NOGCA | National Oesophago-Gastric Cancer Audit

NOGCA short report

Use of evidence-based radiotherapy regimens among oesophago-gastric cancer patients with a palliative treatment plan

NOGCA: short report 2021

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GLOSSARY

Fraction – The full dose of radiation that is given during a course of radiotherapy treatment is usually divided into smaller doses called fractions. These fractions are delivered over a series of sessions. Palliative radiotherapy is often delivered in fewer fractions than radiotherapy courses that aim to cure cancer.

Non-curative treatment – Non-curative treatment includes therapies that reduce symptoms and also extend survival, but do not cure the disease.

Palliation – Palliation describes the easing of pain or other distressing symptoms without curing the disease.

Palliative care – Palliative care is the care given to patients whose disease cannot be cured. It aims to improve quality of life rather than extend survival and concentrates on relieving physical and psychological distress.

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EXECUTIVE SUMMARY

Among patients diagnosed with oesophago-gastric cancer who are unsuitable for curative treatment, radiotherapy plays an important role in the palliation of symptoms. The objective of this report is to examine what proportion of patients who had palliative radiotherapy were prescribed evidence-based palliative regimens, as recommended by the Royal College of Radiologists. The study analysed data on the first planned palliative regimen received by patients diagnosed in England between 1 April 2012 and 31 March 2019 and whose initial treatment plan was described as non-curative.

Among 6,333 patients with oesophageal cancer (including Siewert I and II junctional tumours), and who had a record of palliative radiotherapy, 78.5% had an evidence-based (EB) planned regimen. Of these, the most common planned EB regimen was 20 Grays (Gy) over 5 fractions (20Gy/5F; 43.1%), delivered over a week, while 38.3% received the 30Gy/10F regimen, delivered over two weeks. Among 1,305 patients with stomach cancer (including Siewert III junctional tumours), and who had palliative radiotherapy, an EB regimen was prescribed for 86.1% of patients; of these, 46.0% were prescribed 20Gy/5F and 35.3% were prescribed 8Gy/1F.

The likelihood of an individual being prescribed an EB palliative radiotherapy regimen was not strongly associated with patient characteristics in general, with the notable exceptions of cancer stage for oesophageal cancer and the number of comorbidities for stomach cancer. Patients with stage 4 oesophageal cancer were more likely to have been prescribed an EB regimen than those with stage 0-3 cancer, while stomach cancer patients with multiple comorbidities were less likely to have been prescribed an EB regimen than those with none.

There was significant variation in the rates of planned EB regimen use observed across the 21 regional Cancer Alliances ($p<0.001$). In seven Cancer Alliances, more than 90% of their patients who had palliative radiotherapy had a planned EB palliative regimen, while in four Cancer Alliances, less than 70% of their patients had an EB regimen. OG cancer services in these four regions should investigate the reasons for this.

Some patients with oesophageal tumours were prescribed an EB palliative regimen for stomach tumours (i.e. 8Gy/1F regimen), and vice versa for patients with stomach tumours (i.e. 30Gy/10F regimen). These combinations were classified as an EB regimen because the part of the body to which the radiation was applied is not described precisely in the available data. Nonetheless, it suggests that oncologists may be extrapolating beyond the current evidence in response to the perceived needs of patients or the need to make an evidence based case for revising the recommended regimen.

Recommendations

1. Investigate the use of palliative radiotherapy regimens that are recommended for a different cancer site (i.e. use of regimens recommended for stomach tumours among patients with oesophageal cancer, and vice versa), and consider these findings in the next revision of radiotherapy dose recommendations (Audience: oncologists, multidisciplinary teams, Royal College of Radiologists).
2. Investigate the reasons for low use of evidence-based regimens for palliative radiotherapy and preference for alternative regimens in some regions (Audience: Cancer Alliances delivering low levels of evidence-based regimens, Radiotherapy Operational Delivery Networks).

