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Adherence to NICE Guidelines on Colorectal Cancer Follow-Up: A Cross-Sectional Analysis

Priyancaa Jeyabaladevan[1], Abhinaya Varatharajah[2]

[1] Whipps Cross Hospital, Barts Health NHS Trust
[2] Whipps Cross Hospital, Barts Health NHS Trust

Correspondence: Priyancaa Jeyabaladevan. 27 Stradbroke Grove, Clayhall, Ilford, Essex. IG5 0DN.
Email: p.jeyabaladevan@nhs.net

Abstract
Purpose: Our aims were to determine adherence to National Institute of Clinical Excellence (NICE) guidelines on colorectal cancer (CRC) surveillance and to evaluate local practice patterns determine how it can be further improved. Patients and methods: Patients with colorectal cancer resection between January 1, 2017 and December 31, 2017 were identified, and their records retrospectively reviewed. Results: A total of 18 patients were eligible. Surveillance patterns, including blood tests and colonoscopies, were inconsistent with NICE recommendations in a significant proportion of patients. Follow up appointments and CT imaging occurred more frequently in line with the guidelines. For recurrences detected by surveillance, 66.6% were resectable whereas 0% of those detected by symptoms were resectable. Conclusions: The results prove that a moderately intensive follow-up strategy can positively identify resectable recurrence thus increasing overall survival. Our data highlights the need for local improvement to adherence to NICE guidelines regarding CRC follow-up. We have created a pro forma which is attached to the patient's clinical notes. It will aid clinicians in reminding them when appropriates tests should be completed. A re-audit will be completed in December 2020 which will include looking at the effectiveness of the new pro forma.

Keywords: Colorectal Cancer, Tumor, Follow-Up, Resection, CEA

1. Introduction

1.1 Background

Colorectal cancer (CRC) is the second most common malignancy in the world, with there being around 42,300 new cases in the UK every year (1). At presentation, around two-thirds of these patients will undergo resection with curative intent. The TNM stage at diagnosis is the most important prognostic factor for disease-free and overall survival (OS), with patients with stage II and III CRC having a 5-year OS rates of 70% and 55%,

respectively (2,3) Despite potentially curative surgery and the use of adjuvant chemotherapy, radiation, or chemoradiation, ≤ 40% of patients with stage II/III disease will still develop disease recurrence within three years of their initial diagnosis (4.5). The substantial risk of recurrence highlights the importance of adequate postoperative surveillance, so that appropriate detection and treatment of disease relapse can be offered. There are three purposes of surveillance following CRC resection: (a) detection of residual tumour tissue or local recurrence; (b) detection of metachronous colorectal tumours; and (c) detection of metastases (6-8). For the detection of residual tumour tissue or local recurrence and metachronous colorectal lesions, colonoscopy is the most established examination method and computed tomography (CT) is used to detect metastases. In addition, medical history, physical examination and carcinoembryonic antigen (CEA) measurement are recommended for surveillance (9.)

The ongoing debate regarding the intensity of follow-up investigations is complex. There is a plethora of research that demonstrates intense postoperative surveillance compared with less intensive strategies results in a survival benefit. Proponents of an intensive surveillance regimen argue that early detection of recurrence results in a higher proportion of potentially resectable tumour recurrences and improves OS (10-12). In contrast, advocates for a simpler strategy argue that excessive investigations can lead to increased health care costs, contribute to patient and physician anxiety, and rarely alter the natural course of disease (13,14). To date, there is no universally accepted protocol.

In view of ambiguous protocol, the National Institute of Clinical Excellence (NICE) has published guidelines for managing and surveillance of colorectal cancer in adults. The set of NICE guidelines released in 2011 (and later updated in 2014) recommends a moderately intensive surveillance scheme in which patients are offered follow up clinic in 4-6 weeks after resection, at least two CT Chest, Abdomen & Pelvis (CAP) in the first three years, regular carcinoembryonic antigen (CEA) tests at least every six months in the first three years and offered a colonoscopy one year after surgery (15). Despite the existence of clear guidelines, nationwide surveys of oncologists reveal marked differences in attitudes towards CRC follow up. Research shows the substantial variations in actual surveillance practice amongst cancer centres and in the guidelines published by major cancer societies (16-21). To better understand the protocol practice locally, we conducted this study to determine the adherence rate of NICE guidelines on CRC follow- up to examine the impact of patterns on patient outcomes.

