European Journal of Oncology Nursing 40 (2019) 126–130

Contents lists available at ScienceDirect

European Journal of Oncology Nursing

journal homepage: www.elsevier.com/locate/ejon

Gastroesophageal cancer patients need earlier palliative intervention - Using data to inform appropriate care

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ABSTRACT

Purpose: To evaluate demographics of survival in patients with gastroesophageal cancer so that it informs nursing practice.
Method: Data on 2215 patients diagnosed with gastroesophageal cancer who presented to a specialist referral centre between the years 2000 and 2011 were extracted from a Public Health repository. Survival time was calculated and analysed against clinical and lifestyle factors to reveal whether they had an impact on survival outcomes.
Results: Over 60% of patients had died within the first year, 39% of these died within the first 6 months. Survival outcomes were reduced in advancing age, and in those patients who present as 'emergency' cases. One quarter of patients were seen by a GP, but were not referred urgently through the two week wait system, to specialist care.

Thus, gastroesophageal cancer patients need specific and appropriate treatment options, including earlier referrals to palliative care provision. There is also a need for cancer specific education and information at community and clinical levels.
Conclusions: The globally applied one and five-year statistics applied to cancer survival studies do not adequately capture rates of early demise with gastroesophageal cancer. This study presents a novel approach to statistical analysis, based on patient derived data. It identifies factors linked to earlier deaths. However, rather than a focus on early presentation and diagnosis (which are essential) - it also reveals a significant need to consider early referrals for palliative care and nursing interventions to alleviate pain and suffering in patients with poor prognosis.

1. Introduction

This paper proposes a new vision for a more cancer-specific focus on treatment, diagnosis and care. There are qualitative differences when palliative care is offered as adjunct to oncology services. Palliative care offers patients more information on treatment processes and prognosis, the aim is to assist patient and carer coping strategies, and to develop advanced care planning directives (Thomas et al., 2019). Palliative care is complementary to oncological interventions, it offers family centred care to optimize quality of life, through the anticipation, prevention and alleviation of suffering – it meets intellectual, emotional, spiritual needs to offer autonomy, access to information and informed choice (Dahlin, 2013). Patients should receive dedicated, interdisciplinary palliative support as early as possible in the disease process (Ferrell et al., 2017). Furthermore, knowing the trajectory and survival in certain cancers can guide healthcare delivery and provide intelligence to assert the most appropriate treatment options. For many years, national cancer strategies have focussed on encouraging earlier diagnosis and interventions. However, they must also recognise the importance of timely referrals to palliation services.

This paper presents a quantitative analysis of N2215 patients to challenge the commonly applied 1-year and 5-year survival outcome measures to cancer statistics. Gastroesophageal cancer (GOC), or oesophagogastric cancer, is malignancy of the gastroesophageal junction and upper oesophagus. Global trends show a significant rise, and as the 8th most common cancer diagnosis, it remains relatively overlooked in current literature (World Cancer Research Fund, 2018; Malhotra, 2017). Survival is dependent on surgical removal of the tumour (Whitehead et al., 2018; Altorki and Harrison, 2017). In GOC, the 'red flag warning' physiological symptoms are not always evident until there is major tumour infiltration, so survival outcomes remain poor (NCIN, 2018; Thrift et al., 2012). This means many GOC patients present too late for curative options, despite National Cancer Campaigns to expedite referrals and streamline routes to diagnosis (Ellis-Brookes et al., 2012; NCIN, 2016). During the first year after surgery, GOC tumours commonly re-present and metastases are found in over 80% of patients (Altorki and Harrison, 2017; Whitehead et al., 2018). This means the journey from detection of symptoms is multi-faceted for GOC patients.

Survival outcomes in GOC are influenced by patients' demographic profiles. The mean age at diagnosis is 70 years (SD ± 20), meaning

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https://doi.org/10.1016/j.ejon.2019.04.004
Received 10 October 2018; Received in revised form 19 March 2019; Accepted 26 April 2019

Table 1
Demographic data of the gastroesophageal cancer cohort (N = 2215).

