


Dysphagia progression-free survival in oesophageal cancer patients treated with palliative radiation therapy



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Background: In patients with advanced oesophageal carcinoma, palliation of dysphagia is important to maintain a reasonable quality of life.

Aim: To determine the dysphagia progression-free survival (DPFS) in patients with advanced oesophageal carcinoma treated with palliative radiotherapy (RT).

Setting: Groote Schuur Hospital, Cape Town, between January 2015 and December 2016.

Methods: The medical records of all patients with oesophageal carcinoma were reviewed, and patients who were not candidates for curative treatment and received palliative RT were selected. For these patients, the dysphagia score (DS) was recorded prior to RT, six weeks after RT and at each follow-up visit. The DPFS was calculated as the time from completion of RT to worsening of DS by ≥ 1 point or until death. Other outcomes measured were objective change in DS and survival post RT.

Results: The study population comprised 84 patients. Squamous cell cancer was the primary histological subtype (93%). The median duration of DPFS after RT was 73 days, with approximately two-thirds of remaining patients able to swallow at least liquids and soft diet until death. The difference in median duration of DPFS was not statistically significant in stented versus non-stented patients (54 days vs 83 days, $p = 0.224$). The mean change in DS was 0.45 ± 0.89 points following RT and the post-RT survival was significantly shorter in patients with stent insertion (81 days vs 123 days, $p = 0.042$).

Conclusion: Palliative RT can successfully be used to prolong DPFS in patients with locally advanced and metastatic squamous cell cancer of the oesophagus.

Keywords: oesophageal cancer; locally advanced; dysphagia score; palliative radiotherapy; squamous cell cancer.

Introduction

In 2018, approximately 572 000 new cases of oesophageal cancer were diagnosed worldwide, and this was the seventh most common cancer diagnosed in South Africa.^{1,2,3} Approximately 70% of cases in England, Scotland and Northern Ireland in 2014 were diagnosed at a late stage.¹ Although definitive data are lacking for South Africa, most new cases follow a similar trend, with a high percentage of patients presenting with locally advanced or metastatic disease. One retrospective study conducted in South Africa by Dandara et al.⁴ examining all patients presenting with oesophageal cancer over a 30-year period reported that 76% of patients presented with advanced disease and poor clinical condition requiring palliative care.⁴ In those patients receiving palliative care, the average survival was approximately 4–6 months.^{4,5}

Dysphagia is documented as the most common presenting symptom, prompting patients with oesophageal cancer to seek medical care and has a substantial impact on quality of life which becomes more significant in advanced disease.^{6,7} One large study conducted by the American College of Surgeons⁸ reported dysphagia in 74% of the 5044 patients enrolled. Palliation of this symptom is crucial to maintain an acceptable quality of life in these patients.^{9,10,11}

Currently no consensus guidelines are available for the optimal management of dysphagia in patients with locally advanced and metastatic oesophageal cancer. Options for palliation include stent placement, dilatation, external beam radiotherapy (RT), brachytherapy, chemotherapy, laser treatment, and photodynamic therapy or ablation.^{12,13} Various studies have been carried out comparing the benefit of RT, both external beam radiotherapy (EBRT) and brachytherapy to

endoscopic stenting while evaluating various end points to determine the efficacy of treatment. Retrospective studies demonstrated that endoluminal stenting that provided earlier and more rapid relief of symptoms, however, was associated with recurrent dysphagia in the long-term¹¹ while RT provides more durable response.¹⁴ These studies suggested the optimal management for palliation of dysphagia in these patients is a combination of endoluminal stenting and RT or brachytherapy.^{13,14,15,16} Palliative chemoradiation shows a modest but not significant benefit over RT alone¹⁷; and considering the increased toxicity associated with concurrent chemoradiation, it is not considered a viable option in palliation. Although previous data suggest effective relief of dysphagia in patients with locally advanced and metastatic oesophageal cancer treated with palliative RT,⁵ only limited data are available to suggest the duration of this response. One retrospective study of the use of RT in palliation of dysphagia conducted in the Netherlands by Caspers et al.¹⁸ reports improvement in dysphagia score (DS) in 70.5% of patients with a median dysphagia-free interval of 3.7 months. Another retrospective study conducted in Germany by Welsch et al.¹⁹ between 1994 and 2004, analysing 139 patients with advanced or incurable oesophageal cancer treated with palliative RT, that is, with EBRT, brachytherapy or a combination of both EBRT and brachytherapy, reported subjective symptom relief in 72% of patients with a median response duration of five months.¹⁹ Our study was primarily aimed at examining the overall duration of response to RT in our clinical setting and to identify the contributing factors that may affect the overall response to palliative RT.

