

# Improved survival in resected oesophageal and gastric adenocarcinomas over a decade: the Royal Marsden experience 2001–2010

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## Abstract

**Background** Oesophageal and gastric adenocarcinoma (OGA) treatment remains challenging. Improvements in early diagnosis, staging and management might have contributed to survival prolongation. To examine this hypothesis, we assessed outcomes of resected OGA patients in our institution over 10 years, comparing two time periods, 2001–2005 and 2006–2010.

**Methods** Records from patients who had undergone surgery with radical intent and follow-up for OGA were retrospectively reviewed. Patients followed up at hospitals other than the Royal Marsden Hospital were excluded. Two different cohorts were identified: patients with oesophageal and type I or type II oesophagogastric junction (OGJ) tumours, and patients with gastric and type III OGJ tumours.

**Results** We identified 360 patients: 147 from 2001–2005 and 213 from 2006–2010. The characteristics were comparable across the two time periods. Between 2001–2005 and 2006–2010, the percentage of R0 resections increased (from 67.1 to 81.1 % for proximal tumours and from 76.3 to 95.9 % for gastric and type III OGJ tumours). The mean number of lymph nodes retrieved increased over time. The 5-year overall survival rate increased significantly from 42.3 to 56.6 % for proximal tumours and from 38.8 to 55.3 % for gastric and type III OGJ tumours. Similarly, the disease-free survival rate significantly increased from 34.6

to 53.5 % for proximal tumours and from 35.9 to 51.1 % for gastric and type III OGJ tumours.

**Conclusion** This study comprehensively describes the improvement in survival outcomes in a major UK referral centre over a 10-year period, identifying potentially relevant factors such as increased number of R0 resections and higher lymph node yield.

**Keywords** Oesophageal adenocarcinoma · Oesophagogastric junction adenocarcinoma · Gastric adenocarcinoma · Surgical resection · Clinical management

## Introduction

Oesophageal cancer and gastric cancer are, respectively, the eighth and fifth commonest types of malignancies worldwide [1]. With 107,300 deaths every year, gastric cancer is the fourth leading cause of cancer-related death globally [2]. In the UK, 8,300 new cases of oesophageal cancer (55 % adenocarcinoma) and more than 7,000 new cases of gastric cancer were diagnosed in 2011 [3]. The trends in incidence and mortality are divergent for oesophageal/oesophagogastric junction (OGJ) cancer and true gastric cancer. For distal or antral gastric cancer, mortality has decreased over the past 30 years, with an estimated annual percentage change of –3.7 % in men and –3.4 % in women, and a persisting favourable trend in mortality is predicted up to 2015 [4]. Eradication of *Helicobacter pylori*, cessation of smoking and improvement in food preservation and dietetic habits are factors that have been related to this decrease in incidence and mortality [4]. The opposite trend in incidence has been noted for the other anatomical subtype, OGJ cancer, the rates of which are steadily increasing, possibly related to an increased

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prevalence of obesity-related Barrett's oesophageal neoplasia [5].

Surgery remains the only potentially curative treatment for both gastric adenocarcinoma and oesophageal adenocarcinoma. However, because of poor rates of survival with a surgery-alone approach in locally advanced but resectable disease, and the fact that most patients in industrialised countries have locally advanced disease, combined treatment approaches are usually considered for disease of stage IB or greater [6, 7]. Evidence-based approaches for non-Asian patients include preoperative chemotherapy or chemoradiotherapy for proximal/OGJ tumours, or perioperative chemotherapy or postoperative chemoradiotherapy for both gastric cancer patients and oesophageal/OGJ cancer patients [8–12]. Adjuvant chemotherapy alone is supported by randomised trials in Asian patients but is seldom used in Western patients [13, 14]. However, selection of the optimal treatment approach is dependent on local practice, patient presentation and the characteristics of the underlying tumour for every patient.

Factors which influence the outcome of patients treated with curative intent for gastric cancer include improvements in imaging yielding a consequently more adequate disease staging, the increasingly pivotal role of multidisciplinary teams for treatment planning and the centralisation of surgery in high-volume centres. The largest cooperative population-based study of survival in oesophago-gastric cancer, the EURO-CARE-5 project, highlighted an increase from 23.3 to 25.1 % in the 5-year relative survival rate for patients with gastric cancer diagnosed in the two 3-year periods 1999–2001 and 2005–2007 [15]. We hypothesised that changes in these variables may also have yielded improvements in overall survival in patients undergoing surgery during this period at the Royal Marsden Hospital (RMH), London, UK. To examine this hypothesis, we retrospectively collected data on resected oesophageal and gastric adenocarcinoma (OGA) patients over a decade. This analysis compares demographic, management and surgical outcomes according to the site of the primary tumour between two 5-year time periods: 2001–2005 and 2006–2010.