1.2 Colorectal Cancer Stages

The staging system (Table 1) most often used for colorectal cancer is the American Joint Committee on Cancer (AJCC) TNM system, which is based on 3 key pieces of information:

- The extent (size) of the tumor *(T)*
- The spread to nearby lymph nodes *(N)*
- The spread (metastasis) to distant sites *(M)*

Table 1: AJCC staging system. Describes the extent of disease progression in cancer patients, utilising the TNM scoring system: **T**umour size, Lymph **N**odes affected and **M**etastases (22)

Stage IA	*T1*	*N0*	*M0*
Stage IB	T2	N0	M0
Stage IIA	T2	N0	M0
Stage IIB	T1- T3	N1	M0
Stage IIIA	T1- T3	N2	M0
Stage IIIB	T4	Any N	M0
Stage IV	Any T	Any N	M1

1.3 Surveillance following surgical resection

Table 2 summarizes the recommendations on surveillance following curative survival resection of CRC in the US, EU, and UK (23). In all guidelines, medical history and examination, CEA measurements, CT of chest and abdomen and colonoscopy are recommended after surgery for colon cancer. For rectal cancer, CT pelvis is recommended for all guidelines. Except for colonoscopy for detection of metachronous colorectal tumours, the surveillance period is determined to be five years in every guideline. This is based on previous studies showing that most recurrences and metastases are detected within five years after initial treatment (24-26). Forty percent of patients with stage II and III will develop recurrences (2). It is widely recommended in national guidelines be applied for patients with Stage II and III CRC. Surveillance after surgical resection of cancer in Stage I does not require such intense follow up as there is allow possibility of recurrence, particularly for node negative pT1 cancer. This goes as far as the surveillance recommendations for Stage I cancer is not described in the ASCO guidelines because of minimal data to provide guidance. It is reasonable to note further investigation is necessary to establish more efficient programs for surveillance of pT1 cancer (27,28).

2. Methodology

2.1 Audit standard

The 'Colorectal Cancer Diagnosis and Management' NICE guidelines, published in 2011 and last updated in 2014 (summarized in Table 2) were used as the reference standard on which clinicians adherence to CRC follow up was measured and practice patterns evaluated.

2.2 Study Hospital

Whipps Cross Hospital is a district general teaching hospital located in East London serving a population of around 350,000 people. It houses a General Surgery which provides urgent and emergency services through its accident and emergency department and urgent care centre.

Table 2: Summary of surveillance following colorectal resection secondary to cancer in the US, EU and UK. ASCO, American Society of Clinical Oncology. ESMO, European Society for Medical Oncology. NICE, National Institute of Clinical Excellence. CEA, carcinoembryonic antigen. CT, computed tomography

	ASCO US	ESMO EU	NICE UK
History and physical examination	Every 3-6 months for 5 years after surgery	Every 3-6 months for 3 years and every 6-12 months at years 4 and 5 after surgery	offered follow up clinic in 4-6 weeks after resection
CEA measurement	Every 3-6 months for 5 years after surgery	Every 3-6 months for 3 years and every 6-12 months at years 4 and 5 after surgery	At least every 6 months in the first three years
CT scan of chest, abdomen and pelvis	Every 12 months for 3 years/ every 6-12 months for high risk recurrence patients	Every 6- 12months for the first 3 years for patients at high risk of recurrence	At least 2 scans in the first 3 years
Colonoscopy	AT year 1 and every 5 years thereafter if the findings were normal	At year 1 and 3 -5 years there after	At year 1 and 3 -5 years there after

2.3 Study design

This study is a cross- sectional analysis within the colorectal cancer database with a population – based cohort study to assess the post resection follow up care for adult patients for with colorectal cancer.

2.4 Data collection

This study was conducted upon receiving approval from the General Surgical department lead. Consecutive patients diagnosed with colorectal cancer and underwent curative resection from January 1, 2017 to December 31, 2017 were included. An electronic database compromising a list of the patient that had undergone colorectal resection was made available to all surgical doctors on the hospital shared drive. Surgical juniors were periodically reminded by consultants to ensure patients having colorectal resection secondary to CRC were added to the database for audit purposes. Electronic medical records were respectively reviewed to abstract patient demographics, baseline tumour characteristics, local and systemic treatment history, surveillances practices and clinical outcomes during the first three years of follow-up.

2.5 Sample size

The sample size for this study was determined by the sample size of the Colorectal Database. N = 18. One patient was excluded from data because of death.