Methods

Study aims and objectives

The aim of this study was to assess the benefits of palliative RT in the management of patients with locally advanced and metastatic oesophageal cancer at a single institution.

The primary objective was to determine the median dysphagia progression-free survival (DPFS) after RT in patients with locally advanced or metastatic oesophageal cancer. The secondary objectives were to compare the duration of DPFS in patients with and without oesophageal stenting to determine the overall quantitative objective improvement in DS after receiving palliative RT in patients with advanced oesophageal cancer and to determine the median overall survival (OS) and post-RT survival of patients following palliative RT.

Study population

The records of all new patients who presented with oesophageal cancer to the gastro-oesophageal oncology clinic at Groote Schuur Hospital, Cape Town, between January 2015 and December 2016 were reviewed. Only patients with stage I–III oesophageal cancer, who were not candidates for the potentially curative treatment (i.e. not physiologically fit, tumours involving adjacent organs or multi-station and bulky lymphadenopathy), or with stage IV disease were selected. Further inclusion criteria were patients determined

to have a DS of 1–4 at initial visit or during follow-up using the Knyrim et al.²⁰ dysphagia grading system (see Appendix 1) and were treated with palliative radiation. Patients who were less than 18 years of age, had received chemotherapy for carcinoma of the oesophagus, had percutaneous endoscopic gastrostomy insertion or patients with tracheo-oesophageal fistulae were excluded from the study.

Scientific design

This was a retrospective, observational study. The patients meeting the inclusion criteria were selected for further data collection and analysis.

Treatment

All patients were reviewed in the gastro-oesophageal multidisciplinary team meeting for a treatment decision. Patients were selected for palliative treatment based on the characteristics at presentation such as poor Eastern Cooperative Oncology Group performance status (PS [ECOG]), significant weight loss $\geq 10\%$ baseline body weight, low body mass index (BMI), multiple medical comorbidities and poor general clinical condition. Because of the limited resources, only patients who were being considered for curative treatment were staged with computed tomography (CT) scan of the chest, abdomen and pelvis. All patients who presented with DS grade 3 or 4 were referred to the upper gastroenterology surgical service for assessment of stent insertion. They were reviewed post-stent insertion; an updated DS was assigned based on the current clinical status and they were assessed for palliative RT. The palliative RT was offered to patients who had significant symptoms such as dysphagia and odynophagia and were in reasonable clinical condition. The aim was to maintain swallowing and control pain, whereas patients whose general condition was too poor that the palliative RT was thought not to add any benefit were supportively treated.

The choice of fractionation schedule was at the radiation oncologist's discretion and three fractionation regimes were used at our centre, namely, 4.6 Gy \times 4# (Equivalent dose in 2 Gy fractions [EQD2 = 28.0 Gy]), 4.0 Gy \times 5# (EQD2 = 28.0 Gy) or 3.0 Gy \times 10# (EQD2 = 36.0 Gy), assuming an alpha and beta ratio of 3 for late effects. Patient factors including socio-economic were considered in deciding fractionation schedule; in general, the higher dose of RT was offered to patients were planned using 2-D simulation technique. The patients were positioned supine with head rest, knee and ankle stocks for immobilisation and an anterior image was taken. In patients with a stent *in situ*, the field was placed to encompass the stent and an additional 2 cm margin superiorly, inferiorly and laterally. In patients without a stent *in situ*, 10 mL of barium was given orally and a fluoroscopic image was taken to determine the site of the tumour. The field was then placed to encompass the lesion with an additional 5-cm margin superiorly, inferiorly and 2 cm laterally. The patients were treated with photons, either Cobalt-60 (Co-60) or 6 Megavoltage (MV) X-rays, once per day (Monday–Friday) with a treatment break on weekends.

Patients were reassessed six weeks after completing RT and then routinely every three months or earlier if dysphagia worsens. The medical records of these patients were reviewed for objective worsening of DS at these visits. The DPFS was taken as the date from the completion of RT to worsening of DS by ≥ 1 point. Patients who died without returning to follow up with complaint of increasing dysphagia were assumed to have DPFS from the time of radiation therapy until death. This information was used to calculate the median DPFS in the patient population and to compare the median DPFS in patients with and without stent insertions. The objective improvement in DS was calculated by determining the change in DS after RT for each patient. These values were used to determine the mean objective improvement in DS. The OS and post-RT survival were measured from the date of diagnosis and date of completion of RT, respectively, to the date of death.