		Total	Gender	
			Male	Female
Age Group	< 44	36 (2%)	26	10
	45–55	174 (7%)	127	47
	56–64	457 (21%)	355	102
	65–74	707 (32%)	523	184
	75–84	621 (28%)	386	235
	85 +	220 (10%)	98	122
Socioeconomic Status (IMD 10)	Least deprived	351 (16%)	251	100
	Not deprived	505 (23%)	336	169
	Mid	467 (21%)	317	150
	Deprived	391 (18%)	268	123
	Most deprived	501 (23%)	343	158
Morphology	Neoplasm (not specified)	13 (.5%)	9	4
	Epithelial neoplasm	128 (6%)	84	44
	Papilliary and squamous cell carcinoma	620 (28%)	280	340
	Adenocarcinoma	1337 (60%)	1050	287
	Cystic and mucinous	100 (5%)	77	23
	Mixed neoplasms	17 (1%)	15	2

patients frequently die from age related conditions (Coupland et al., 2012). This cancer is also linked with lifestyle factors (smoking, obesity and alcohol ingestion) which also bring associated comorbidities. (CRUK, 2017; Parkin, 2010).

Despite this, GOC tends to be amalgamated with other cancers for research studies. Frequently merged with head and neck, gastric and gastrointestinal tract cancers, survival outcomes specific to GOC are not always easy to separate from these other cancer groups. This is important to note, because different people with different cancers require different approaches to care and interventions. Thus, the requirement to evaluate cancer specific data and align care options to the patient demographics, is paramount.

Therefore, this research evaluates the demography of survival in patients with GOC. The sole purpose is to adequately profile a cancer so that it informs intervention strategies (such as interdisciplinary palliative care) – to improve quality of life, alleviate pain and suffering and bring family centred care to those patients with a poorer prognosis.

2. Methods

A retrospective cohort analysis of every patient referred to a specialist UK cancer centre by 6 National Health Service sites and multiple primary care referral centres between the years 2000–2011 (N2215).

2.1. Statistical analysis

Data were retrieved from the United Kingdom, National Cancer Public Health England (PHE) datasets. PHE provide information from hospital episode statistics and cancer registry to 95% CI accuracy and are accessible through the Office of Data Release, subject to National Health Service Ethics Approval and Confidentiality Advisory Group assurance of Information Governance and Data Protection conformity (NCIN, 2016).

Date of histological confirmation to date of death was calculated to reveal mean survival in days. Tukeys Hinges quartiles were applied to group survival outwith the usual 1-year statistic, so groups reflected actual mortality.

Linear correlations for continuous variables (such as advancing age) were assessed through pearsons product moment correlation coefficient. Between group differences were analysed through parametric and nonparametric tests and these included: Kruskal Wallis for groups exceeding 2, ANNOVA where there was homogeneity and t-distribution was analysed for dichotomous variables (Gender). Cox Proportional survival analysis was undertaken to reveal survival functions against morphology. Cohen's (1988) guidelines for effect sizes were applied where d = 0.2 represents a 'small' effect size, 0.5 represents a 'medium' effect size and 0.8 a 'large' effect size.

To reveal the demographic elements of survival with GOC, three groups were developed. Group 1 captured the full cohort (N2215) who presented between January 2000 and June 2011. This was useful to identify age ranges, socioeconomic status, calculate days survival and morphology of the cancer. Group 2 captured a sub-cohort (patients presenting after 2006 with recorded routes to diagnosis) – to evaluate whether routes to diagnosis impacted on survival outcomes (N1097). Group 3 related to all patients diagnosed 2000 to 2011 with full TNM staging data (N121) to confirm whether advanced stage is a predictor of early demise.

