NATIONAL BOWEL CANCER AUDIT

Optimal time interval between neoadjuvant long-course radiotherapy and major resection in English rectal cancer patients diagnosed between 2011 and 2014

NBCA: Short report 3

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Introduction:

Historically rectal cancer has had a high local recurrence rate, often with poor functional outcomes. Improvements in MRI scanning has led to more accurate assessment of local recurrence risk prior to treatment,(1) whilst improvements in surgical technique and the introduction of pre-operative radiotherapy have reduced the risk of local recurrence.(2)

Neoadjuvant chemo-radiotherapy (CRT) combines radiation treatment to inhibit tumour growth and low-dose chemotherapy to increase the sensitivity of the tumour to radiation. It is used to reduce the risk of local recurrence and has the potential to induce tumour downsizing, which in turn may improve sphincter preservation and pathological complete response (pCR) rates.(3)

Current NICE guidelines advise that treatment of rectal cancer is guided by the risk of local recurrence defined by the pre-treatment MRI scan. They recommend that preoperative CRT, with an interval before surgery to allow tumour response and shrinkage, is offered to patients with high-risk primary rectal cancer. Patients deemed to have borderline moderate and high risk disease should also be considered for CRT.(4)

Although the interval between the end of radiotherapy and surgery is traditionally quoted as 6-8 weeks (based on a randomised controlled trial from the 1990s (5)), there is no consistent evidence as to the optimal time delay. Previous cohort studies suggest that there is wide variation in practice as to the interval between CRT and surgery.(6) An on-going randomised trial is investigating the outcomes of surgery at 6 or 12 week time intervals; in the short-term they found significantly greater tumour downstaging and improved pCR with a longer delay.(7) Another recent trial compared delays of 7 and 11 weeks, but did not find an increase in pCR rate.(8)

This study investigates the impact of time to surgery after CRT on circumferential margin status, tumour downstaging, rate of complete response, 18 month stoma presence and 24 month mortality in patients with rectal cancer.

Methods:

Data from the National Bowel Cancer Audit for patients diagnosed with rectal cancer between 2011 and 2014 were linked to administrative hospital data (Hospital Episode Statistics), the National Radiotherapy Dataset and ONS mortality data. The total number of attendances for radiotherapy was used to define whether a patient received CRT. Time to

surgery was defined as the number of days between the estimated finish date of radiotherapy and date of elective surgery.

In total, 4,164 patients with rectal cancer who received CRT 28-182 days (4-26 weeks) prior to surgery were included.

Results:

- Median time from CRT to surgery was approximately 12 weeks (85 days (IQR 71-100 days))
- < 10% of patients had surgery within 8 weeks of finishing radiotherapy
- Patients who waited longer tended to be older and less healthy (more co-morbidities and higher ASA grade) (Table 1)
- Patients who waited longer were more likely to have a stoma 18 months after surgery (Figure 1a) and
    - were more likely to have a surgical procedure leading to a permanent stoma (44% at 4-10 weeks vs 60% at 14-26 weeks)
    - were less likely to have a stoma reversed after an anterior resection (72% at 4-10 weeks vs 60% at 14-26 weeks)
- The lowest rate of positive circumferential margins occurred between 4-14 weeks (Figure 1b)
- The highest rates of complete response and downstaging occurred between 10-14 weeks (Figure 1c/d)
- There was no evidence that time to surgery had an effect on mortality at 24 months after starting CRT ($p=0.46$ (2dp))

Conclusions:

The median time to surgery within our cohort is longer than that previously reported. The best tumour response appears to occur between 10-14 weeks. A longer delay to surgery is associated with an increased risk of having a stoma 18 months after surgery.