Statistical analysis

Formal sample size calculations were not performed. The number of subjects was chosen based on the feasibility of data collection and was considered sufficient to meet the study objectives.

The data collected was stored in the REDCap (Research Electronic Data Capture) database and the interface was used to process the data and analyse the variables relevant to the study. The data collected using REDCap software was only accessible to the primary investigator and the student investigator.

Stata MP version 14 software was used for data processing and analysis. Continuous variables were presented as mean/standard deviation (s.d.) or median/interquartile range (IQR) depending on data distribution. Continuous data were analysed using independent *t* test or Mann–Whitney U test.

Kaplan–Meier survival analysis was performed to determine the DFPS, OS and post-RT survival; and log-rank test was performed to test for significant differences in the probability of survival by stent insertion. Time 0 was defined as the day the patient completed RT. To determine the variables associated with DPFS, change in DS and post-RT survival, multiple linear regression analysis was performed. The variables analysed were gender, age, PS(ECOG), DS at presentation, time of RT and post-RT, histological subtype, site of primary tumour, RT fractionation schedule, stent insertion and weight loss $> 10\%$ of baseline. Variables with $p < 0.20$ in the univariate analysis (i.e. simple linear regression) were entered into the adjusted model. Model building was then performed using a backward elimination technique, and p -values ≤ 0.05 were considered statistically significant. These results were displayed as charts and tables.

Ethical considerations

The study proposal was approved by the Human Research and Ethics committee of the Faculty of Health Sciences at University of Cape Town. HREF: 106/2018

Results

A total of 84 patients presenting to the gastro-oesophageal carcinoma clinic between the period January 2015 and December 2016 met the inclusion criteria for the study. The patient- and disease-specific factors were grouped by variables such as gender, age group, PS (ECOG), histological subtype and location of primary tumour are provided in Table 1.

A slight predominance of male patients 46 (54.8%) versus female patients 38 (45.2%) was observed. The mean age was 59 years and the modal age group was 51–60. More than 50% of all patients were between 50 and 70 years. No patients in our study population were younger than 31 years of age. Most patients were observed to have a PS (ECOG) 2 or 3. Regarding the duration of symptoms, most patients had symptoms for > 3 –6 months prior to

TABLE 1: Demographics and disease-related variables in the study population.

Variable	Patients	
	<i>n</i>	%
Gender		
Male	46	54.8
Female	38	45.2
Age group (years)		
18–24	0	0.0
25–30	0	0.0
31–40	3	3.6
41–50	16	19.0
51–60	30	35.7
61–70	19	22.8
71–80	13	15.5
> 80	3	3.6
Performance status (ECOG)		
0	0	0.0
1	27	32.1
2	33	39.3
3	21	25
4	3	3.6
Histological subtype		
Squamous cell carcinoma	78	92.9
Adenocarcinoma	6	7.1
Location of primary tumour		
Upper 1/3	13	15.5
Middle 1/3	46	54.8
Lower 1/3	16	22.6
Gastro-oesophageal junction	6	7.1
Duration of symptoms		
< 1 month	1	1.2
> 1 –3 months	22	26.2
> 3 –6 months	34	40.5
6–12 months	20	23.8
1–2 years	6	7.1
> 2 years	1	1.2
Loss of weight		
Yes	73	86.9
No	11	13.1
$< 10\%$	13	17.8
$> 10\%$	60	83.2

ECOG, Eastern Cooperative Oncology Group.

presentation; and the mean duration of symptoms was 6.1 months before seeking medical attention. The most common presenting symptoms were dysphagia and weight loss. More than 85% of patients had reported weight loss as shown in Table 1; of these > 75% reported losing more than 10% of their baseline body weight.

The most common histological subtype was squamous cell cancer (78 patients; 92.9%) versus adenocarcinoma (6 patients; 7.1%). The most common subsite among all patients was the middle third of the oesophagus (46 patients; 54.8%) followed by the lower third of the oesophagus (16 patients; 22.6%). The least common subsite was the gastro-oesophageal junction (6 patients; 7.1%).

