Assessment of a rapid referral pathway for suspected colorectal cancer in Madrid

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Objective. To assess the results achieved with a rapid referral pathway for suspected colorectal cancer (CRC), comparing with the standard referral pathway.

Methods. Three-year audit of patients suspected of having CRC routed via a rapid referral pathway, and patients with CRC routed via the standard referral pathway of a health care district serving a population of 498 000 in Madrid (Spain). Outcomes included referral criteria met, waiting times, cancer diagnosed and stage of disease.

Results. Two hundred and seventy-two patients (mean age 68.8 years, SD 14.0; 51% male) were routed via the rapid referral pathway for colonoscopy. Seventy-nine per cent of referrals fulfilled the criteria for high risk of CRC. Fifty-two cancers were diagnosed: 26% Stage A (Astler–Coller), 36% Stage B, 24% Stage C and 14% Stage D. Average waiting time to colonoscopy for the rapid referral patients was 18.5 days (SD 19.1) and average waiting time to surgery was 28.6 days (SD 23.9). Colonoscopy was performed within 15 days in 65% of CRC rapid referral patients compared to 43% of standard pathway patients \( (P = 0.004) \). Overall waiting time for patients with CRC in the rapid referral pathway was 52.7 days (SD 32.9); while for those in the standard pathway, it was 71.5 days (SD 57.4) \( (P = 0.002) \). Twenty-six per cent Stage A CRC was diagnosed in the rapid referral pathway compared to 12% in the standard pathway \( (P < 0.001) \).

Conclusion. The rapid referral pathway reduced waiting time to colonoscopy and overall waiting time to final treatment and appears to be an effective strategy for diagnosing CRC in its early stages.

Keywords. Colorectal cancer, early detection of cancer, rapid referral, waiting times.

Introduction

Colorectal cancer (CRC) is the second most common form of cancer in the majority of developed countries; only lung cancer causes more cancer-related deaths. In Europe, 413 000 estimated cases of CRC were diagnosed in 2006—some 12.9% of all cancers newly diagnosed—and ~207 400 people died of this disease.\(^1,2\)

In Spain, CRC is also the second most important neoplasm with ~22 000 new cases being diagnosed every year. In 2007, it caused 13 495 deaths. Although the incidence of CRC in Spain and its associated mortality are lower than the average figures for Europe, mortality is higher than in France, Italy and the UK, and incidence appears to be increasing over time (mean annual increase 2.6% for men and 0.8% for women).\(^3,4\)

Disease stage at the time of diagnosis is the most important factor determining patient survival.\(^5–7\) Reaching a diagnosis rapidly for patients in whom CRC is suspected, and reducing diagnosis-to-treatment times is a priority of all health systems. However, controversy exists regarding the effectiveness of pathways designed to shorten the waiting time to treatment.\(^8\)

In August 2004, a rapid referral pathway between primary and specialized care in a Madrid (Spain) health care district was introduced for patients suspected of having CRC.\(^9\) In line with similar ventures,\(^5,10–15\) the goal of this pathway was that such patients should undergo colonoscopy within 15 days.

The aim of the present work was to assess the results achieved with this rapid referral pathway over the first 3 years of its functioning. The waiting times to diagnosis and treatment, and the stage of disease at diagnosis in patients finally diagnosed with CRC, are compared with figures for the standard referral pathway.
Methods

This study included all patients who entered a rapid referral pathway for suspected CRC in a Madrid health care district (serving 498,000 people in the southeast Madrid area) between August 2004 and October 2007.

The rapid referral pathway between primary and specialized care in a Madrid health care district included patients suspected of having CRC seeking advice from a GP. All patients meeting some high-risk criterion for CRC (Table 1) were routed via the rapid referral pathway ideally in order to undergo colonoscopy within 15 days. The sequential implementation of the rapid referral pathway was done in two phases: 97 GPs from 10 primary health care centres were in first phase, and 315 GPs from 28 primary health care centres were finally included in the second one. The rapid referral pathway allows direct referral of patients for colonoscopy without the need of a specialist consultation and reducing the delay of CRC diagnosis. In both phases, there were six specialists performing the referred colonoscopies at the district’s tertiary hospital.