Table 1 Demographics and pre-treatment staging

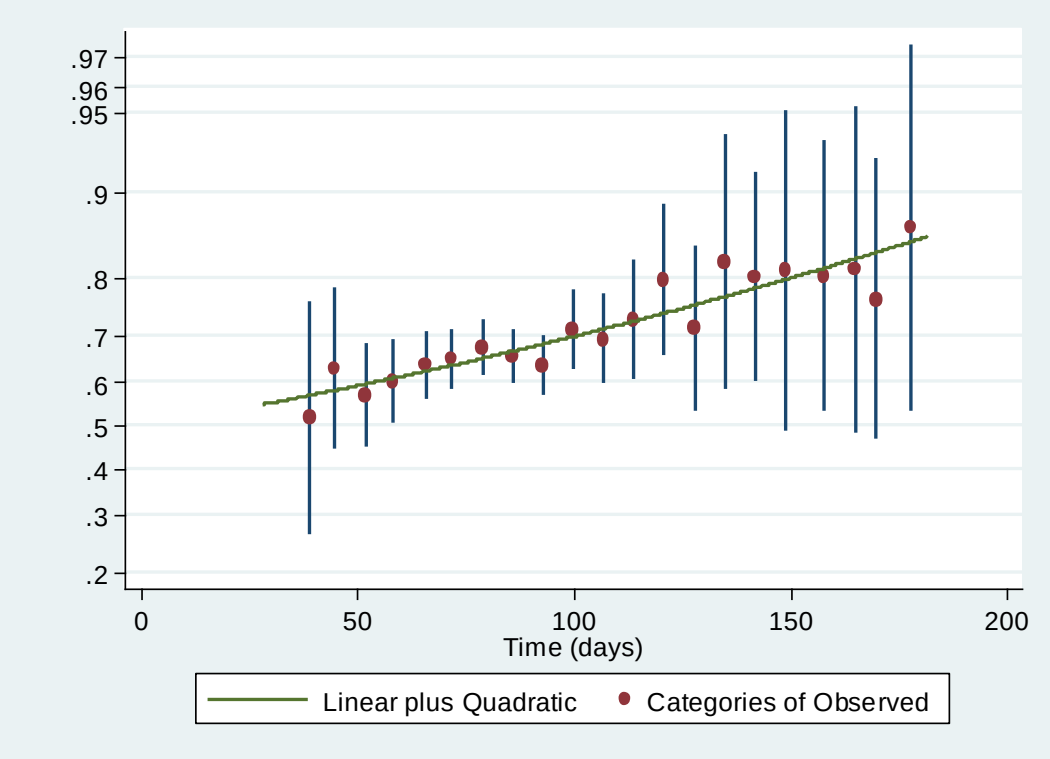
		4-10 weeks		10-12 weeks		12-14 weeks		14-26 weeks	
		N	%	N	%	N	%	N	%
		990		1,025		1,000		1,149	
Age Group (years)	18-64	533	53.8	503	49.1	517	51.7	522	45.4
	65-74	288	29.1	335	32.7	332	33.2	395	34.4
	75-84	161	16.3	182	17.8	147	14.7	220	19.1
	>=85	8	0.8	5	0.5	4	0.4	12	1.0
Gender	Male	664	67.2	664	64.8	662	66.2	765	66.6
	Female	324	32.8	361	35.2	338	33.8	383	33.4
	Missing		2 (0.2)		0 (0.0)		0 (0.0)		1 (0.1)
Comorbidities (Charlson Score)	0	710	71.7	723	70.5	663	66.3	719	62.6
	1	220	22.2	250	24.4	271	27.1	337	29.3
	2+	60	6.1	52	5.1	66	6.6	93	8.1
ASA grade	1	190	20.7	190	19.7	179	19.1	149	14.0
	2	589	64.2	629	65.3	591	63.1	664	62.5
	>=3	138	15.0	144	15.0	166	17.7	250	23.5
	Missing		73 (7.4)		62 (6.0)		64 (6.4)		86 (7.5)
IMD quintile of deprivation	least 1	160	16.3	190	18.7	160	16.2	244	21.5
	2	166	16.9	191	18.8	213	21.6	213	18.8
	3	205	20.9	209	20.6	189	19.1	207	18.3
	4	233	23.8	218	21.5	183	18.5	233	20.5
	most 5	217	22.1	206	20.3	243	24.6	237	20.9
	Missing		9 (0.9)		11 (1.1)		12 (1.2)		15 (1.3)