More than 90% of the patients had a DS ≥ 2 at presentation. Approximately half of the patients had insertion of oesophageal stent (43 patients, 51.2%). Most patients presenting with DS ≤ 2 did not have oesophageal stent insertion. Of the patients with grade 4 dysphagia who were referred for stent insertion, one failed to have the procedure because of poor PS (ECOG) (Table 2). After stent insertion, 100% of patients had an improvement in DS by ≥ 1 point.

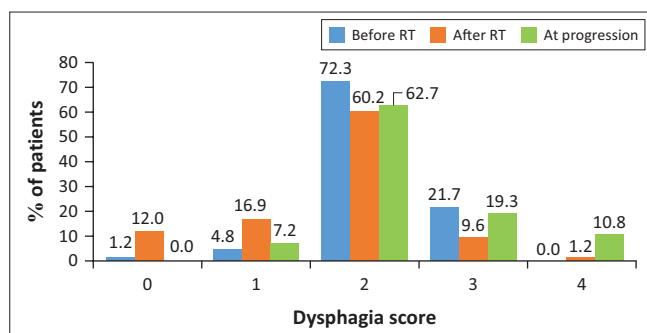
For the delivery of palliative RT, three fractionation regimens were used, namely, 18 (21%) of patients received 20.0 Gy in 5#, 60 (71%) received 18.4 Gy in 4# and 6 (7%) received 30.0 Gy in 10#.

The DS as assessed prior to starting RT, after RT and at the time of progression of dysphagia is shown in Figure 1. One patient was lost to follow-up and hence the data for the remaining 83 patients were analysed. Prior to RT, the

TABLE 2: Dysphagia score at presentation and in patients having stent insertion.

Dysphagia score	Total		Stent insertion	
	n	%	Yes	No
0	2	2.4	0	2
1	5	6.0	0	5
2	40	47.6	14	26
3	22	26.2	15	7
4	15	17.9	14	1
Total	84	-	43[†]	41[‡]

[†], 51.2%; [‡], 48.8%.

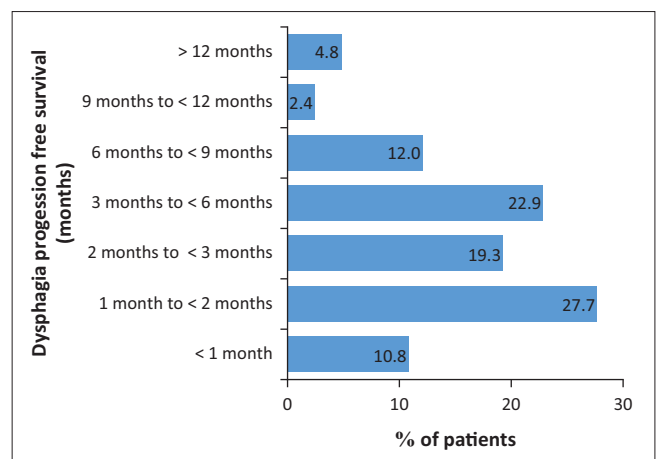


RT, radiotherapy.

FIGURE 1: Bar chart showing Dysphagia score at various time intervals.

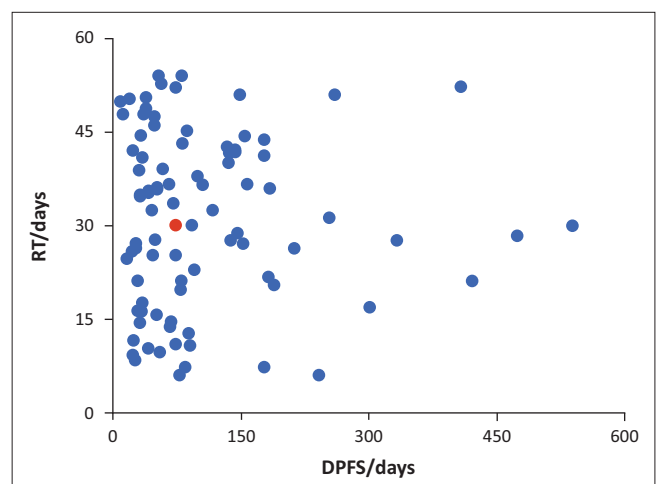
majority of patients (94%) had DS of grade 2 or 3. Our study did not include any patients with grade 4 dysphagia at the time of RT as all patients seen post-stent insertion with DS of grade 4 either did not meet the inclusion criteria or died prior to receiving RT. At the post-RT review, 58 patients (68.9%) had DS of grade 2 or 3. One patient (1.2%) had a deterioration in DS to grade 4 following RT.