2.6 Statistical Analysis

Descriptive statistical analysis was conducted to summarize the baseline patient demographics and tumour characteristics. The NICE guidelines on CRC surveillance were used to estimate the appropriate number of surveillance interventions over a three-year follow-up period. Statistical analysis was conducted using Microsoft Excel. All visits and tests prompted by patient symptoms or abnormal laboratory and imaging results as well as investigations occurring after disease relapse were excluded from our tally and analysis of surveillance interventions. Study participants were compared with respect to imaging, follow up and CEA testing results. The primary outcomes were the proportion of patients with curative intent, who since completing treatment had:

- received a follow up clinic report which has been uploaded onto the electronic system
- two CT Chest, Abdomen & Pelvis reports in the first three years
- CEA tests at least every six months in the first three years, this a total of six CEA values in three years
- colonoscopy reports one year after resection

3. Results

3.1 Follow up pattern

83% (15/18) of the patients received two CT CAPs within three years. The remaining 17% (3/18) had two CT CAPs done within four years. 22% (4/18) patients had colonoscopy one-year post surgery. Of the remaining patients, 47% (7/18) had flexible sigmoidoscopy and 47% (7/18) had no further scopes. 5% (1/18) had six-monthly CEA tests. 17/18 (95%) had four CEA tests within three years, with the average length of time between tests being 8.4 months between each test. 61% (11/18) of patients were seen in clinic within 4-6 weeks. Of those not seen in recommended time, 29% (2/7) were seen between 8-12 weeks, 43% (3/7) within 12-24 weeks and 29% (2/7) between 24-40 weeks.

3.2 Tumour recurrence

In total there were four recurrences. Table 3 outlines the characteristics of disease recurrences. Among those who experienced recurrence, 75% (3/4) were detected by surveillance and the remaining 25% (1/4) by patient symptoms. 66.6% (2/3) of those recurrences detected by surveillance were amenable to resections. The one recurrence discovered by patient symptoms was not suitable for resection. CT CAP was the method of diagnosis for 100% of recurrences, followed by a colonoscopy and CEA test in 25% (1/4).

4. Discussion

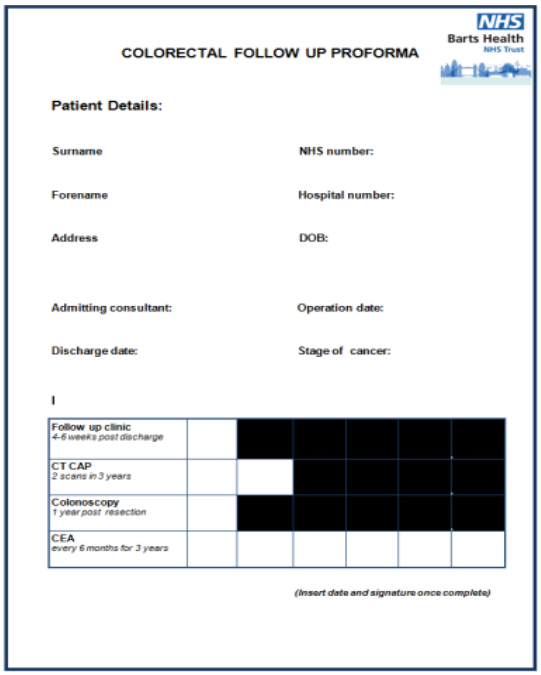
It is evident from the results that there was much scope for improvement. Majority of the CT scans and follow-up appointments were completed as per NICE recommendations, nonetheless the colonoscopy and CEA testing were poor. CEA has been illustrated to detect disease two - five months prior to any other means and therefore remains as a crucial component in diagnosing and managing colorectal cancer. Regarding the importance of colonoscopy during follow – up, it is performed with two intentions; 1. to detect metachronous tumours and 2. to detect anastomotic recurrences (9). Three percent of patients develop metachronous tumour within 5 years of surgery, and 50% of these develop within one year (29). The poor adherence to NICE guidelines in some aspects of testing is evident in this study and indicates the need for better education and widespread implementation of evidence-based guidelines. To try and achieve this we have held a teaching session at the weekly surgical departmental meeting. We presented our audit research and discussed with the department the reasons as to why we adherence to guidelines is not 100%. From this, it was decided a pro forma (Figure 1) would aid in reminding clinicians to ensure patients are followed up in the advised timeline. This pro forma has been implemented by being attached to the front of the physical patient notes folder which the clinician running the clinic will be required to fill in.

Table 3: Outline of disease recurrence characteristics by stage of cancer, type of cancers and site of resectable recurrences.