Table 2: Surgical procedure

		4-10 weeks		10-12 weeks		12-14 weeks		14-26 weeks	
		N	%	N	%	N	%	N	%
		990		1,025		1,000		1,149	
Surgical Procedure	AR	548	55.4	517	50.4	516	51.6	455	39.6
	APER/PE	381	38.5	447	43.6	410	41.0	575	50.0
	Hartmanns	47	4.7	51	5.0	61	6.1	109	9.5
	Other	14	1.4	10	1.0	13	1.3	10	0.9
Stoma at time of surgical procedure	None	30	3.0	18	1.8	15	1.5	13	1.1
	Ileostomy	476	48.1	433	42.2	458	45.8	360	31.3
	Colostomy	484	48.9	574	56.0	527	52.7	776	67.5

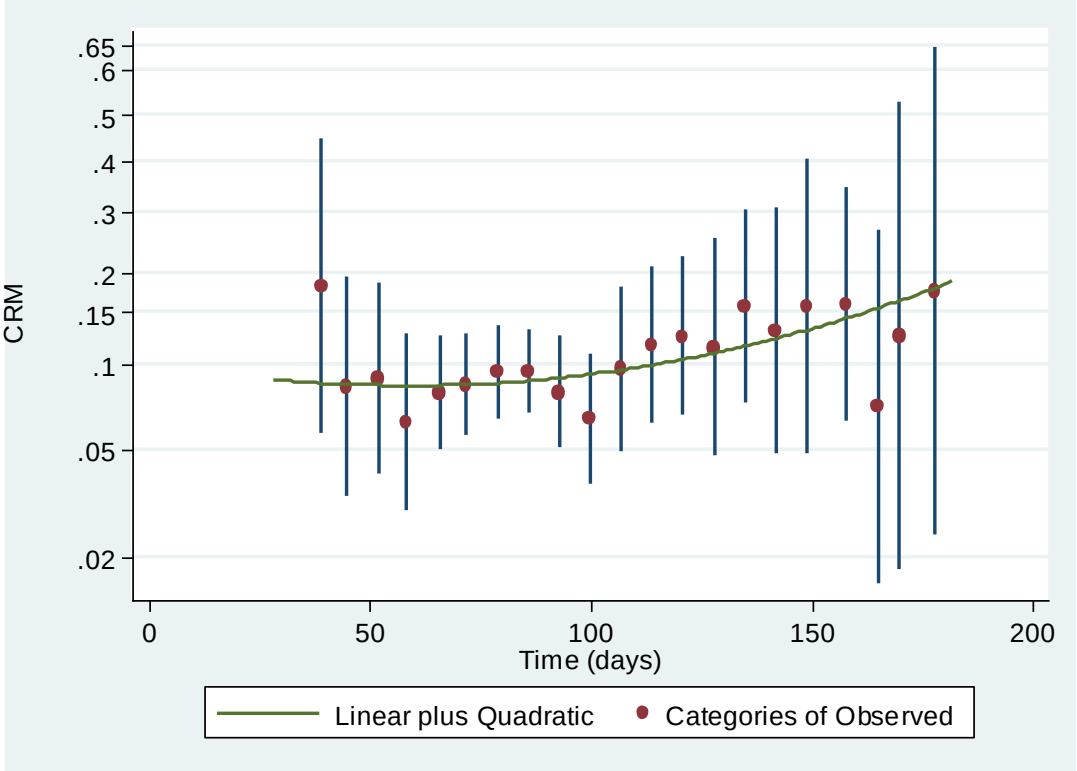
Figure 1: Relationships between outcome and time to surgery