The duration of DPFS is represented in the column chart (Figure 2) and scatter plot (Figure 3). The median DPFS calculated using the ungrouped data was 73 days (IQR: 35–145) (Figure 4). Simple and multiple linear regression analyses were performed to assess the association between DPFS and several variables. The median DPFS appeared to have a numerically significant difference between those with and without stent insertion, with patients with a stent having a shorter duration of DPFS (median 54 days; [IQR: 31–98]) than those without a stent (median 83 days; [IQR: 45.5–176.5]) (Figure 5). However, this result in conjunction with the log-rank test ($p = 0.224$) confirmed no statistical significance between DPFS in patients who were stented and those who were not.



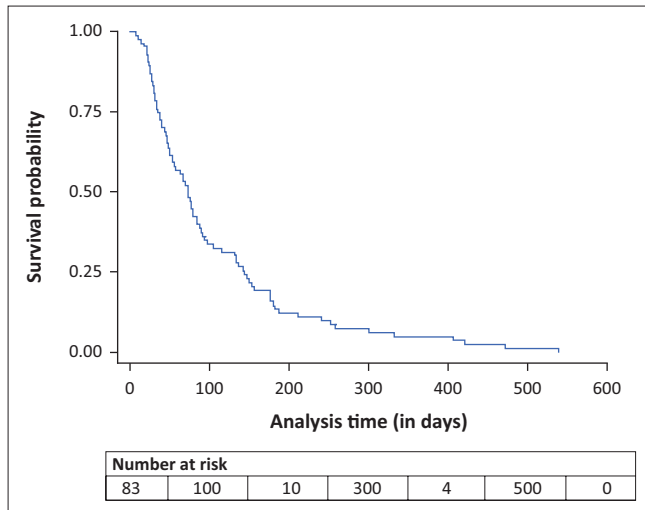
DPFS, dysphagia progression-free survival.

FIGURE 2: Duration of dysphagia progression free survival.



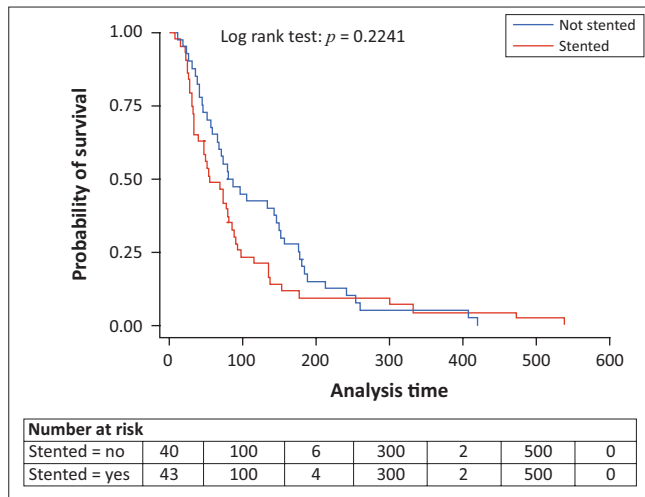
DPFS, dysphagia progression-free survival; RT, radiotherapy.

FIGURE 3: Scatterplot showing distribution of DPFS (ungrouped data).



DPFS, dysphagia progression-free survival.

FIGURE 4: Kaplan-Meier survival estimate for DPFS in all patients who received palliative RT.



DPFS, dysphagia progression-free survival.

FIGURE 5: Kaplan-Meier survival estimates for DPFS in patients with or without stent insertion who received palliative RT.

A simple regression analysis showed the median duration of DPFS significantly differed by DS at presentation ($p = 0.045$), DS after RT ($p < 0.0001$) and PS (ECOG) ($p = 0.036$) (Table 3). Using multiple linear regression, only the DS after RT ($p < 0.0001$) was found to be significantly associated with DPFS. From this analysis, for every 1 point increase in DS, the DPFS decreased by 61 days.