Characteristic	**Recurrence detected by Surveillance n=3 (%)**	***Recurrence detected by symptoms n=1 (%)***
Stage		
Stage II	1 (33.3%)	-
Stage III	2 (66.7%)	1 (100%)
Type of Cancer		
Colon	3 (100%)	1 (100%)
Rectal	-	-
Resectable	2 (66.7%)	-
Unresectable	1 (33.3%)	1 (100%)
Site of resectable recurrences		
Liver	1 (50%)	-
Local	1 (50%)	-

Surveillance for disease recurrence is an integral component in the management of many tumours once active treatments such as surgery, chemotherapy, and/or radiation have been completed. Although there is emerging evidence to suggest that intensive post - treatment monitoring with periodic imaging results in earlier detection of asymptomatic recurrences and potentially more opportunities for cure, these benefits must be weighed against the physical, psychologic, and economic detriments of unnecessary and repeated assessments (30). Our study supports the periodic imaging notion as 100% of the resectable recurrences were detected by CT scans, thereby endorsing the use of imaging studies during follow-up. Several large meta-analyses have indicated a possible survival advantage from intensive follow-up, whereas competing studies have found that a conservative, symptom-based approach provides equivalent outcomes (31-33). In a recent prospective, multicentre, randomized, controlled trial, Rodriguez-Moranta et al did not demonstrate any statistically significant differences in OS between patients who

underwent simple versus intensive follow-up (4). However, interestingly, an exploratory subgroup analysis of the stage II CRC cohort did reveal a trend toward improved survival among patients randomized to the intensive arm as a result of a higher rate of resection at the time of recurrence . The trial consisted of 259 patients and perhaps underpowered to detect survival differences in the entire patient sample. The lack of conclusive evidence from this and previous studies drives the surveillance controversy and contributed to wide variations in current follow-up programs (34).



COLORECTAL FOLLOW UP PROFORMA

NHS Barts Health NHS Trust

Patient Details:

Surname | NHS number:

Forename | Hospital number:

Address | DOB:

Admitting consultant: | Operation date:

Discharge date: | Stage of cancer:

I

Follow up clinic *4-6 weeks post discharge*		■	■	■	■	■
CT CAP *2 scans in 3 years*			■	■	■	■
Colonoscopy *1 year post resection*		■	■	■	■	■
CEA *every 6 months for 3 years*						

(Insert date and signature once complete)

Figure 1: Colorectal Cancer Clinic Pro forma. aid in reminding clinicians to ensure patients are followed up in the advised timeline. Implemented by being attached to the front of the physical patient notes folder which the clinician running the clinic will be required to fill in.

Our results confirm that there are noticeable departures from evidence-based surveillance guidelines. Many patients satisfy the minimum number of clinic visits and CT CAP but were hugely missed out when it came CEA testing and post-operative colonoscopies. The accessibility to organise clinic dates and in house imaging may be the reason that patients would more routinely receive follow up clinic and imaging whereas the increased number of people involved in organising CEA testing with the GP/ hospital phlebotomy service or arranging scoping with the Endoscopy department led to patients more likely to fall through the gaps.

In terms of limitations of the study, the sample size was small and the data we had used was collected by predecessors and therefore we were unable to be certain that it contained a complete list of all patients that were diagnosed with malignant colorectal cancer in 2017. It is also possible that some patients may have not had the relevant electronic documentation, therefore we were unable to clarify whether the patient was lost to follow up, had moved to a different hospital trust, if patient had declined further tests or if it was documented on paper notes. As the data and results were collated in April 2020, and we used a patient database that had patients diagnosed with colorectal cancer in 2017, a proportion of the patients still had the remaining year to have their CT CAP as the recommended follow up guidelines was over a three-year period. Going forth, it will be vital to add all patients to the database to guarantee no one is by-passed accidentally and all notes are electronically recorded. Additionally, we are aware that other national CRC surveillance recommendation exist, and only NICE guidelines were used as the reference standard because it had the broad appeal and applicability to a UK audience. Finally, resectability of recurrence was chosen as the main outcome instead of measuring OS. Although OS arguably is preferable, the logistic difficulties to detect OS differences has led research to recognises resectability of recurrence as an acceptable alternative for survival analysis. A re-audit will be completed in December 2020 which will include looking at the effectiveness of the new pro forma.

5. Conclusion

In summary, our data shows that locally there is need for improvement in adherence to NICE guidelines regarding CRC follow- up. The results prove that a moderately intensive follow-up strategy can positively identify resectable recurrence this increasing overall survival. However, this study also adds to the plethora of research the highlights the impetus to find a scientifically agreed follow up strategy that balances patients' benefits vs risks vs cost effectiveness.

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