INTRODUCTION

Oesophago-gastric (OG) cancer is among the top five cancers in the UK, with around 13,000 individuals diagnosed with OG cancer each year in England and Wales [1]. Patients with early or localised disease are candidates for curative treatment, in the form of surgery either alone or in combination with chemotherapy and/or radiotherapy, definitive chemo-radiotherapy (for patients with oesophageal squamous cell carcinoma or those with oesophageal adenocarcinoma who are not suitable for surgery) or endoscopic resection for early stage tumours.

Around 60% of patients diagnosed with OG cancer are unsuitable for curative treatment [1]. These patients may receive palliative chemotherapy, radiotherapy and/or endoscopic / radiological interventions. The National Oesophago-Gastric Cancer Audit reported that among the patients diagnosed with OG cancer between April 2017 and March 2019 who were on a non-curative care pathway, 56% had a treatment plan for chemotherapy and/or radiotherapy [1].

Radiotherapy uses high doses of radiation to eliminate or control the growth of cancer cells and can thereby reduce tumour size. When the treatment intent is palliative, the main aim is symptom control, and two types of radiotherapy may be used. Most patients have external beam radiotherapy but there is also the possibility of brachytherapy (in which the radiation source is placed internally). The type of palliative radiotherapy offered to patients with OG cancer depends on several factors such as cancer type and stage, tumour size and location, and patient comorbidities [2]. In a palliative radiotherapy regimen, the overall dose of radiation is typically lower than the dose delivered in a curative regimen. These palliative regimens are also delivered over shorter courses.

The objective of this report is to describe the pattern of planned palliative radiotherapy treatments for OG cancer patients with a non-curative treatment plan, and estimate the proportion who had an evidence-based palliative radiotherapy regimen, as recommended by the Royal College of Radiologists (RCR) [3]. The analysis has been limited to patients treated in England because it relied on the regimen dose information held in the national radiotherapy dataset (RTDS) which is maintained by the National Cancer Registration and Analysis Service (NCRAS) [4]. This information was not available in the data available for patients treated in Wales.

METHODS

The National Oesophago-Gastric Cancer Audit (NOGCA) collects information to assess the quality of care received by OG cancer patients in England and Wales. This report is based on an extract of the NOGCA dataset including all patients diagnosed between 1 April 2012 and 31 March 2019 in England and whose initial treatment plan was described as non-curative.

The records in the NOGCA extract were linked to the individual's records of radiotherapy contained in the RTDS. The RTDS records are organised into a hierarchical data structure that distinguishes between three different levels:

- Episodes which correspond to a course of radiotherapy treatment,
- Prescriptions (or regimens) within each episode which describe the planned radiotherapy dose in Grays (Gy) and the planned number of fractions,
- Hospital visits which repeat information about the planned radiotherapy dose and fractions, but also report the actual radiotherapy dose delivered as well as the actual number of fractions (visits).

Classification of prescription doses and fractions

As noted above, a radiotherapy regimen is characterised by the total radiation dose and the number of fractions over which it is delivered. These radiotherapy regimens reported in RTDS were classified as evidence-based (EB) according to the RCR guidelines on palliative radiotherapy dose fractionation for upper GI cancer [3], or as non-evidence-based. The types of evidence and the grading of recommendations used within this RCR guideline are based on those proposed by the Oxford Centre for Evidence-Based Medicine [5]. Table 1 below shows the radiotherapy doses and fractions that are classified as EB for palliative treatment.

Table 1: List of evidence-based palliative radiotherapy regimens as per the Royal College of Radiologists guideline [3] for OG cancer patients

Oesophageal Cancer			Stomach Cancer		
Dose (Grays) / Fractions	**Duration of regimen**	**Evidence Grade [5]**	**Dose (Grays) / Fractions**	**Duration of regimen**	**Evidence Grade [5]**
12Gy / 1F	N/A	B	6-8Gy / 1F	N/A	D
12-16Gy / 2F	No recommendation	B	20Gy / 5F	1 Week	D
20Gy / 5F	1 Week	D			
30Gy / 10F	2 Weeks	C			
35Gy / 15F	3 Weeks	C			
40Gy / 15F	3 Weeks	D			

N/A – not applicable, single dose recommended. Grade A reflects a high-level evidence base; Grade D reflects a low-level evidence base.

