for Medical Research and Development, The National Cancer Center Research and Development Fund, and Health, Labour and Welfare Science Research

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Author contributions

T.K. prepared the manuscript and conducted the literature search; T.K. reviewed and edited the manuscript; and T.K., A.T., H.W., H.H., H.K., H.N., J.H., K.M., K.Y., M.T., M.F., M.N., N.N., N.U., N.A., S.S., T.K., T.T., T.S. and N.S. reviewed the manuscript. All authors have read and approved the final manuscript.

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