The objective changes in DS when reassessed at six weeks after palliative RT were as follows: 4 (4.8%) of patients had worsening of DS, 48 (57.8%) of patients had no change in DS from baseline; however, 31 patients (37.3%) had an improvement in DS following RT; 21 patients (25.3%) reported an improvement in DS by 1 point, 8 patients (9.6%) reported an improvement by 2 points and 2 patients (2.4%) reported an improvement by 3 points. The mean objective change in DS was 0.45 ± 0.89 points in all patients at six weeks post-RT treatment and 0.28 ± 0.80 points in stented and 0.63 ± 0.95 points in non-stented patients. Independent t test showed that the difference in mean objective

TABLE 3: Simple linear regression analysis for variables associated with dysphagia progression-free survival.

Variable	Simple linear regression analysis		
	Beta coeff.	95% CI	p
Stent insertion (Ref: No)	-24.26	-70.65–22.13	0.301
Age category (Ref: <60)	-6.12	-52.77–40.54	0.795
DS at presentation	-24.94	-49.25–-0.63	0.045*
DS at time of RT	-40.33	-82.56–-1.89	0.061
DS after RT	-60.88	-85.05–-36.71	< 0.0001*
PS (Ref: PS 1/2)	-53.66	-103.74–-3.57	0.036*
Gender (Ref: Female)	-13.43	-60.17–33.31	0.569
Histology (Ref: SCC)	42.43	-47.20–132.05	0.349
Site of tumour (Ref: Upper 1/3)			
Middle 1/3	-13.25	-81.53–55.03	0.700
Lower 1/3	28.36	-49.31–106.02	0.470
GEJ	54.08	-51.23–159.40	0.310
RT fractionation scheduled (Ref: 20.0 Gy/ 5#)			
18.4 Gy in 4#	-32.94	-89.89–24.02	0.253
30 Gy in 10#	-58.44	-158.15–41.26	0.247
Weight loss (Ref: No)			
Yes, $\leq 10\%$	4.38	-85.58–94.3	0.923
Yes, $> 10\%$	8.88	-64.17–81.93	0.809

RT, radiotherapy; PS, performance status; GEJ, gastro-oesophageal junction; CI, confidence interval; coeff., coefficient.

*, Statistically significant.

TABLE 4: Simple linear regression analysis for variables associated with mean objective change in dysphagia score.

Variable	Simple linear regression analysis		
	Beta coeff.	95% CI	p
Stent insertion (Ref: No)	-0.35	-0.73–0.04	0.076
DS at presentation	-0.03	-0.24–0.18	0.776
DS at time of RT	0.56	0.22–0.90	0.001*
PS (Ref: PS 1/2)	-0.16	-0.59–0.27	0.465
Histology (Ref: SCC)	-0.12	-0.87–0.63	0.749
Site of tumour (Ref: Upper 1/3)			
Middle 1/3	-0.004	-0.58–0.58	0.990
Lower 1/3	0.16	-0.50–0.82	0.626
GEJ	-0.08	-0.98–0.81	0.854
RT fractionation scheduled (Ref: 20.0 Gy/ 5#)			
18.4 Gy in 4#	-0.17	-0.65–0.30	0.477
30 Gy in 10#	-0.61	-1.44–0.22	0.147
Weight loss (Ref: No)			
Yes, $\leq 10\%$	0.32	-0.43–1.06	0.404
Yes, $> 10\%$	0.13	-0.47–0.74	0.663

DS, dysphagia score; RT, radiotherapy; PS, performance status; GEJ, gastro-oesophageal junction; CI, confidence interval; coeff., coefficient.

*, Statistically significant.

change in DS between the stented and non-stented groups was not statistically significant ($p = 0.0757$).

Simple regression analysis showed DS at time of RT was the only variable significantly associated with the mean objective change in DS ($p = 0.001$) (Table 4). Using multiple linear regression, only the DS at the time of RT ($p = 0.001$) was found to be significantly associated with DS. From this analysis, for every 1 point increase in DS at the time of RT, the mean objective change post RT decreased by 0.56 points.

The median OS of patients receiving RT was 150 days (IQR: 131–169). The median OS in the RT patients without stents was 154 days (IQR: 99–211) while the median OS in the RT

TABLE 5: Simple linear regression analysis for variables associated with post-radiotherapy survival.