Cohort definition and statistical analyses

The study included patients (diagnosed April 2012 - March 2019) who had a radiotherapy episode within 12 months of the date of their OG cancer diagnosis (as recorded in NOGCA). Episodes of radiotherapy delivered more than 12 months after a patient's diagnosis (or 6 months before) were excluded because these episodes may not relate to treatment of the primary tumour. The analysis was limited to patients who were identified as having a non-

curative treatment plan in NOGCA. However, among these patients, a number of cases had planned regimens that corresponded to courses of radiotherapy consistent with curative treatment. These patients were excluded as it is likely they were being treated with curative intent. The analysis considered only the first planned regimen recorded in the RTDS because the dose / fractionation of subsequent regimens may justifiably deviate from the RCR recommendations, for example, due to how a patient responds to the initial regimen.

The unadjusted rates of planned EB palliative regimens for the overall cohort and patient subgroups (by age, sex, cancer stage, tumour site, and number of comorbidities recorded at time of diagnosis) were derived using the planned dose / fraction and were expressed as percentages. The unadjusted rates of EB regimen use were also compared across geographical regions (Cancer Alliance). The statistical significance of differences in the proportions across patient subgroups was tested using a Chi-square test.

A multivariable logistic regression model was used to assess which patient characteristics were associated with the likelihood of being prescribed an EB palliative regimen. All statistical tests were two-sided and used a significance level of 0.05.

RESULTS

Patient cohort

Among the patients diagnosed with OG cancer in England between 2012 and 2019, a total of 8,855 were reported to have a non-curative treatment plan in NOGCA and had a record of radiotherapy in RTDS. Of these, 742 patients were excluded because the date of prescribed radiotherapy treatment in RTDS was either more than one year after (n=708) or more than 6 months before (n=34) the date of diagnosis. A further 475 patients were excluded because they had a planned regimen that corresponded to a recommended curative treatment regimen. This left 7,638 patients for the analysis.

The majority of patients in the cohort were men (70%), and over 60% were aged 70 years or over. Among the patients with a known clinical stage, 46% had stage 4 (metastatic) disease, while another 34% had stage 3. Patients who had stage 1-2 disease were typically older patients (79% were aged ≥70 years) suggesting they may have not been sufficiently fit for curative treatment.

Planned radiotherapy regimens

Within the study cohort of patients with a non-curative treatment plan and a record of radiotherapy, 79.8% had a prescription that corresponded to an EB palliative regimen for OG cancer:

- Among 6,333 patients with oesophageal cancer (including upper junctional Siewert I and II cancers), 78.5% had an EB planned regimen. Of these, the most frequently

prescribed regimen was 20 Gy over 5 fractions (20Gy/5F; 43.1%), followed by 30 Gy over 10 fractions (30Gy/10F; 38.3%)

- Among 1,305 patients with stomach cancer (including lower junctional Siewert III cancer), 86.1% had an EB planned regimen, a higher proportion than among the oesophageal group ($p<0.001$). Of these, 46.0% were prescribed 20Gy/5F and 35.3% were prescribed 8Gy/1F.

Some patients with oesophageal tumours were found to have a planned regimen recommended by the RCR for the palliative treatment of stomach tumours, and vice versa for patients with stomach tumours. In the first situation, there were 807 patients with an oesophageal tumour (among the 4,971 classified as having an EB regimen) who were prescribed the 8 Gy/1F regimen. Among the 1,124 patients with stomach cancer who were classified as having an EB regimen, there were 199 who were prescribed the 30 Gy/10F regimen recommended for oesophageal tumours. These patients were included in the proportions of EB regimen estimates because the location of some tumours, particularly those at the gastro-oesophageal junction, may be difficult to determine precisely. As the exact site of radiation was not included in the available data, it was not possible to determine whether the prescribed regimen matched the appropriate site of radiotherapy.

Non-evidence-based regimens

Among those patients with a prescription that did not correspond to an EB palliative radiotherapy regimen, many different regimens were recorded (Table 2). The most common non-EB radiotherapy regimens were 27 Gy/6F and 36 Gy/12F, which accounted for over a third of all non-EB palliative regimens.