## Methods

On the basis of surgical procedure codes, we identified all patients who underwent surgery for cancer of the oesophagus, OGJ or stomach at RMH between January 2001 and December 2010 from the hospital electronic patient record. Eligible patients had (1) a histological diagnosis of adenocarcinoma, (2) had curative-intent resection of the malignancy at RMH, (3) were 18 years or older, and (4) had postsurgical follow-up performed at RMH. Patients

with histological diagnoses or unquestionable radiological evidence of metastatic disease before the date of surgery and patients for whom no data besides the date of surgery were available in the electronic patient record or for whom the date of surgery coincided with the last contact were excluded.

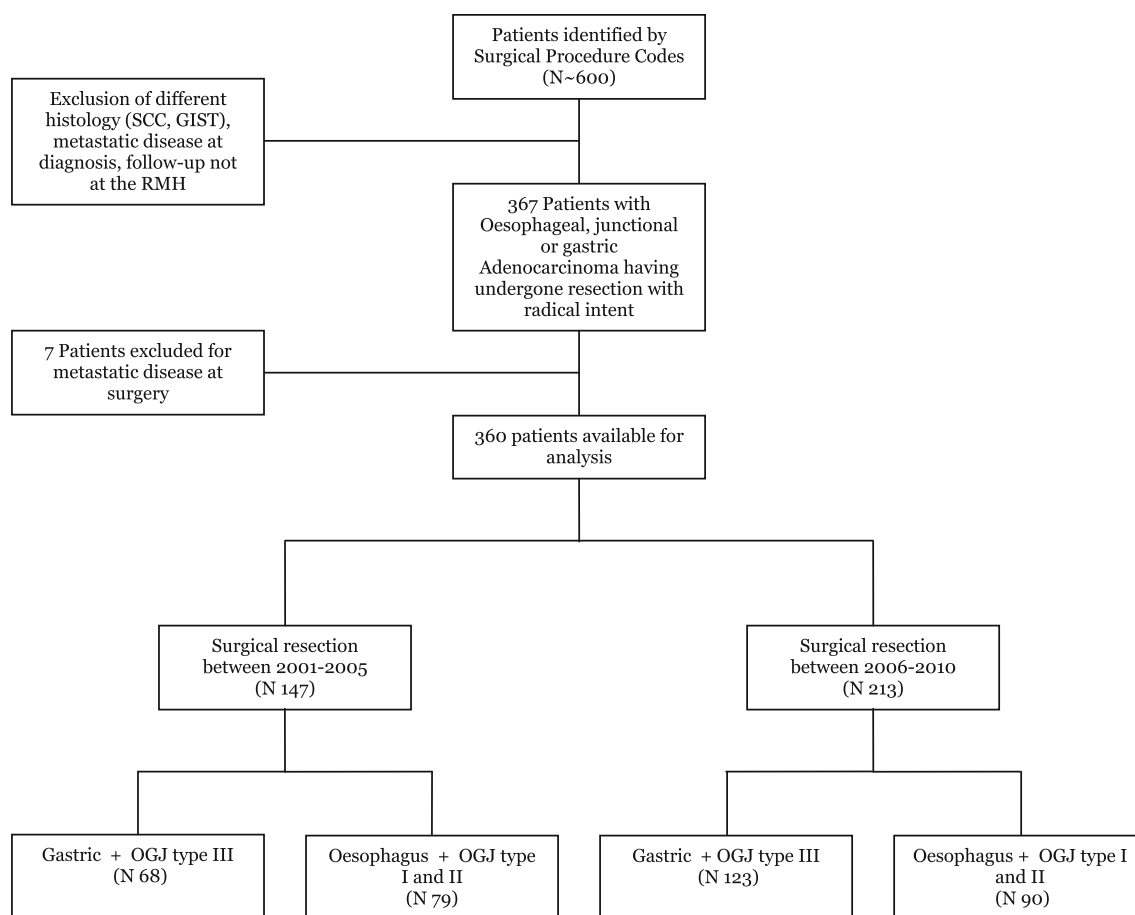
The data collected included patient demographics, the site of the primary tumour, preoperative computerised tomography (CT) staging, preoperative TN staging obtained by endoscopic ultrasonography (EUS) when performed, the type of surgery, the number of lymph nodes collected and the perioperative treatments received (including schedules and number of cycles for chemotherapy and the dose in grays and the fractions for radiotherapy). Histological details collected included pathological TNM stage, grade of differentiation and resection margins, defined as positive in the presence of tumour within 1 mm of the circumferential margin (CRM) [16]. On the basis of the date of surgery, two different cohorts were defined: patients from 2001–2005 and patients from 2006–2010. Considering the substantially different surgical approach between oesophageal and gastric cancer, we analysed demographic, management and outcomes according to the site of the primary tumour (type I and type II OGJ tumours vs gastric and type III OIG tumours, according to the Siewert classification) with descriptive statistics [17]. Disease-free survival, overall survival and survival beyond relapse were estimated by the Kaplan–Meier method; covariates were compared by the log-rank test and hazard ratios were calculated by Cox regression within the two time periods. Approval for this project was obtained before study commencement from the Institutional Review Board (Service Evaluation 3407).