a) Stoma presence 18 months after any surgery



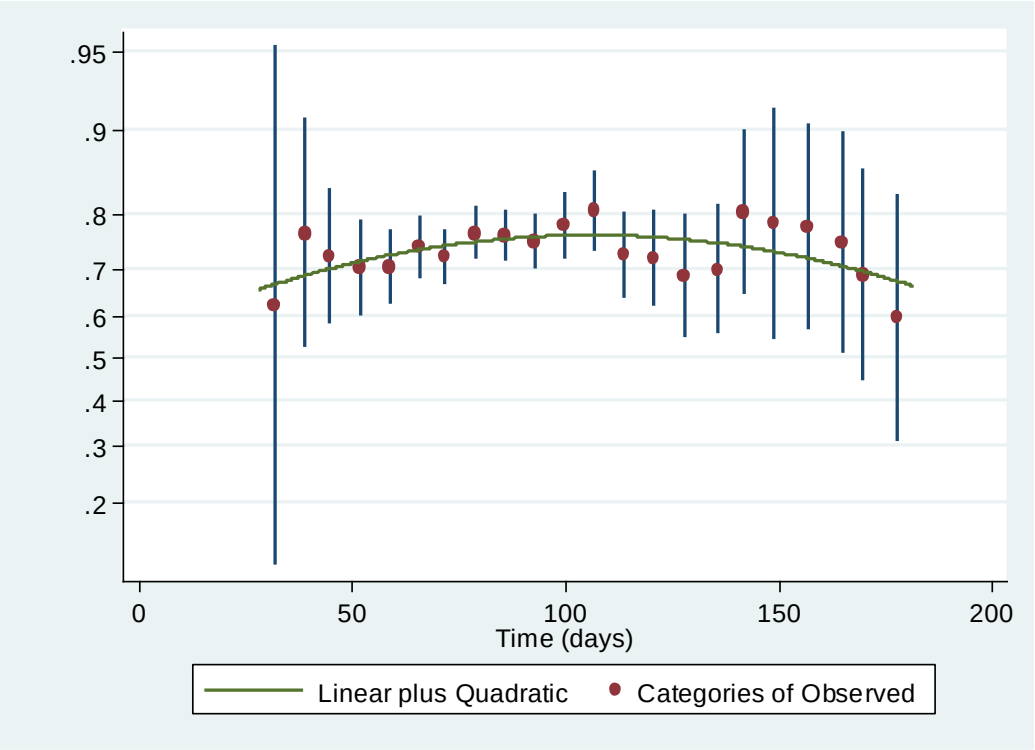
p value for relationship over time <0.0001

b) Positive circumferential margin



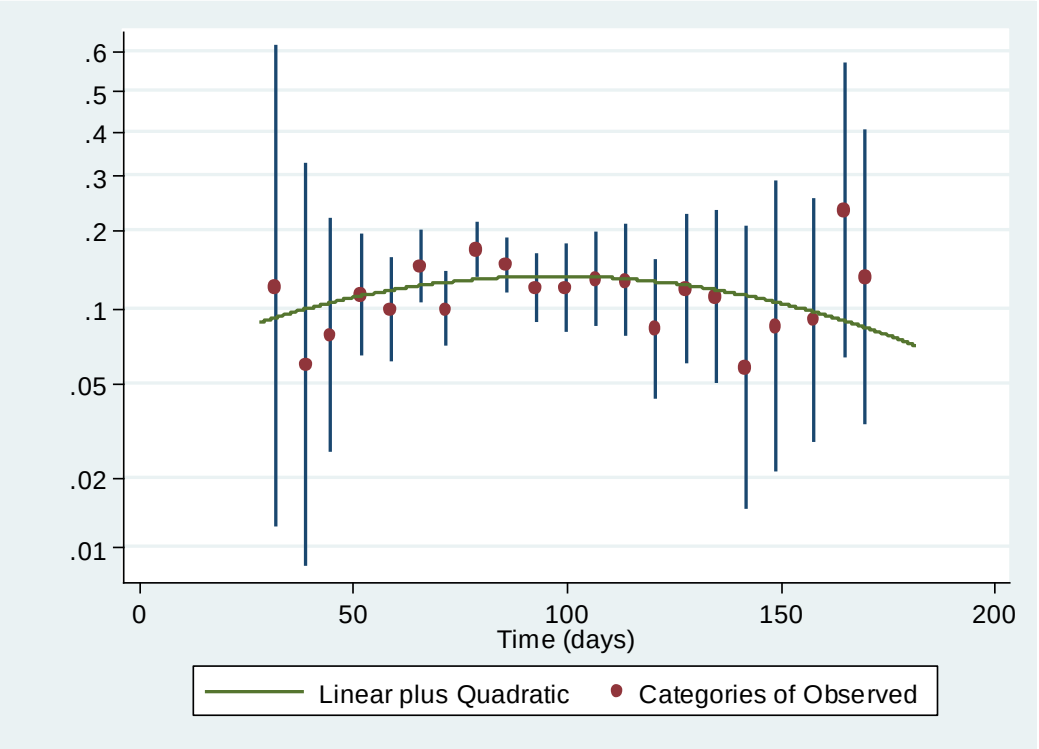
p value for relationship over time 0.03 (2dp)