Table 2: Most commonly prescribed non-EB regimens among patients receiving palliative therapy (2012-19), arranged by fraction

Fractions	Dose [a]	No. of patients	% of all non-EB regimens
6	27	264	17%
12	36	257	17%
4	12, 16, 20	179	12%
1	2-5, 10	124	8%
3	6, 9, 12	74	5%
10	20, 25, 30	44	3%
2	6, 8, 9	30	2%
8	20-24	19	1%
9	27-30	19	1%
5	15, 20-25	18	1%

[a] – Some doses are given as a range, as several values within the range were identified in the prescribed dose.

Use of evidence-based palliative regimens and patient characteristics

Table 3 shows the proportion of patients with oesophageal and stomach cancer prescribed an EB palliative regimen by age group, sex, clinical stage and number of comorbidities present at cancer diagnosis. The differences in the proportions across the different age groups, and between men and women were generally small. There was a much greater range in values across the different cancer stages, particularly among patients with oesophageal cancer. Here, patients diagnosed with stage 4 (metastatic) cancer were more likely to be prescribed an EB palliative regimen (p<0.001).

Table 3: The proportion of patients prescribed an EB palliative regimen by tumour site

Patient characteristics	No. of pats	Patients prescribed an evidence-based regimen for palliative radiotherapy treatment, n (%)		
		Oesophageal cancer N=6,333	Stomach cancer N=1,305	All patients N=7,638
Age group (years)				
<60	1,161	785 (81.5%)	172 (86.9%)	957 (82.4%)
60-69	1,821	1,230 (77.6%)	200 (85.1%)	1,430 (78.5%)
70-79	2,370	1,531 (77.7%)	334 (83.5%)	1,865 (78.7%)
≥80	2,286	1,425 (78.6%)	418 (88.6%)	1,843 (80.6%)
Sex				
Female	2,279	1,471 (76.4%)	294 (83.3%)	1,765 (77.5%)
Male	5,351	3,497 (79.4%)	827 (87.2%)	4,324 (80.8%)
Missing	8			
Clinical stage				
0/1	386	222 (71.0%)	65 (89.0%)	287 (74.4%)
2	901	480 (71.0%)	196 (87.5%)	676 (75.0%)
3	2,251	1,513 (74.6%)	184 (82.1%)	1,697 (75.4%)
4	3,061	2,073 (84.0%)	514 (86.7%)	2,587 (84.5%)
Missing	1,039			
Number of comorbidities				
0	3,997	2,691 (80.0%)	568 (89.5%)	3,259 (81.5%)
1	2,056	1,324 (77.6%)	300 (85.7%)	1,624 (79.0%)
2 or more	1,585	956 (75.6%)	256 (80.0%)	1,212 (76.5%)

Patients with multiple comorbidities were less likely to be prescribed an EB palliative regimen than those with one or no significant comorbidities (p<0.001). This association was stronger for stomach cancers than oesophageal cancers.

The adjusted odds ratios for these patient characteristics from the multiple regression model are shown in Table 4. The results confirm the association between the use of EB planned regimens and clinical stage for oesophageal tumours, and the presence of multiple

comorbidities for stomach tumours. The association between the use of EB planned regimens and the other patient factors were not statistically significant.