## Results

Approximately 600 patients underwent surgery for oesophageal or gastric cancer at RMH between 2001 and 2010. After exclusion of patients with tumour histological type different from adenocarcinoma and patients who had palliative surgery or were followed up at a hospital other than RMH, 360 eligible patients were identified for the analysis. Of these, 147 underwent surgery during the first time period (2001–2005) and 213 underwent surgery during the second time period (2006–2010) (Fig. 1).

### Characteristics of patients

Approximately half of the patient population had a primary tumour localised at the OGJ, 40 % in the stomach and less than 10 % had a lower oesophageal adenocarcinoma; the proportion of patients with type III OGJ tumours and



**Fig. 1** Selection of patients. *GIST* gastrointestinal stromal tumour, *OGJ* oesophagogastric junction, *RMH* Royal Marsden Hospital, *SCC* squamous cell carcinoma

gastric tumours increased over time. Patients with lower oesophageal cancer or type I and type II OGJ cancer were younger and more frequently male than patients with type III OGJ cancer and gastric cancer. Most of the patients had an Eastern Cooperative Oncology Group performance status of 0–1. These baseline characteristics were comparable across the two time periods (Table 1).

### Tumour staging

Preoperative staging is detailed in Table 2. In the oesophageal and type I and type II OGJ cancer population, the use of EUS for preoperative T and N category definition increased over time, from 72 to 83 %. Overall, almost 60 % of patients had a T3–T4 tumour and more than 60 % had lymph node involvement.

In the gastric cancer cohort, the proportion of patients with preoperative CT stage T1–T2 cancer significantly increased over time, from 13 to 40 %. Approximately 50 % did not demonstrate preoperative lymph node involvement on CT. The use of positron emission

tomography (PET)–CT as a further staging technique also significantly increased over time for both anatomical tumour locations, extending to 46 % of oesophageal and type I and type II OGJ tumours in the later time period.

### Clinical management

Treatments and pathological findings are detailed in Table 3. Most patients received neoadjuvant or perioperative chemotherapy. In exceptional circumstances, a non-standard adjuvant approach was adopted, mainly due to patients' choice or comorbidities, or alternatively when emergency surgery was required or after surgical upstaging. There was a significant increase in the proportion of patients treated with a perioperative approach over time, whereas the use of neoadjuvant chemotherapy alone declined over time.

The surgical approach consisted of Ivor Lewis oesophagogastric resection for the most of the oesophageal and type I and type II OGJ cancer patients. In the gastric and type III OGJ cancer population, most patients underwent distal

**Table 1** Patient characteristics according to the site of the primary tumour and the period of surgery

Characteristics	Oesophagus and OGJ, types I and II			Stomach and OGJ, type III		
	Surgery between 2001 and 2005	Surgery between 2006 and 2010	<i>P</i>	Surgery between 2001 and 2005	Surgery between 2006 and 2010	<i>P</i>
Total patients	79	90		68	123	
Age (years)			0.317			0.264
Median	64	62		70	67	
Range	42–81	33–83		24–84	39–89	
Sex			0.52			0.681
Male	71 (89.9 %)	78 (86.7 %)		50 (73.5 %)	87 (70.7 %)	
Female	8 (10.1 %)	12 (13.3 %)		18 (26.5 %)	36 (29.3 %)	
Ethnicity			0.030 <sup>b</sup>			0.182 <sup>b</sup>
Afro-Caribbean	0 (0 %)	1 (1.1 %)		3 (4.4 %)	10 (8.1 %)	
East Asian	0 (0 %)	2 (2.2 %)		1 (1.5 %)	6 (4.9 %)	
Indian subcontinent	1 (1.3 %)	0 (0 %)		5 (7.4 %)	2 (1.6 %)	
Western	77 (97.4 %)	80 (88.9 %)		58 (85.3 %)	95 (77.2 %)	
Not recorded	1 (1.3 %)	7 (7.8 %)		1 (1.5 %)	10 (8.1 %)	
Performance status			0.041 <sup>c</sup>			0.491 <sup>c</sup>
0	16 (20.3 %)	33 (36.7 %)		13 (19.1 %)	36 (29.3 %)	
1	26 (32.9 %)	24 (26.7 %)		19 (27.9 %)	41 (33.3 %)	
2	1 (1.3 %)	0 (0 %)		4 (5.9 %)	7 (5.7 %)	
Not recorded	36 (45.6 %)	33 (36.7 %)		32 (47.1 %)	39 (31.7 %)	
Site of primary tumour						
Oesophagus	17 (21.5 %)	12 (13.3 %)				
OGJ, type I	35 (44.3 %)	42 (46.7 %)				
OGJ, type II	27 (34.2 %)	36 (40 %)				
OGJ, type III				14 (20.6 %)	31 (25.2 %)	
Stomach				54 (79.4 %)	92 (74.8 %)	
Elevated levels of tumour markers <sup>a</sup>			0.329			0.579
Yes	19 (24.1 %)	26 (28.9 %)		13 (19.1 %)	30 (24.4 %)	
No	49 (62.0 %)	47 (52.2 %)		26 (38.2 %)	75 (61 %)	
Unknown	11 (13.9 %)	17 (18.9 %)		29 (42.7 %)	18 (14.6 %)	