Socioeconomic data were taken from recorded IMD status at the time of diagnosis. Variables such as age, gender, and tumour morphology were taken as recorded in the PHE dataset. Routes to diagnosis were taken from the pre-determined cancer outcomes metrics (NCIN, 2016).

This research is a part of a larger study into spatiality of gastroesophageal cancer survival. The larger study used data captured between 2000 and 2013, (N2785) however, for purposes of a 5-year cut point and survival analytics, this paper is based on presentations between 2000 and 2011. Ethics approval was granted by NHS (IRAS ID 161434), and the host University ethics committee.

3. Results

3.1. Demographics, survival and mechanisms of presentation

A total 2215 (living) patients presented to a regional referral centre and had histologically confirmed GOC between 2000 and 2011. Table 1 identifies age, gender IMD status and tumour morphology for all patients. The average age at presentation was 70 (SD11) and male female divide 70:30%. There was an increase in diagnoses for males between ages 65–74. 71% of the male cohort presented with adenocarcinoma (ADC), whereas females were diagnosed with ADC and squamous cell carcinoma (SCC) (43% and 47% respectively).

In the full cohort, 867 (39%) patients died within the first six months, and a further 471 (21%) after the initial 6 months, but within the first year. Over 60% of the total cohort died on or before 1-year following diagnosis. A further 617 (28%) patients survived between 1 and 5 years. Only 260 (12%) patients remained alive at 5 years after the date of histological confirmation. The median survival time (in days) was 264 days (Tukeys Hinges quartiles ranged 107 lower – to 634 higher day survival range) (See Fig. 1).

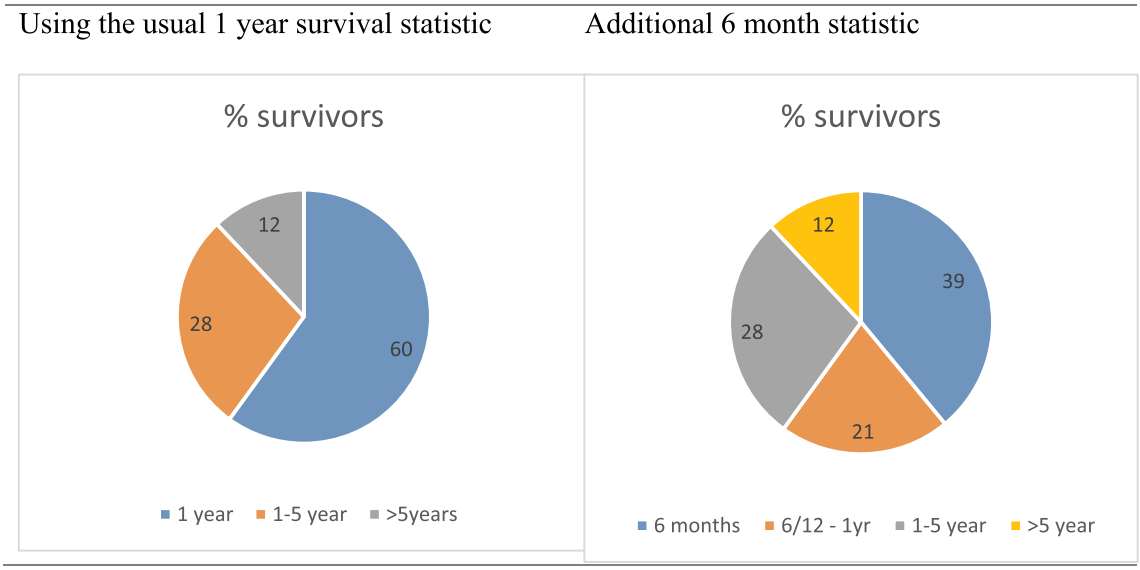

Fig. 1. Proposed survival groups.