The rapid referral pathway was developed and coordinated by a committee consisting of hospital and primary care managers and specialists involved in the health care process. To improve the compliance with the rapid referral pathway, the high-risk criteria for CRC were actively disseminated through educational meetings and brief reminders for GPs participating in the process. In each primary health care centres, a coordinator of the referral pathway, in continuous communication with the specialist involved at the hospital, was appointed. Standardized documentation and data registry were also implemented to ensure the referral criteria compliance.

In the study, the sociodemographic data of all patients were recorded prospectively in a database, as well as their symptoms and signs of disease, the referral criteria, the results of colonoscopy, the waiting times between stages of assistance and the stage of disease and surgery performed in patients finally diagnosed with CRC. The results for these patients were compared to those of patients also diagnosed via colonoscopy but who were referred through the district’s standard referral pathway. The data for the latter pathway were recorded retrospectively via the examination of the patients’ clinical records.

A descriptive analysis was made of the results obtained with the rapid referral pathway: referral criteria met, waiting times, number of cancers diagnosed, endoscopic polypectomies performed, surgery for CRC and the stage of disease at surgery. The waiting times recorded (in days) were those between the request for colonoscopy made by the GP and its performance by a specialist (waiting time to colonoscopy), that between firm diagnosis and surgery (waiting time to surgery) and the overall delay to surgery (waiting time between the request for colonoscopy by GP until surgery including any time required for anatomopathological diagnosis). The target waiting times for the rapid referral pathway were: ≤15 days waiting time to colonoscopy, ≤30 days waiting time to surgery and ≤90 days overall waiting to surgery. These target waiting times were established from those recorded as desirable in the literature.

The waiting times and disease stage at diagnosis for the two pathways were compared by analysis of variance and the chi-square test as required. Significance was set at P < 0.05.

Results

A total of 272 patients were referred via the rapid referral pathway during the study period; 51% (138) were male; the average age of patients was 68.8 years (SD 14.0 years). The study involved the participation of 28 primary care centres and 315 GPs belonging to the selected health care district, together with six colorectal specialists at the district’s tertiary hospital.

A total of 252 (92.6%) rapid referral pathway patients finally underwent colonoscopy. Twenty patients were excluded from the colonoscopy study: 13 failed to attend their colonoscopy appointment, 5 had significant co-morbidity precluding colonoscopy and 2 patients rejected the procedure.

The most common symptom for which patients were routed via the rapid referral pathway was a change in bowel habits (49.8%), followed by rectal bleeding (23.9%), rectal bleeding plus a change in bowel habits (7.7%) and iron deficiency anaemia (10.1%).

Overall, 200 of the 252 above patients (79.4%) fulfilled at least one high-risk criterion for rapid referral. The remaining 52 (20.6%) patients did not meet any rapid referral criterion. Of these latter 52, 31 (12.3%) symptomatic patients met none of the symptomatic

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**Table 1** CRC high-risk symptoms and signs

<table>
<thead>
<tr>
<th>All ages</th>
<th>Patients ≥50 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpable mass in the right hemiabdomen</td>
<td>Recent changes in bowel habits (increased number of defecations and/or reduced stool consistency) lasting &gt;6 weeks</td>
</tr>
<tr>
<td>Rectal tumour detected during manual exploration</td>
<td>Persistent rectal bleeding with associated anal symptoms lasting over 3 weeks</td>
</tr>
<tr>
<td>Rectal bleeding associated with changes in bowel habits (increased number of defecations and/or reduced stool consistency) lasting &gt;4 weeks</td>
<td></td>
</tr>
<tr>
<td>Unexplained ferropenic anaemia (Hb &lt; 11 g/dl in men and Hb &lt; 10 g/dl in postmenopausal women)</td>
<td></td>
</tr>
<tr>
<td>CRC strongly suspected given prior imaging results</td>
<td></td>
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</tbody>
</table>
| Overall, 200 of the 252 above patients (79.4%) fulfilled at least one high-risk criterion for rapid referral. The remaining 52 (20.6%) patients did not meet any rapid referral criterion. Of these latter 52, 31 (12.3%) symptomatic patients met none of the symptomatic
criteria defined or had symptoms/signs of too long a history; 10 (4.0%) had a family history of CRC—a criterion not considered in the present rapid referral pathway, and 11 (4.4%) were routed for rapid referral but without any pertinent information being recorded.