OGJ oesophagogastric junction

<sup>a</sup> Either carcinoembryonic antigen or CA 19-9 or both at presentation

<sup>b</sup> Western versus others in the 2001–2005 group versus the 2006–2010 group according to the site of the primary tumour

<sup>c</sup> Performance status 0 versus performance status 1–2 in the 2001–2005 group versus the 2006–2010 group according to the site of the primary tumour

subtotal or total gastrectomy. No significant difference was observed in the surgical approach between the two time periods. The mean number of lymph nodes collected significantly increased over time in both cohorts (Fig. 2). In oesophageal and type I and type II OGJ tumours, the 30- and 90-day mortality rates were not statistically different between the two time periods (1.3 and 3.8 %, respectively, in 2001–2005 and 1.1 and 3.3 %, respectively, in 2006–2010). A significant difference over time was identified in the gastric and type III OGJ cancer group: the 30- and 90-day mortality rates were, respectively, 10.3 and 14.7 % in 2001–2005 and 0 and 1.6 % in 2006–2010.

## Pathological findings

The percentage of R1 resections decreased over time in both populations. In oesophageal and type I and type II OGJ tumours it decreased from 28 to 19 %; in almost all specimens the margin involved was the circumferential one (26 % in 2001–2005 vs 18 % in 2006–2010). In gastric and type III OGJ tumours, the R1 resection rate decreased from 14 to 4 %; in most cases, the margin involved was the longitudinal one (10 % in 2001–2005 vs 2 % in 2006–2010).

Overall, oesophageal and type I and type II OGJ tumours were more frequently found to be of a more

**Table 2** Preoperative staging according to the site of the primary tumour and the period of surgery

Characteristics	Oesophagus and OGJ, types I and II				Stomach and OGJ, type III					
	Surgery between 2001 and 2005		Surgery between 2006 and 2010		<i>P</i>	Surgery between 2001 and 2005		Surgery between 2006 and 2010		<i>P</i>
	No. of patients	%	No. of patients	%		No. of patients	%	No. of patients	%	
Total patients	79		90			68		123		
CT T category					0.932 <sup>a</sup>					0.001 <sup>a</sup>
T1–T2	11	13.9	13	14.4		9	13.3	50	40.7	
T3–T4	44	55.7	50	55.6		30	44.1	39	31.7	
TX	7	8.9	15	16.7		16	23.5	16	13	
Unknown	17	21.5	12	13.3		13	19.1	18	14.6	
CT N category					0.746					0.114
N0	33	41.8	39	43.3		33	48.5	56	45.5	
N1–N2	28	35.4	37	41.1		16	23.5	48	39	
Unknown	18	22.8	14	15.6		19	27.9	19	15.5	
Baseline EUS performed	57	72.2	75	83.3	0.079					
EUS T category					0.068 <sup>a</sup>					
T1	2	3.5	7	9.3						
T2	9	15.8	18	24						
T3–T4	44	77.1	47	62.7						
TX	1	1.8	1	1.3						
Unknown	1	1.8	2	2.7						
EUS N category					0.318					
N0	20	35.1	19	25.3						
N1	35	61.4	49	65.3						
Unknown	2	3.5	7	9.3						
EUS/CT concordance					1					
Yes	22	38.6	30	40						
No	22	38.6	30	40						
Unknown	13	22.8	15	20						
Baseline PET performed					<0.001					0.001
Yes	12	15.2	46	51.1		2	2.9	33	26.8	
FDG avid	9	75	42	91.3		2	100	24	72.7	

CT computed tomography, EUS endoscopic ultrasonography, FDG fluorodeoxyglucose, OGJ oesophagogastric junction, PET positron emission tomography

<sup>a</sup> T1–T2 versus T3–T4 in the 2001–2005 group versus the 2006–2010 group according to the site of the primary tumour

advanced pathological T category than gastric and type III OGJ tumours; there was a trend towards a higher proportion of early-stage T category cancers resected in the later time period for both subsites. More than 50 % of patients who underwent surgery in the later time period (2006–2010) regardless of the site of the primary tumour did not demonstrate lymph node involvement.

### Survival outcomes

At the time of analysis, the median follow-up time was 95.5 months [95 % confidence interval (CI) 73.9–112.2 months] for patients who underwent surgery in

the first time period (2001–2005) and 58.6 months (95 % CI 54.2–60.6 months) for those who underwent surgery in the second time period (2006–2010). Survival outcomes according to the site of the primary tumour and the time period are shown in Table 4.