This proposed 6 month statistic captures the following groups:

1) Deaths within 6 months of presentation to cancer specialist services n = 867 (39%) (Patients presenting with aggressive tumours, or too late for curative treatment)
2) Deaths up to 1 year n = 471 (21%) (> 6 month presentations, may have had surgical interventions, but with limited curative options.
3) Death 1–5-years n = 617 (28%) Patients who have received surgical intervention of a curative or palliative nature
4) Survival > 5-years n = 260 (12%) Considered as patients who have survived, or are in remission of the disease process.

Data on routes to diagnosis have been recorded in the UK cancer statistics since January 2006. Table 2 uses a 6 month survival cut point in addition to the 1 year survival, for analysis against the general 'routes to presentation'. It illustrates the general patient journey from diagnosis to death. Emergency and two week wait routes were common to those who died within the first 6 months. There was a stochastic dominance in the emergency presentation group, linking emergency presentation with reduced days survival x^2 (5, n = 1097) = 112, p = < 0.05. Those alive after 6 months, but who died before 1 year more commonly presented through the '2-week wait' referrals. Over a quarter of this cohort (54 patients out of a total 222), presented to their GP but their symptoms were not considered appropriate for referrals through the 2-week wait system. Survivors and those dying between 1 and 5 years tended to present via 2-week wait, or through a non-urgent GP referral.

3.2. Lifestyle and demographic variables

Demographic variables were explored against survival, thus allowing isolation of the effects of treatments, from the effects of other variables. It was used *a priori* as other variables, such as advancing age, date of presentation and poor initial vital status have been shown to have an impact on long term survival.

Preliminary exploration of data exploring relationships between advancing age and survival revealed that there were no violations of the assumptions of normality, linearity and homoscedasticity. A statistically significant difference in survival days between the 6 different age groups was identified (gp 1 N = 36: 0–44 yrs, gp 2 N = 174: 45–54 yrs, gp 3 N = 457: 55–64 yrs, gp 4 N = 707: 65–74 yrs, gp 5 N = 621: 75–84 yrs, gp 6 N = 220: 85plus) X2 (5, N = 2215) = 20.1 p = 0.001. There was a small negative correlation between age and survival, (r = −0.28, n2215, p < 0.01) meaning advancing age decreases survival outcomes, but that only 7% of variance in survival can be explained by advancing age (r^2 = 0.729). Patients over the age of 65 experienced fewer days alive after their GOC diagnosis (Md = 350 N = 1374) when compared to those under 65 (Md171 N = 841) U 39661p = 0.001. z = −12.4 r = 0.3.

There was no significant difference in mean survival scores between males (524 days) and females (469 days) (t (2215) = 2.07, P 0. 04 (two tailed)). The magnitude of the differences in means (95% ci 3.0–106.5) was very small (eta squared = 0.001).

Survival time has increased over the duration of this cohort timescale X^2 (11, N = 2215) = 31.54, p = 0.01. Patients presenting after the year 2006 had improved survival outcomes, when compared with those presenting before 2006. The pre 2006 group displayed worse survival in days (Median 234, n 1116), whereas the post 2006 group exhibited a small improvement in survival outcomes (Median N = 310, n 1099 U = 535907, Z = −5.1, P = 0.01, r = 0.1). Mean survival outcomes were greater in patients who were offered surgical intervention (p = 0.005).

Table 2
Mechanisms of presentation against survival.

	N of patients in with mechanism of presentation cohort (N = 1097)					
	Emergency	Standard GP referral	Inpatient	Outpatient (other)	Two Week Wait	Unknown 21
Deaths *within* 6 months	134	81	23	11	126	4
Deaths *up to 1 year*	28	54	18	8	113	1
Death 1–5-years	38	91	35	11	158	11
Survival > 5-years	12	41	23	7	64	5
Median days survival across presentation	122 days	353 days	463 days	359 days	349 days	593 days

Table 3
Site and Morphology of cancer in the new survival groups.

