Can the National Health Service Cancer Plan timeline be applied to colorectal hepatic metastases?

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ABSTRACT

INTRODUCTION The National Health Service (NHS) Cancer Plan guidelines recommend a maximum 2-week wait from referral to first appointment, and 2 months from referral to treatment for primary cancers. However, there are currently no guidelines available for metastatic disease. In the UK, nearly half of all colorectal cancer patients develop hepatic metastases. Timely, surgical resection offers the potential for cure. The aim of this study was to audit current practice for colorectal liver metastases in a regional hepatobiliary unit, and compare this to the NHS Cancer Plan standards for primary disease.

PATIENTS AND METHODS A retrospective review of the unit's database was performed for all hepatic metastases referrals from January 2006 to December 2008. The dates of referral, first appointment, investigations and initiation of treatment, along with patient's age and sex, were recorded on Microsoft Excel and analysed. Time was expressed as mean $\pm$ SD in days.

RESULTS A total of 102 patients with hepatic metastases were identified. Five were excluded due to incomplete data. The average time from referral to first appointment was 10.6 ± 9.4 days and the average time from referral to treatment was 38.5 ± 28.6 days. Seventy-five (72.7%) had surgical intervention, of whom 37 also had chemotherapy.

CONCLUSIONS The data compare favourably to the NHS Cancer Plan guidelines for primary malignancy, demonstrating that a regional hepatobiliary unit is capable of delivering a service for colorectal liver metastases that adheres to the NHS Cancer Plan. Therefore, the NHS Cancer Plan can be applied to this cohort.

KEYWORDS

NHS Cancer Plan – Timeline – Colorectal hepatic metastases

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Colorectal cancer is the second most common cause of cancer-related death in the Western world, with 221 people dying from colorectal cancer in 2006 and an annual incidence of 1060 people in 2006, and 1153 in 2007, in Northern Ireland alone.¹

Between 35–50% of colorectal cancer patients develop liver metastases, with the detection of these either at the time of initial surgery or during follow-up.² With recent advancements in surgical technique, anaesthesia and peri-operative care, curative surgery now offers a 5-year survival rate of up to 64%.³ This, therefore, highlights the importance of an efficient, prompt management plan for patients with hepatic colorectal metastases in order to maximise their potential for cure.

The National Health Service (NHS) Cancer Plan provides a major programme of action linking prevention, diagnosis, treatment, care and research. Overall, it aims to improve survival rates and achieve the appropriate professional support for patients.⁴ Guidelines have been drawn up in the

form of a timeline for primary malignancy in the UK, in which the following recommendations are made:

14 days from referral to initial appointment.

31 days from referral to diagnosis.

62 days from referral to initiation of treatment.

Currently, no such guidelines exist for the treatment of metastatic disease. The second point listed above in the timeline cannot be applied to metastatic disease, since the diagnosis has been established prior to tertiary referral. However, the aim of this study was to determine if these guidelines can be applied to the management of hepatic colorectal metastatic disease, in order to streamline the delivery of care, cut waiting times, optimise survival and give patients more certainty, for what is now seen as a potentially curable disease.

Patients and Methods

This study was performed in the Mater Hospital, Belfast, which is the sole regional referral centre for hepatobiliary surgery in Northern Ireland. All patients, over a period of 36 months, who were referred for the management of hepatic colorectal metastases, were identified. The population was compiled from a combination of sources, including referral letters and theatre records of hepatectomies performed during this time period. Data were obtained from the electronic hospital database, which contained out-patient letters, operation details and discharge letters. The initial referral letters, along with the radiological data and histology records also helped ensure as complete capture of the total patient population as possible. No exclusion criteria were applied.

The pre-operative staging protocol of the hepatobiliary surgical unit is for all patients, where possible, to have a positron emission tomography (PET-CT) scan. Evidence of extrahepatic disease is deemed to be exclusion for surgery, unless this is in the form of isolated resectable deposits. Other pre-operative investigations include multislice computerised tomography (CT), magnetic resonance imaging (MRI) and laparoscopic staging.

Details of the pathology and treatment of the primary disease were obtained, in addition to the dates of initial referral, first appointment time, investigations and initiation of treatment. Basic demographic details, such as age and sex, as well as any treatment undertaken and follow-up for the metastatic disease were recorded. These data were subsequently recorded on Microsoft Excel, and analysed. Time was expressed as mean $\pm$ SD in days.

Results

A total of 102 patients with hepatic metastases were referred to the regional hepatobiliary unit between 1 January 2006 and 31 December 2008. Five patients were excluded due to incomplete data.

The mean age of this population was 64.3 ± 10.1 years, with 40 (41.2%) females and 57 (58.8%) males. All these patients had previous surgery for colorectal adenocarcinoma, with 56 (57.7%) having hepatic metastases at initial presentation. Primary colorectal tumour staging demonstrated no T1s, 5.9% T2, 73.5% T3, and 20.6% T4. Thirty-two patients had adjuvant chemotherapy.