Variable	Simple linear regression analysis		
	Beta coeff.	95% CI	<i>p</i>
Age category (Ref: < 60)	-5.04	-57.67–47.60	0.849
DS at presentation	-30.52	-57.54–-3.49	0.027*
DS at time of RT	-43.85	-90.97–-3.27	0.068
Change in DS	39.73	11.49–67.97	0.006*
PS (Ref: PS 1/2)	-61.65	-117.67–-5.69	0.031*
Gender (Ref: Female)	-13.35	-66.10–39.41	0.616
Histology (Ref: SCC)	41.86	-67.11–150.83	0.447
Site of tumour (Ref: Upper 1/3)			
Middle 1/3	-3.64	-79.86–72.57	0.924
Lower 1/3	38.94	-48.48–126.38	0.378
GEJ	76	-41.29–193.29	0.201
RT fractionation scheduled (Ref: 20.0 Gy/5#)			
18.4Gy in 4#	-30.11	-95.45–35.23	0.362
30Gy in 10#	-44.26	-156.77–68.24	0.436
Weight loss (Ref: No)			
Yes, ≤ 10%	46.73	-55.96–149.43	0.368
Yes, > 10%	12.79	-71.97–97.54	0.765

DS, dysphagia score; RT, radiotherapy; PS, performance status; GEJ, gastro-oesophageal junction; CI, confidence interval; coeff., coefficient.

*, Statistically significant.

patients with stents was 136 days (IQR: 71–206). The difference between these values compared by Mann–Whitney U test was not statistically significant ($p = 0.387$).

The median survival following RT in the study population was 95 days (IQR: 41–154). In the stented group of patients, the median survival was 81 days (IQR: 30–135) compared to 123 days (IQR: 58–181) in the non-stented group of patients. The Mann–Whitney U test was used to assess the correlation between post-RT OS and stent insertion and showed that median survival post-RT was significantly shorter in patients who had a stent insertion ($p = 0.0482$).

Simple regression analysis showed that the only variables which significantly affected post-RT OS were DS at presentation ($p = 0.027$), change in DS post RT ($p = 0.006$) and PS (ECOG) ($p = 0.031$) (Table 5). Using multiple linear regression, DS at presentation ($p = 0.002$) and change in DS post RT ($p < 0.0001$) were found to be significantly associated with post-RT OS. From this analysis, for every 1 unit increase in DS at the time of RT, the duration of post-RT survival decreases by 75 days, holding other variables constant and for every 1 unit increase in the change in DS, the duration of post-RT survival increases by 56 days, holding other variables constant.

Discussion

From our study, the median DPFS after palliative RT was 73 days; the median DPFS in patients without stent insertion was approximately 1 month longer than that in the stented subgroup of patients (83 days vs 54 days); however, this result was not statistically significant between the two groups ($p = 0.224$). Patients having DS 1 or 2 at presentation or post-RT or PS (ECOG) ≤ 2 had significantly better DPFS. No other variables were associated with DPFS.

Because of the assumption that patients who died were considered to have had dysphagia progression at the time of death, the estimated value for median DPFS in our study represents the worst-case scenario and is most likely to represent a minimum value as the cause of death may not directly be related to failure to swallow in these patients.

Following palliative RT, the median change in DS was 0, with most patients (57.8%) remaining unchanged following treatment. The mean objective change in DS was calculated as 0.45 ± 0.89 points. This value is much lower than that described in studies examining the impact of stent insertion as the sole intervention⁵ which suggests that patients receiving RT have a less dramatic improvement in dysphagia than patients who have stent insertion. Existing literature reports approximately 60%–70% of patients have improvement in DS immediately following stent insertion.^{14,21,22} The relief of dysphagia following RT is slower usually taking approximately 4–6 weeks to improve post RT.^{11,23} From our data, at 6 weeks post RT, only 37.5% of patients reported improvement in DS, thus supporting previous data that stenting provides a more rapid relief of dysphagia than RT.

In our study population, the median OS was 150 days, the median OS in the RT patients without stents was 154 days while the median OS in the RT patients with stents was 136 days. Previous data suggested the median OS to be 62 days in patients with only covered stent insertion.¹⁰ Thus, our data suggest that the RT with or without stenting leads to an improved median OS.

The median post-RT survival in the study population was 95 days. The post-RT survival was significantly longer in the non-stented group than in the stented group of patients (123 vs. 81 days; $p = 0.0482$). Both PS (ECOG ≤ 2) and DS ≤ 2 at presentation and after RT were significantly associated with improved median post-RT survival on simple linear regression analysis. Using the DPFS curve for all patients who received radiation, at the time of 95 days (median post-RT survival), 40% of patients still did not have any progression of dysphagia. This validates the use of RT as an effective method of palliation of dysphagia to ensure that most patients are able to swallow at least liquids and soft diet until the time of death.