TOTAL COHORT (N = 2215)	Site of cancer			Morphology		
	Oesophagus unspec	Upper oesophagus	GO Junctional	SCC	ADC	Other
Deaths *within* 6 months of presentation to cancer specialist services n = 867 (39%) (Patients presenting with aggressive tumours, or too late for curative treatment)	348	72	470	280	490	112
Deaths *up to 1 year* n = 471 (21%) (> 6 month presentations, may have had surgical interventions, but with limited curative options.	158	48	225	120	280	52
Death 1–5-years n = 617 (28%) Patients who have received surgical intervention of a curative or palliative nature	219	58	350	132	394	60
Survival > 5-years n = 260 (12%) Considered as patients who have survived, or are in remission of the disease process.	98	24	145	80	180	8

There was a very small, but statistically significant difference in survival days between lower socioeconomic groups and higher (IMD 1& 2 versus IMD 4&5) ($P < 0.005$ eta squared = 0.02) though these findings must be considered against the lower effect size. Analysis revealed statistically significant differences in survival days between groups. x^2 (4, n = 2215) = 38.6, p = 0.05, suggesting an association between lower deprivation scores and poor survival.

The main GOC morphology in the survival cohort (N2215) was adenocarcinoma (ADC) with papillary and squamous cell (SCC) second. Cancers labelled as 'other' included neoplasms and cystic/mucinous morphology and these were diagnosed in 258 cases (Table 3).

Mean days survival after diagnosis in squamous cell carcinoma was 485, Adenocarcinoma was 543 and all other cancers was 368 days. For SCC, 61% of the cohort died within a year and 11% survived to 5 year. 57% of ADC sufferers died within a year of diagnosis and 13% survived over 5 year.

There was a statistically significant difference in days survival post diagnosis between the three morphology groups (SCC n = 620, ADC N = 1337, Other N = 258). X2 (2, N = 2215) = 16, p = 0.005. The ADC groups had a higher median score in days survived (MD291) than the other two groups, with values of MD 245 and 212. Cox proportional survival anaysis revealed survival functions decrease with time in all 3 groups (CI 95%, P= < 0.05).

4. Discussion

The aim of this study was to evaluate the demographics of survival in gastroesophageal cancer, to reveal elements of the care trajectory which can inform appropriate interventions. By offering analysis of this large group of patients with gastroesophageal cancer, it was evident that a significant percentage would have benefitted from an holistic care package and early intervention palliative care and support.

Several significant factors were identified in this research. Namely – that the 1 year survival statistic does not articulate GOC, that patients with advanced symptoms have worse outcomes, that over ¼ of patients presented to their GP – but were not referred urgently for GOC screening, and that increasing age, emergency presentation and socioeconomic deprivation is linked to impaired survival.

Fig. 1 illustrated the significant proportion of patients who had died within 6 months of their diagnosis. They would ordinarily be missed and merged into the 1 year 'commonly applied' survival statistic. Thus, a generic '1 year' statistic does not fully capture the extent of mortality across the total timeframe. This intelligence can be used to drive initiatives to instigate palliative care, to reduce suffering and to deliver the appropriate care to those patients and their families who were most at need.

Findings illustrated that use of the 1 year survival statistic missed a full 39% of patients dying before 6 months. A further 21% died before the 1-year survival statistic. A biologically plausible explanation for this would be to suggest those patients who died within the first 6 months, either had other comorbidities, presented at a very late stage, or had extremely aggressive tumours.

However, this information is crucial to inform healthcare. Those 39% of patients dying within 6 months would be more appropriate for alternative interventions. For example, early diagnosis strategies are not necessarily going to have an effect on these patient groups. Instead, the focus should be on palliative care, alleviation of pain, and further research into practices which alleviate symptoms exacerbated by this cancer (such as dietetics and nutrition, pain management, palliative care options, counselling). This study's findings are commensurate with existing literature (CRUK, 2017; Coupland et al., 2012). However, this is the first study to generate survival data and identify the need for a 6 month cut point. By applying gold standard 'interval measures' for cancer research (Weller et al., 2012), this study proposes new parameters to support gastroesophageal cancer survival analysis - one which represents death rates at 6 months.