c) Improvement in T/N stage



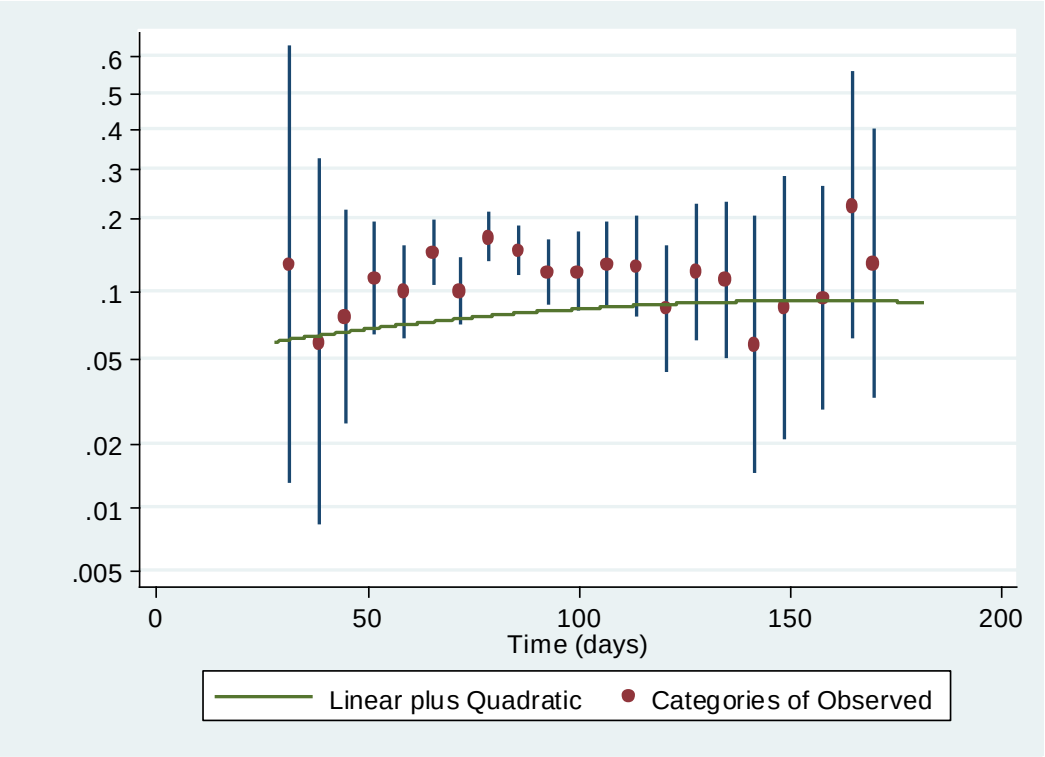
p value for relationship over time 0.09 (2dp)

d) Complete response



p value for relationship over time 0.10 (2dp)

e) Mortality 24 months after starting CRT



p value for relationship over time

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