Fifty-two (20.6%) of the rapid referral patients were finally diagnosed with CRC. In 62.7% (32 patients), the cancer was located in the colon and 37.3% (19) in the rectum or at the recto-sigmoid junction. Some 87.8% of the detected cancers were colonic adenocarcinomas; three patients had carcinoma-in-situ. Twenty-six per cent (13 patients) of those diagnosed with CRC had Astler–Coller Stage A disease, 36% (18) had Stage B disease, 24% (12) Stage C and 14% (7) Stage D. Forty-nine patients (94.2% of those diagnosed with CRC) underwent surgery; curative surgery was performed in 39 (79.6%). The three patients who did not undergo surgery had Stage D disease; these received palliative oncological treatment.

Colonoscopy also detected 73 patients (29% of the 252 who underwent the procedure) with high-risk lesions: 64 (25.4%) had adenomatous polyps, 8 (3.2%) had inflammatory bowel disease (IBD) and 1 patient (0.4%) was diagnosed with both polyps and IBD. Twenty-one patients (32.3%) received polypectomy during colonoscopy; biopsies were taken in 7 of these patients.

The mean waiting time to colonoscopy for the patients in the rapid referral pathway was 18.5 days (SD: 19.1 days); the median waiting time was 15 days (range 0–138 days), and the P75 was 20 days. The waiting time to colonoscopy for patients with CRC decreased to 13.8 days (SD: 8.8 days) compared to 33.8 days (SD 38.7) in the standard pathway; P < 0.001. Some 64.7% of patients underwent colonoscopy in ≤15 days compared to 43.0% of patients in the standard referral pathway (P = 0.004). No significant differences were seen in the waiting time to surgery for the two referral routes [28.6 days (SD 23.9) in the rapid referral pathway and 31.0 days (SD 34.4) in the standard pathway: P = 0.559]. Sixty-four per cent of patients in the standard referral pathway underwent surgery within 30 days of diagnosis compared to 61.2% patients in the rapid referral pathway; nevertheless, it should be noted that the number of patients who underwent surgery increased from 48% in the first year to 73% in the third. The overall waiting time was also significantly shorter for the patients in the rapid referral pathway [52.7 days (SD 32.9) compared to 71.5 days (SD 57.4) in the standard pathway]. Some 91.7% of patients in the rapid pathway had an overall waiting time of <3 months compared to 74.4% patients in the standard pathway (P = 0.008).

No differences were found between the patients of the two referral pathways in terms of the location of cancers, the proportion of patients who underwent surgery within 30 days of diagnosis and the overall waiting time.
surgery nor the aim of surgery (curative/palliative) (Table 3). However, the stage of disease at diagnosis was influenced by the referral route. With the rapid referral pathway, 26.0% of cancers were diagnosed at Stage A, while the standard referral pathway only diagnosed 11.6% at this stage ($P = 0.007$). The difference was maintained after stratifying by cancer site; 25.8% of colon cancers were diagnosed at Stage A in the rapid pathway patients compared to 11.0% in standard route patients ($P = 0.030$) and 22.2% of rectum cancers at Stage A in the rapid pathway patients compared to 12.5% in the standard pathway patients ($P = 0.276$).