In the earlier time period group (2001–2005), 67 of 147 patients (45.6 %) experienced a relapse. The presence of an anastomotic relapse as a single site of relapse was confirmed in 3 % of the population. No significant difference was demonstrated in the pattern of relapse (anastomotic only vs any other site) in both cohorts over time. Almost 50 % of patients who experienced a relapse were treated with at least one cycle of first-line palliative chemotherapy

**Table 3** Treatment and pathological details according to the site of the primary tumour and the period of surgery

Characteristics	Oesophagus and OGJ, types I and II				Stomach and OGJ, type III					
	Surgery between 2001 and 2005		Surgery between 2006 and 2010		<i>P</i>	Surgery between 2001 and 2005		Surgery between 2006 and 2010		<i>P</i>
	No. of patients	%	No. of patients	%		No. of patients	%	No. of patients	%	
Total patients	79		90			68		123		
Surgery					0.207 <sup>c</sup>					0.580*
Ivor Lewis oesophagostrectomy	77	97.5	84	93.3		6	8.8	14	11.3	
Total gastrectomy	2	2.5	6	6.7		27	39.8	51	41.5	
Subtotal gastrectomy						35	51.4	58	47.2	
Resection					0.116					0.005
R0	53	67.1	73	81.1		52	76.5	118	95.9	
R1	22	27.8	17	18.9		10	14.7	5	4.1	
Unknown	4	5.1	0	0		6	8.8	0	0	
Grade					0.354 <sup>d</sup>					0.178 <sup>d</sup>
Poor	39	49.4	41	42.2		46	67.7	75	61	
Moderate	29	36.7	38	45.6		18	26.5	42	34.2	
Good	2	2.5	6	6.7		0	0	4	3.3	
Unknown	9	11.4	5	5.6		4	5.9	2	1.6	
Tumour T category					0.043 <sup>e</sup>					0.167 <sup>e</sup>
T0	3	3.8	6	6.7		3	4.4	6	4.9	
T1–T2	32	40.5	49	54.4		37	54.5	83	67.5	
T3–T4	42	53.2	35	38.9		24	35.3	34	27.6	
TX	2	2.5	0	0		4	5.8	0	0	
Nodal status					0.57					0.169
N0	39	49.4	49	54.4		26	38.2	63	51.2	
N1–N3	38	48.1	40	44.4		38	55.9	60	48.8	
Unknown	2	2.5	1	1.1		4	5.9	0	0	
Perioperative treatment					0.012 <sup>f</sup>					0.016 <sup>f</sup>
Adjuvant <sup>a</sup>	2	2.5	0	0		5	7.4	5	4.1	
Neoadjuvant	61	77.2	46	51.1		22	32.4	26	21.1	
Perioperative <sup>b</sup>	9	11.4	23	25.6		13	19.1	62	50.4	
None	7	8.9	21	23.3		28	41.2	30	24.4	

OGJ oesophagogastric junction

<sup>a</sup> Because to patients' choice (3), emergency surgery (2), surgical upstaging (3) and comorbidities (4)

<sup>b</sup> Nineteen patients received postsurgical chemoradiotherapy, 18 OGJ cancer patients and one gastric cancer patient because of R1 resection; two OGJ cancer patients received presurgical chemoradiotherapy because of tumour burden persistence

<sup>c</sup> Oesophagostrectomy versus the others in the 2001–2005 group versus the 2006–2010 group according to the site of the primary tumour

<sup>d</sup> Poor versus the others in the 2001–2005 group versus the 2006–2010 group according to the site of the primary tumour

<sup>e</sup> T0–T2 versus T3–T4 in the 2001–2005 group versus the 2006–2010 group according to the site of the primary tumour

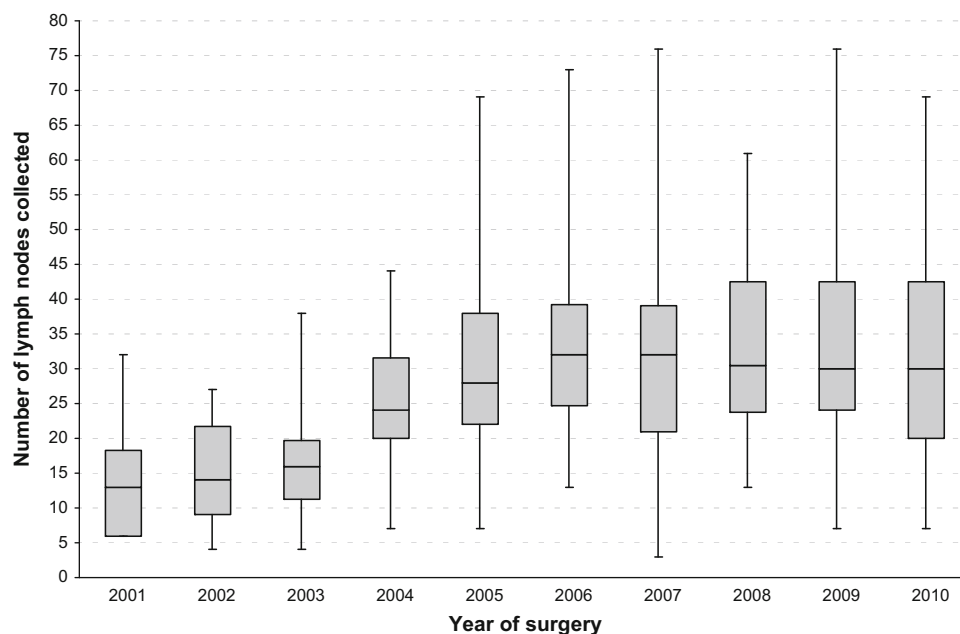
<sup>f</sup> None versus any other adjunct treatment in the 2001–2005 group versus the 2006–2010 group according to the site of the primary tumour