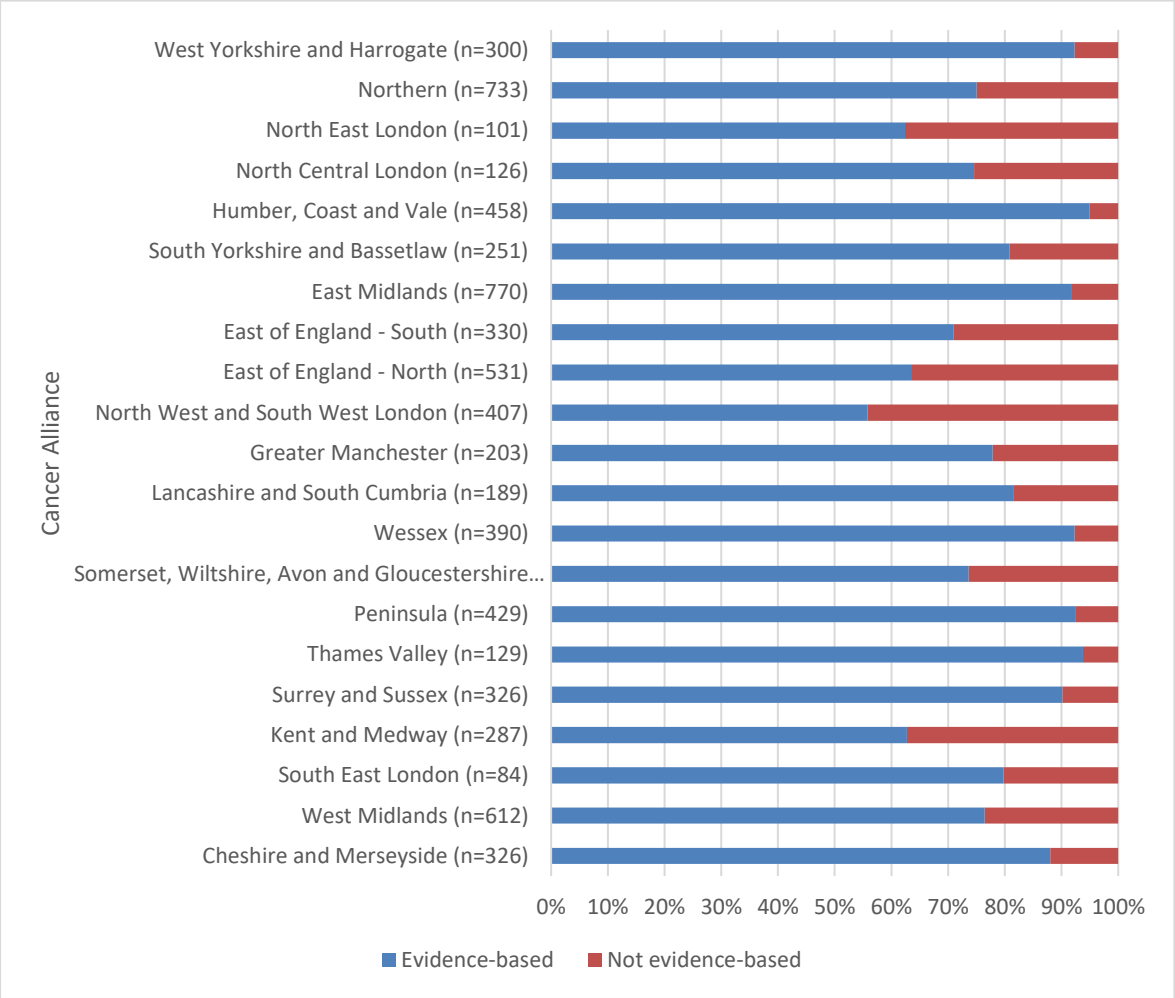
Table 4: Adjusted odds ratios (OR) for the association between use of planned EB palliative regimens and various patient characteristics

	Oesophageal cancer		**Stomach cancer**	
	Adjusted OR	**(95% CI)**	**Adjusted OR**	**(95% CI)**
Age group (years)				
<60	1		1	
60-69	0.841	0.680 to 1.041	0.898	0.500 to 1.614
70-79	0.956	0.775 to 1.179	0.881	0.512 to 1.518
≥80	1.096	0.877 to 1.369	1.337	0.749 to 2.388
Sex				
Female	1		1	
Male	1.125	0.977 to 1.395	1.329	0.910 to 1.941
Clinical stage				
0/1	0.453	0.344 to 0.596	1.281	0.575 to 2.853
2	0.451	0.568 to 0.556	1.051	0.645 to 1.710
3	0.555	0.477 to 0.646	0.744	0.482 to 1.149
4	1		1	
Number of comorbidities				
0	1		1	
1	0.917	0.786 to 1.070	0.703	0.455 to 1.087
2 or more	0.852	0.721 to 1.006	0.416	0.273 to 0.635

Significant variation in the unadjusted rates of planned EB palliative regimen use was observed across the 21 Cancer Alliances ($p<0.001$). In seven Cancer Alliances, more than 90% of their OG cancer patients had been presribed an EB palliative radiotherapy regimen, while in four Cancer Alliances, less than 70% of their patients had an EB regimen (Figure 1).