Most patients who had stents inserted had worse DS at presentation which can be attributed to more advanced disease and possibly more aggressive tumour biology. Cumulatively, these factors could lead to decreased tumour response and control following palliative RT and hence account for the poorer response in all measured outcomes in the stented subgroup of patients in our study population. Other than DS and PS (ECOG), no other patient or tumour factors significantly affected the outcomes in our patients treated with palliative RT. As such, PS and DS at presentation can be used to guide patient selection for those who will benefit the most from palliative RT, which

can be useful in the setting of limited resources. Additionally, the DS and mean objective change in DS after RT can also be used to determine which patients are likely to have a longer survival and hence may benefit from further palliative therapies.

A major problem in the developing countries such as our setting revolves around access to care and health education, resulting in a high proportion of patients presenting late with advanced stage disease.²⁴ In our study, approximately 75% of patients reported having symptoms for more than three months and almost 10% of patients had symptoms for more than a year. Approximately 70% of patients presented had PS (ECOG) ≥ 2 and more than 80% of patients presented had significant weight loss of more than 10% baseline body weight. This can be attributed to the advanced DS at presentation, with more than 90% of patients having a DS of at least grade 2. This affects nutritional status and PS (ECOG) and contributes to the poor general physical condition that precludes many oesophageal cancer patients from receiving radical treatment.^{6,7}

When examining patient and disease characteristics, a male predominance is seen in our study (54.8%), with a higher incidence of squamous cell cancer (92.9%) and a predominance of tumours on the upper and middle oesophagus (70.3%). Previous data report oesophageal cancers located in the upper oesophagus are primarily squamous cell cancers and are associated with lifestyle and cultural factors such as diet, smoking and heavy alcohol consumption²⁵ and generally tend to be more prevalent in lower socio-economic populations.² These factors are also noted in a large proportion of our study population.

At our centre, the standard fractionation schedule used is 18.4 Gy in four fractions, which has the same EQD2 as 20 Gy in five fractions, a frequently used palliative fractionation schedule.²⁶ Notably, the fractionation schedule did not impact the objective response to RT. This is of significance in low- and middle-income countries where resources are scarce as a shorter fractionation schedule (i.e. 18.4 Gy in four fractions) can improve the workflow. The acute toxicity and complication associated with this regimen from our experience are tolerable, however were not described in the study; and hence, further research is necessary for comparison in this regard to other fractionation schedules.

A limitation of our study was that the impact of RT on the other symptoms associated with locally advanced oesophageal cancer such as odynophagia, pain and regurgitation was not assessed. Existing data suggest benefits of radiation for palliation of these symptoms but the duration of response is unknown.²⁷ In addition, an objective assessment of the DS was involved following RT; however, the impact on nutritional status and weight gain was not assessed. These represent areas requiring further work in locally advanced and metastatic oesophageal cancer.

Conclusion

Radiotherapy is beneficial to palliation of dysphagia associated with locally advanced and metastatic squamous cell cancer of the oesophagus with respect to DPFS and improvement in DS. The median duration of DPFS following RT was 73 days; in relation to the post-RT survival, this was effective in palliating dysphagia in approximately 60% of patients until the time of death. Patients who have stent insertions had a shorter duration of response compared to patients without stent insertions. In the setting of patients with locally advanced and metastatic oesophageal cancer who are receiving palliative treatment, PS (ECOG) and DS at presentation can be used as a surrogate to determine which patients will benefit the most from RT. A short course of RT can be an effective method of palliation in these patients in a limited resource setting. Additional investigations on the quality of life and impact of RT on relief of other symptoms may be beneficial to further quantify the magnitude of benefits in these patients.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

N.B. was responsible for the literature research, data analysis and write up of the manuscript. N.B., V.B., A.H., G.C. and B.R. were responsible for reviewing the manuscript prior to submission.

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Data availability

Raw data will be provided by corresponding author upon reasonable request.

Disclaimer

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Appendix 1

TABLE 1-A1: Dysphagia score grading system.

Grade	Description
Grade 0	Able to eat all solids/no dysphagia
Grade 1	Able to eat only some solid foods
Grade 2	Able to eat only soft foods
Grade 3	Able to drink liquids only
Grade 4	Complete dysphagia

Source: Knyrim K, Wagner HJ, Bethge N, Keymling M, Vakil N. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. *New Engl J Med.* 1993;329(18):1302–1307. <https://doi.org/10.1056/NEJM199310283291803>