and 14 (20.1 %) were treated with a second-line treatment. In the later time period group (2006–2010), 80 of 213 patients (37.6 %) experienced a relapse. Of these, 50 patients (62.5 %) were treated with at least one cycle of first-line palliative chemotherapy and 17 (21.2 %) also received a second-line treatment. One patient in the earlier

time period group and five patients in the later time period group received a third-line treatment.

Fifty-three percent of the population died (54.6 % of oesophageal and type I and type II OGJ cancer patients and 50 % of gastric cancer patients). The 5-year overall survival rate significantly increased over time in both

**Fig. 2** Number of lymph nodes collected by year



cohorts: from 42.3 to 56.6 % [hazard ratio 0.64 (95 % CI 0.41–0.98),  $P = 0.040$ ] for oesophageal and type I and type II OGJ cancer patients and from 38.8 to 55.3 % [hazard ratio 0.51 (95 % CI 0.34–0.76),  $P = 0.001$ ] for gastric and type III OGJ cancer patients. Similarly, the 5-year disease-free survival rate significantly increased over time in both cohorts: from 34.6 to 53.5 % [hazard ratio 0.61 (95 % CI 0.41–0.92),  $P = 0.019$ ] for oesophageal and type I and type II OGJ cancer patients and from 35.9 to 51.1 % [hazard ratio 0.56 (95 % CI 0.38–0.82),  $P = 0.003$ ] for gastric and type III OGJ cancer patients (Fig. 3). The survival time from relapse to the last follow-up was between 8 and 10 months for oesophageal and type I and type II OGJ cancer patients and 6 months for gastric and type III OGJ cancer patients. No significant improvement was demonstrated over time.

## Discussion

In this study we examined patient and tumour characteristics, preoperative staging, treatment and outcomes of a large cohort of patients with gastric and gastroesophageal cancers selected from a single cancer centre over a period of 10 years. We then analysed any differences in treatment pathways and survival over two 5-year periods: 2001–2005 and 2006–2010. Our findings demonstrate a significant improvement in disease-free and overall survival in the later time period. We postulate that the significant increase in the number of R0 resections and the higher lymph node yield are the main factors affecting outcomes. As advances in surgical techniques do not always translate into

significant differences in outcomes, we speculate that improved patient selection for those truly amenable to curative resection and exclusion of those patients making rapid progress with neoadjuvant treatment may also be partly responsible for these results. However, this contribution remains speculative because of the nature of this study, which did not allow the description of stage migration phenomena.

Changes in the pattern of the use of chemotherapy as an adjunctive treatment might also contribute to improved outcomes. This large dataset is reflective of the practice at RMH, which is a major tertiary referral cancer centre. The population served by RMH is diverse and is broadly representative of the UK population as a whole. Several practice-changing clinical trials were ongoing during the decade under investigation, and this activity might have impacted on both management and outcomes. When the Medical Research Council OE02 study was reported in 2002 [18], the strategy adopted for patients with lower-third oesophageal or cardia tumours consisted of two cycles of preoperative cisplatin and 5-fluorouracil chemotherapy. From November 2004, the same population was eligible for the Medical Research Council OE05 trial [19], which randomised patients to receive either two cycles of cisplatin and 5-fluorouracil chemotherapy or four cycles of epirubicin, cisplatin, and capecitabine chemotherapy. Following the publication of the UK Medical Research Council MAGIC trial in 2006, perioperative chemotherapy for tumours staged as T2 or greater became a standard treatment for both gastric and lower-third oesophageal adenocarcinomas [10]. Finally, in October 2007 a further multicentre study for patients with operable

**Table 4** Survival outcomes according to the site of the primary tumour and the period of surgery

	Oesophagus and OGJ, types I and II			Stomach and OGI, type III		
	Surgery between 2001 and 2005	Surgery between 2006 and 2010	<i>P</i>	Surgery between 2001 and 2005	Surgery between 2006 and 2010	<i>P</i>
Median follow-up time (months)	97.3	59.3		82.6	57.3	
5-year OS rate	42.3 % (31.0–53.1 %)	56.6 % (44.6–66.9 %)	0.04 (0.41–0.98)	38.8 % (27.1–50.2 %)	55.3 % (45.4–64.2 %)	0.001 (0.34–0.76)
5-year DFS rate	34.6 % (24.2–45.1 %)	53.5 % (42.5–63.3 %)	0.019 (0.41–0.92)	35.9 % (24.6–47.3 %)	51.1 % (41.3–60.1 %)	0.003 (0.38–0.82)