The use of the most commonly prescribed non-EB regimens (27 Gy/6F and 36 Gy/12F) was concentrated within a few regions, with Cancer Alliances tending to use one of the two regimens, rather than both. The use of 27 Gy/6F was observed most frequently in the East of England Cancer Alliances (North (n=105) and South (n=75)), while 36 Gy/12F was prescribed most commonly in North West & South West London (n=113) and Kent & Medway (n=65). The other Alliance used these regimens in no more than 30 patients.

Figure 1: Regional variation in the use of planned evidence-based palliative radiotherapy regimens, by Cancer Alliance



CONCLUSION

Palliative radiotherapy is a common form of treatment among patients with oesophageal cancer who are unsuitable for curative therapy. This analysis of patients diagnosed between 2012 and March 2019 found that 78.5% of the 6,333 patients with oesophageal cancer (including upper junctional Siewert I and II cancers) had a planned EB palliative radiotherapy regimen, with two regimens (20 Gy over 5 fractions and 30 Gy over 10 fractions) accounting for 81% of these EB regimens.

Compared with oesophageal cancer, palliative radiotherapy is used among far fewer patients with stomach cancer and there is a more limited number of EB regimens recommended by the RCR. This analysis included 1,305 patients with stomach cancer (including lower junctional Siewert III cancer), of whom 86.1% were prescribed an EB palliative regimen.

In undertaking the analysis, we found that some patients with oesophageal tumours were prescribed a regimen recommended by the RCR for the palliative treatment of stomach tumours (ie, the 8 Gy/1F regimen), and vice versa for patients with stomach tumours (ie, the 30 Gy/10F regimen). It was decided to classify these combinations as an EB regimen because the part of the body to which the radiation is applied is not described precisely in the available data, and this approach was considered preferable to under-estimating the proportion of patients with an EB planned regimen. It is possible that the radiation was applied to a tumour in the appropriate anatomical site. Nonetheless, it may also suggest that oncologists are extrapolating beyond the current evidence in response to the perceived needs of patients, or the need to make an evidence based case for revising the recommended regimen.

> **Recommendation 1**: Investigate the use of palliative radiotherapy regimens that are recommended for a different cancer site (i.e. use of regimens recommended for stomach tumours among patients with oesophageal cancer, and vice versa), and consider these findings in the next revision of radiotherapy dose recommendations (Audience: oncologists, multidisciplinary teams, Royal College of Radiologists).

Of more concern was the observed levels of regional variation. The results suggest a number of Cancer Alliances prescribed lower levels of EB palliative regimens than might be expected, while the use of the most commonly prescribed non-EB regimens was concentrated in a few regions. The evidence grade associated with some of the regimens in the RCR recommendations is low (Grade C or D), therefore the use of specific non-EB regimens is likely to reflect clinician preference in light of low grade evidence.

> **Recommendation 2**: Investigate the reasons for low use of evidence-based regimens for palliative radiotherapy and preference for alternative regimens in some regions (Audience: Cancer Alliances delivering low levels of evidence-based regimens, Radiotherapy Operational Delivery Networks).

The likelihood of an individual being presribed an EB palliative radiotherapy regimen was not strongly associated with patient characteristics in general, with the notable exceptions of cancer stage (oesophageal) and the number of comorbidities (stomach). The lack of a relationship between patient age at diagnosis and the likelihood of being prescribed an EB regimen suggests age is not influencing what type of regimen is offered. A limitation of the data is that we do not have information on the reasons for selecting a particular non-EB regimen. Factors such as comorbidities may necessitate modified regimens due to interrruptions to treatment, e.g. reduced fractions to account for missed radiotherapy sessions.

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