For those patients with records of 'routes to diagnosis' (n = 1097), the two week wait was the most common route (42% of the cohort). This national cancer strategy, to expedite care and treatment has been effective in increasing diagnoses of GOC (NICE, 2015; Meecham et al., 2012; Vedstead and Olessen, 2011; Hamilton et al., 2015). However, this study identified that 25% of the total cohort did receive a GP referral, but this was not considered urgent enough for the two week wait system. This is important information for those working in primary care, as it highlights the need for education and training in detection of GOC symptoms.

Unsurprisingly, this study linked advancing age with reduced survival. This may be biologically attributed to the ageing process, which frequently manifests with comorbidities and frailty (Chang et al., 2018; Hogan, 2018; Hirani, 2017). The mean age of diagnosed patients was 70 years, so the skew to an older population in gastroesophageal cancer means the cohorts studied will be subject to the many confounding variables of ageing. The fact that male diagnoses increased between the ages 65–74 would suggest that nurses working with patients over 50, could consider offering patients information on specific signs, symptoms and nature of the disease.

Modifiable risk factors such as smoking, diet, physical activity and increased BMI are more commonly identified in deprived groups, and are attributed to reduced survival outcomes in several studies on cancer (Coupland et al., 2012; Hastert et al., 2016; Danzig et al., 2014; Hagedoorn, 2016 Worsley et al., 2011). This study showed a small but significant correlation between socioeconomic deprivation and poor survival and this finding is supported by other studies (Arnold et al., 2015; Abnet et al., 2018; Xie and Leggegren, 2018).

4.1. Strengths and weaknesses of this study

Although this study was based on referrals made to only one UK Cancer regional referral centre this did constitute a population catchment area of an estimated 1682000 and covers a number of healthcare

institutions. Furthermore, although these data represent one geographical region, the demography of this region is diverse providing a good example of other healthcare areas in the UK.

A major aspect of the rigour of this study lies in the reliance of English cancer registry data, which is highly regarded for its quality and completeness (95%CI CRUK, 2017). The incomplete data on TNM staging in this database is common in gastroesophageal cancer studies (Mahar et al., 2018; Anandavadivelan et al., 2018; Islami, 2018; Neal, 2015).

5. Conclusion and recommendations for further research

This paper identified some factors which are crucial to informing care at the end of life. Working with gastroesophageal cancer patients means providing the most relevant treatment to meet their needs. This research identified a significant skewed survival trajectory, which supported early integrated palliative care strategies. Nurses, as significant providers of palliative care, can use these statistics to ensure they are involved in the systematic planning of care for these patients.

However, as with any form of change in systems and healthcare delivery, this has financial and resource implications. Further study would be required to review how earlier palliative nursing care interventions will impact resources. Longer term care delivery options may improve individualised care outcomes – but the evidence remains unclear on costs (Salamanca-Balen et al., 2018). They may prevent hospital admissions and length of stay, but the evidence remains uncertain on cost-effectiveness.

This paper offers an information source for nurses to prepare patients (and families) for the disease trajectory and prognosis. Cancer care, treatment and support is an interdisciplinary process, but nurses are key to this process. They must use information and evidence effectively, supporting an interdisciplinary team to provide the best possible care for GOC patients.

The overall message is that the globally ageing population means gastroesophageal cancer incidence will potentially increase. Therefore, more resources will be required to deliver the most appropriate care for patients. Survival analysis should reflect the survival trajectory, and missing a significant proportion of patients who die within the first 6 months after GOC diagnosis is unacceptable. This information offers a key driver to inform palliative and alternate care strategies – to engage interdisciplinary led palliative care which addresses the actual needs of patients (and their families) who have this cancer.

Conflict of interest

No conflict of interest has been declared by the author(s).

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