The 95 % confidence interval is given in parentheses

DFS disease-free survival, HR hazard ratio, OGJ oesophago-gastric junction, OS overall survival

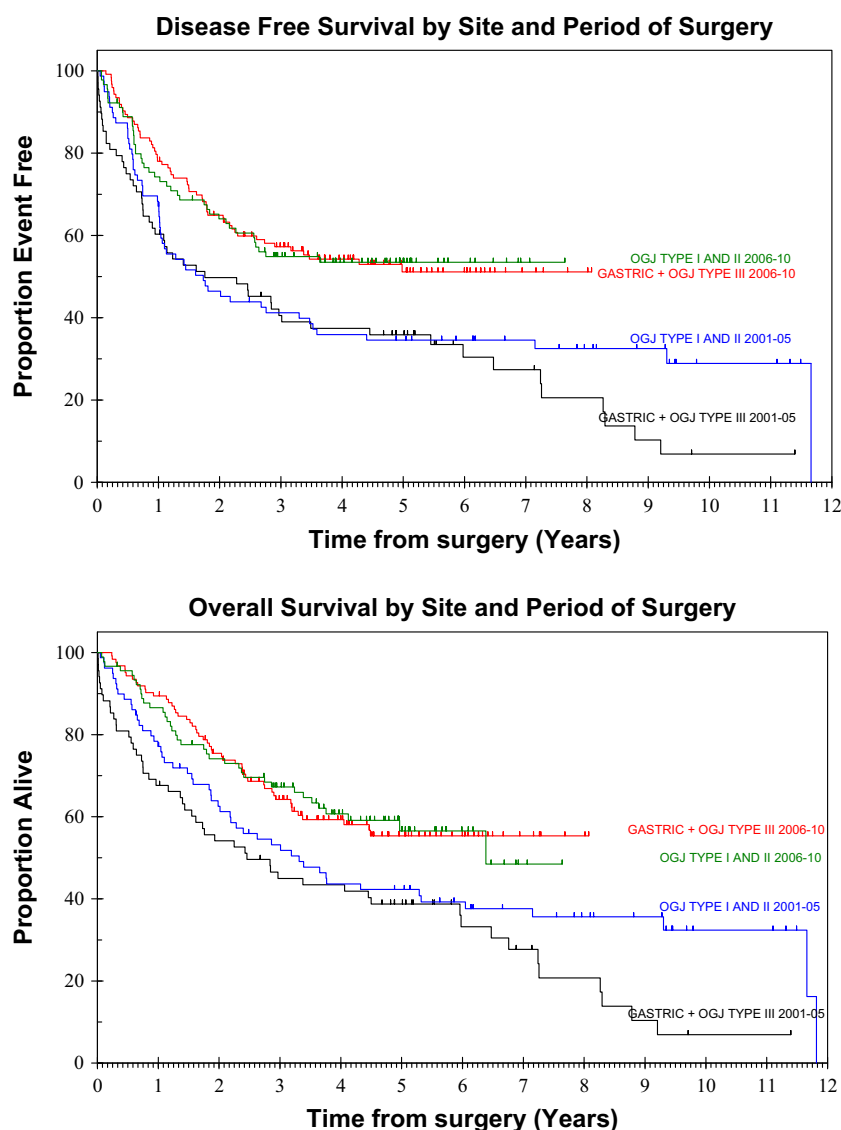
oesophago-gastric adenocarcinoma, the Medical Research Council ST03 trial, which randomised patients to receive perioperative epirubicin, cisplatin, and capecitabine chemotherapy with or without bevacizumab therapy, opened for recruitment [20]. Participation of patients in these studies contributed to promotion of an adjunctive perioperative chemotherapy strategy; this is supported by the fact that both in 70 % of patients the cancer was staged as greater than T2 and the same proportion received at least a preoperative treatment. We acknowledge that patients may experience superior outcomes in a research-active environment [21]. Therefore, it is possible that the high levels of research activity at RMH may result in longer survival for patients, not just those who are participants in clinical trials; however, this would apply equally across both time periods.

With respect to preoperative staging, an increase in the proportion of early-stage tumours was noted in both groups over time, reaching statistical significance in the gastric cancer cohort. We hypothesise that the increased use of PET-CT might be contributory in excluding patients with occult advanced disease, leading to selection of patients with earlier-stage disease as candidates for surgery. However, as PET-CT did not become a standard of care in our institution until 2009, it is difficult to estimate its effect on stage migration and survival without an analysis of pre-PET and post-PET time periods, which may be confounded by other variables. The percentage of EUS performed at the baseline in the proximal cancer cohort also significantly increased over time. A more accurate definition of the depth of tumour invasion and local lymph node involvement might have contributed to changes in decision making regarding adoption of a preoperative treatment strategy or surgery alone. As intention-to-treat data were not collected in this study, we cannot accurately determine the potential impact of the increased use of EUS on treatment decisions.