### Discussion

The rapid referral pathway reduced the waiting time to colonoscopy, thus shortening the overall waiting time in patients diagnosed with CRC. The present rapid pathway for identifying and referring patients with symptoms suggestive of CRC is similar to others that have been implanted in other countries, e.g. in the UK (two-week standard rule). However, while these programs aim for rapid referral from primary to specialist care, the aim of the present pathway was to allow direct referral for colonoscopy from primary care within 15 days without the need to first consult with a specialist.

The direct referral of patients for colonoscopy is a practical and effective means of reducing the number of specialist consultations and reduces the delay to diagnosis for the patient. In order for GPs to make the request for colonoscopy, a number of highly predictive criteria were established that allowed rapid attention to be sought for high-risk patients while avoiding unjustifiable colonoscopies (and therefore avoiding the risks the procedure entails). These criteria also try to avoid the rapid referral pathway saturating the resources of the health district’s digestive medicine departments and thus increasing the waiting times of patients referred via the standard pathway—a problem referred to in other studies.

Overall compliance with the referral criteria was ~80%; this reaches 100% if only those patients eventually diagnosed with CRC are taken into account. Patients who met none of the criteria for rapid referral

### Table 3 Cancer characteristics according to referral route

<table>
<thead>
<tr>
<th>Cancer location</th>
<th>Rapid pathway</th>
<th>Standard pathway</th>
<th>$P$</th>
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</thead>
<tbody>
<tr>
<td>Colon</td>
<td>62.7% (32)</td>
<td>60.5% (185)</td>
<td>0.995</td>
</tr>
<tr>
<td>Recto-sigmoid junction</td>
<td>9.8% (5)</td>
<td>10.8% (33)</td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>27.5% (14)</td>
<td>28.8% (88)</td>
<td>0.307</td>
</tr>
<tr>
<td>Surgery</td>
<td>94.2% (49)</td>
<td>89.7% (279)</td>
<td>0.375</td>
</tr>
<tr>
<td>Curative</td>
<td>90.7% (39)</td>
<td>84.1% (207)</td>
<td>0.265</td>
</tr>
<tr>
<td>Palliative</td>
<td>9.3% (4)</td>
<td>15.9% (39)</td>
<td></td>
</tr>
</tbody>
</table>

### Figure 1 Waiting times for patients with CRC attended to via the rapid and standard referral pathways. *Statistically significant
made up ~4% of all inappropriate referrals, while those who did not explicitly meet the established criteria even though they had symptoms and a family background of CRC made up ~16% of inappropriate referrals. The compliance rates reported in other studies for other rapid referral pathways are lower at 50% and 73% for patients suspected of having CRC, and 85–92% for those finally diagnosed with cancer. In contrast, Maruthachalam et al. report a compliance rate of 99%; however, in this latter study, very different referral criteria were followed.

The most common symptoms shown by the patients routed via the rapid referral pathway were changes in bowel habits and rectal bleeding; these findings agree with those reported by other authors. The patients routed via the standard pathway more often showed more than one symptom, and more often had asthenia/anaemia. This might indicate that these patients had more advanced disease. However, such an interpretation should be understood with caution given the lack of data for many of the standard pathway patients.

For patients with CRC, the rapid referral pathway reduced the waiting time to colonoscopy to 14 days compared to the 34 days for the standard pathway. Other authors report similar reductions in waiting time: 9–14 days compared to 24–29 days via the standard pathway. However, it should be remembered that these studies report the waiting time until seeing a specialist able to request colonoscopy not the waiting time to direct access colonoscopy via a GP. Maruthachalam et al. who compared the waiting time to colonoscopy via a specialist visit with direct access colonoscopy via a GP also showed a reduction in waiting time to colonoscopy (9 days compared to 52 days).

The overall waiting time to colonoscopy (for all patients irrespective of the final diagnosis) in the rapid referral pathway was 18.5 days (median 15 days). Fifty-six per cent of patients underwent colonoscopy in under 15 days—less than the 85–100% reported in other studies. Although the present rapid referral pathway needs adjusting to bring it closer into line with the 15 day standard, it should be noted that 75% of patients received a colonoscopy within 20 days and that those who were eventually diagnosed with CRC had a smaller waiting time than those without cancer (13.8 compared to 19.7 days). It may be that those patients strongly suspected of having CRC received a colonoscopy more quickly. Reducing the waiting time to colonoscopy to 15 days depends on the availability of resources and their adequate use. Since the selected health district has no dedicated colonoscopy unit to which patients can be referred, the proper organization/distribution of patients suspected of having CRC is essential if the 15 day standard is to be met and the waiting times of standard pathway patients not increased.