During the 3-year period, the mean time from referral to first appointment was 10.6 ± 9.4 days (Fig. 1). The mean time from referral to first investigation was 1.5 ± 6.4 days, reflecting the fact that most patients had the appropriate investigations carried out prior to the tertiary referral. Ninety-five (98%) patients had a PET-CT scan, 72 (74.2%) patients had a CT scan, 27 (27.8%) patients underwent an MRI scan, while only 6 (6.2%) patients had staging laparoscopy carried out.

Figure 1 Mean time from referral to first appointment.

The mean time from referral to initiation of treatment was 38.5 ± 28.6 days (Fig. 2). Seventy-five (77.3%) patients underwent surgical intervention in the form of lobar or segmental hepatectomy. Of these 75 patients, 67 had clear resection margins on histology, although all had macroscopic clearance intra-operatively. In this operative subgroup, 12 (16%) had pre-operative chemotherapy and 25 (33.3%) had postoperative chemotherapy. In the entire group, 19 (19.6%) patients had chemotherapy alone, while three were provided with palliative symptomatic support only.

Discussion

The NHS Cancer Plan guidelines provides an efficient time-frame in which to see, investigate, and diagnose patients with red flag symptoms for primary malignancy, thereby providing a prompt service for this already anxious patient group. Delays in the UK have also been associated with disease progression and, therefore, more advanced disease equates to poorer survival rates.⁴

Figure 2 Mean time from referral to initiation of treatment.

The liver is the most common site for metastatic spread of colorectal cancer, due to the direct portal venous drainage. Approximately 15–25% of patients have hepatic metastases at the time of initial primary diagnosis, while a further 25–50% develop metachronous liver metastases within 3 years following primary resection.⁵ If left untreated, the natural history of this disease has a median survival of 10 months. However, a 10-year study reported 1-, 3-, and 5-year survival rates following resection of colorectal liver metastases of 89.6%, 67.5%, and 49.9%, respectively, and 1-, 3-, and 5-year disease-free survival of 65.4%, 31%, and 27.2%, respectively.⁶ A Canadian study of 423 patients with hepatic metastases demonstrated a 47% survival at 5 years, and 28% survival at 10 years following hepatic resection.⁷ These survival rates demonstrate the importance of providing colorectal cancer patients with an efficient service for the management of hepatic metastases, for which timely surgical resection offers the potential for cure. Another study suggested that liver resection, in colorectal liver metastatic patients, can result in complete cure in one-third of patients without negative prognostic factors.⁸

Within the regional hepatobiliary unit in Northern Ireland, on average 3.2% of all colorectal patients will undergo liver resection. These patients are, on average, seen within 10.6 days from referral to first appointment, therefore falling within the 2-week time period recommended by the NHS Cancer Plan for primary cancer. The single centre nature, in Northern Ireland, of the referral pattern suggests that such centralisation of specialist services is appropriate and does not impact upon the time for patients to be reviewed. It also supports the application of the first aspect of the timeline guidelines nationally for management of metastatic disease.

Since the majority of pre-operative investigations were performed prior to tertiary referral, an average time from referral to investigation of less than 2 days is likely to be artificially low. This is a weakness in the data, as the time to achieve all investigations prior to referral could not be obtained. It does, however, highlight that our regional practice accords with the British Society of Gastroenterology guidelines for the resection of colorectal liver metastases, which recommends CT chest, abdomen and pelvis should be performed prior to tertiary referral with liver specific imaging being performed as per local protocol.⁹ PET-CT is our investigation of choice for liver metastases, with 98% of all patients having had this investigation. A recent meta-analysis of 61 studies evaluating colorectal liver metastases showed that FDG-PET had a sensitivity of 95%, significantly better than CT (65%) and MRI (76%).¹⁰ However, diagnosis can also be aided by CT, MRI and staging laparoscopy.

For primary malignancy, the NHS Cancer Plan recommends that treatment should be initiated within 62 days of the initial referral. In the case of hepatic metastases within our unit, the mean time from referral to initiation of treatment was 38.5 days. Subsequently, a majority (89%) had a margin-

clear resection, which is associated with a better long-term prognosis.¹¹ This average time indicates that the third aspect of the NHS Cancer Plan timeline could be successfully applied to metastatic disease, bearing in mind the caveat of pre-referral times and investigations already discussed.

Majeed and Price¹² reported a resection rate of 39% of all patients referred to a specialist hepatobiliary service, compared to our resection rate of 77.3%. This difference may be explained by the use of PET-CT scans and the fact that the majority of our investigations have been carried out prior to referral and, therefore, only those patients thought to be resectable were subsequently referred to the hepatobiliary unit.

Conclusions

These data compare favourably to the NHS Cancer Plan guidelines for primary malignancy, demonstrating a regional hepatobiliary unit is capable of delivering a service for colorectal liver metastases that adheres to the NHS Cancer Plan.

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