No significant difference in the type of surgery performed was demonstrated. However, surgical outcomes changed significantly over time; specifically, a higher lymph node yield was demonstrated in the later time period. Furthermore, the rate of R0 resections for patients with gastric and type III OGJ tumours dramatically increased from 76.5 to 95.9 % over time. These data compare favourably with the National Oesophago-gastric Cancer Audit 2013 data [22]. Although not statistically significant, an increase in the R0 resection rate in the group of patients with proximal tumours was demonstrated, from 67.1 to 81.1 %. In most cases the CRM was involved, in 26 and 18 % of cases in the earlier and later periods, respectively. These figures are consistent with the National Oesophago-gastric Cancer Audit 2013, which reported a CRM rate of 27 % [22]. The involvement of the CRM is clearly a major



**Fig. 3** Survival outcomes. *OGJ* oesophagogastric junction



challenge in oesophageal and OGJ tumours. As such, introduction of preoperative chemoradiotherapy regimens such as that used in the CROSS trial is a rational and effective approach in the treatment of these tumours [9].

Service provision for oesophagogastric cancer in the UK underwent a major reconfiguration over the past decade, following publication of the Department of Health's document entitled "Guidance on Commissioning Cancer Services: Improving Outcomes in Upper Gastro-intestinal Cancers" [23]. In 2002, national guidelines for the management of this disease were introduced, with specific recommendations in terms of diagnosis, staging, pathology report and treatment [24]. A concerted effort was made to centralise specialised cancer surgery in high-volume centres, where multidisciplinary teams are responsible for patient management. As a consequence, the number of patients referred to specialised centres such as RMH may

have increased and consolidated the experience of the multidisciplinary team there. Furthermore, in 2004, the Joint Advisory Group on Gastrointestinal Endoscopy [25] provided dedicated guidelines for training, appraisal and assessment of trainees in gastrointestinal endoscopy. This may also have contributed to improvements in the national endoscopy service, with consequent increases in early detection of cancer, as suggested by the significant increase in the proportion of early-stage cancer patients.

In the case of recurrent cancer following surgery, median survival improved over time for proximal tumours, without reaching statistical significance. In the later time period, approximately two thirds of patients received treatment on relapse, whereas this proportion was lower in the earlier time period. On the basis of the COUGAR-02 study, second-line chemotherapy was not adopted as a standard RMH practice until 2012, although selected

patients did receive it before then [26]. Additionally, the monoclonal antibody trastuzumab used in the treatment of human epidermal growth factor receptor 2 positive disease was not available in the UK until 2011, and only two patients in this study received it in a first-line metastatic setting [27]. Owing to the increasing availability of these treatments, it is likely that there has now been a further improvement in postrelapse survival over time, although the treatment intent currently remains palliative in this setting.

This study has a number of limitations principally because of the retrospective nature of the data collection. This has prevented our accurately identifying the total number of cases evaluated over the study period, which does not allow us to report the surgical resection rate. However, the results do demonstrate the outcome for a large cohort of patients considered fit for radical treatment (performance status less than 2) with locally operable disease. Using the comparison of the two time-period groups as an internal control, we have demonstrated improved outcomes over time in the selected population. All comparisons in this analysis were made between the average of variables considered from the two consecutive time periods. As a result, differences in management and outcomes between the two tails of the decade might be underestimated; limiting our analysis to these restrictive time points would reduce our power to draw statistically sound conclusions. During the study, neoadjuvant or perioperative chemotherapy became the standard UK practice for treatment of oesophageal and gastric cancer. Recent data from the CROSS trial have demonstrated higher R0 resection rates with a chemoradiotherapy regimen compared with surgery alone. We acknowledge the issue of the most appropriate perioperative management remains to be fully established and that the UK practice may change in relation to cases with a threatened CRM [9].

In conclusion, the findings of this study demonstrate that survival of patients with resected OGJ adenocarcinoma at RMH improved during the decade from 2001 to 2010. Relevant factors may include an increase in the R0 resection rate and a progressively higher lymph node yield. A more accurate staging of the disease preoperatively by the use of CT-PET and EUS, leading to exclusion from surgery of those patients with CT-occult metastatic disease, and an increase in chemotherapy use as a surgical adjunct may also be contributory. Clinically, ongoing expert multidisciplinary team input is essential to maintain this quality of care. Although oesophageal and gastric cancer remain lethal diseases, this is currently an area of intense research and improvements in survival are anticipated. The results recently published by The Cancer Genome Atlas Research Network [28] have contributed to a better understanding of tumour biology and molecular profiles, and it is hoped that

this will promote the identification of prognostic and predictive biomarkers fundamental in personalisation of the chemotherapeutic and surgical pathway for this disease.

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#### Compliance with ethical standards

**Ethical standards** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Approval for this project was obtained before study commencement from the Institutional Review Board (Service Evaluation 3407).

**Conflict of interest** The authors declare that they have no conflict of interest.

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