No significant differences were seen between the two referral pathways with respect to the waiting time to surgery, which was ~30 days. This is less than the 36-day wait reported for both types of referral pathway by Chohan et al. Both referral pathways in the present work met the waiting time targets set, showing the excellent organization between the district’s gastroenterology and surgery departments.

The overall delay for patients diagnosed with CRC was reduced by the rapid referral pathway from 72 to 53 days; much of this via the reduction in the waiting time to colonoscopy. Other studies report reductions in this respect from 65–75 to 49–55 days. Thus, some 92% of patients with CRC in the present rapid referral pathway were diagnosed and received treatment in under 3 months—meeting the standard set. Chohan et al. established a standard of 62 days for treatment to be received; 69% of patients were treated within this time, similar to the 71% of patients who were treated in under 2 months in the present work.

The rapid referral pathway allowed a greater number of cancers to be detected at Stage A of disease (26%) compared to the standard pathway (12%). Other studies have failed to demonstrate that the stage of detection is influenced by the referral pathway, in fact one even suggests that rapid pathways might refer patients with more advanced stages of disease. Once CRC presents clinically, the stage of disease is the most important factor influencing survival. At Stage A, the cancer is localized and survival is 75–90%, reflecting the need to treat early. Survival studies are required to confirm the suspected impact of the present rapid referral pathway’s detection of tumours at earlier stages of development. Such an undertaking was beyond the scope of the present work.

The aim of rapid referral pathways is to reduce waiting times in order for an early diagnosis to be made and hopefully improve survival. Only Iversen et al. have shown that a diagnostic/therapeutic delay of over 60 days is associated with reduced survival in patients with rectal cancer; no other studies have been able to show this. However, independent of its potential effect on patient prognosis, a delay in arriving at a diagnosis generates great anxiety for patients. The length of this delay is also a marker of the quality of assistance patients receive.

The percentage of patients eventually diagnosed with CRC routed via the rapid referral pathway was 21% over its first 3 years of functioning. In the final year of the study period, this percentage was 17%, higher than the 8–14% reported in other studies. Some 14% of all cancers detected in the final year were at Stage A, a figure similar to that reported for other rapid referral pathways (9–19%).

During the study period, 447 new cases of CRC were diagnosed in the selected health care district, 52
(12%) via the rapid referral pathway, 311 (69%) via the standard pathway and 84 (19%) in the emergency room. In the final year of this period, during which 148 cases were detected, 18% were detected via the rapid pathway, 59% via the standard pathway and 22% in the emergency room. These results for the rapid pathway are similar to those reported by Eccersley et al.\textsuperscript{10} but lower than the 22% and 41% reported by other authors.\textsuperscript{11–15} As the present rapid referral pathway becomes more extended in the primary health care setting, the number of cancers detected through its use should increase.

The present study suffers from a number of limitations. The monitoring of the patients routed via the rapid pathway was prospective in nature, while the results for the standard pathway patients were collected retrospectively. This could introduce bias into patient selection and data gathering. The organization of the rapid referral pathway, the characteristics of the health care area and the resources destined to it means it is difficult to extrapolate the present results to other settings, although the results published in the literature are similar.

The use of the present rapid referral pathway led to substantial improvements in waiting times to colonoscopy over the standard pathway. Cancers were diagnosed at earlier stages; this is the first time such results have been reported. Although the results appear promising, further monitoring is required for them to be confirmed. Long-term studies should also examine the survival and quality of life of patients to determine the impact of this rapid referral pathway in clinical practice and on health related outcomes.

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Conflict of interest: none.

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