Short Report

Disease presentation, treatment and survival for Italian colorectal cancer patients: a EUROCARE high resolution study

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We analysed presentation, treatment and survival in a representative population-based sample of 3753 Italian colorectal cancer cases, diagnosed 2003–05: 70% were >65 years, 44% stage I–II, 27% stage IV and 92% received surgery. Chemotherapy was given to 58% of stage III colon cases, radiotherapy to 25% of rectal cases. Four percent of surgical cases underwent endoscopic polypectomy, and in 57% ≥11 lymph nodes were examined. Five-year relative survival was good (60%), independent of sex and site. Adherence to treatment guidelines was satisfactory, but wider use of faecal blood testing and colonoscopy will anticipate stage at diagnosis and likely improve survival.

Introduction

Colorectal cancer is one of the commonest cancers in Europe, with higher incidence in Western than Central and Southern Europe. Although internationally agreed guidelines for diagnosis and treatment are available, and screening can effectively identify early-stage lesions, survival varies markedly across Europe. Thus, 5-year relative survival (RS) for European colorectal patients alive at some point in 2000–02 ranged from 30% to 65% (60% overall).1 Such variation might be owing to differences in stage at diagnosis or variable adherence to treatment guidelines.2

The present EUROCARE-5 high-resolution (HR) study provides an overview of colorectal cancer presentation, treatment and survival for Italian patients diagnosed in 2003–05. The overview was obtained by analysis of a representative population-based sample of cases archived in eight Italian cancer registries (CRs), with detailed information on stage at diagnosis, treatment, etc., obtained by consultation of clinical records.

Methods

In conformity with the Italian EUROCARE-5 HR protocol, 500 primary colorectal cancers diagnosed in 2003–05 were selected for each of the participating CRs (Biella, Modena, Romagna, Reggio Emilia, Firenze, Napoli, Ragusa and Sassari) by a random procedure balanced for year of diagnosis, from cases archived in the Italian Association of Cancer Registries database. International Classification of Diseases, 3rd revision, codes identified right colon (C18.0–C18.5), left colon (C18.6–C18.7), unspecified colon (C18.8–C18.9) and rectal (C19.9–C21.3) sites. After excluding cases with unspecified colon subsite, 3753 cases were analysed. Cases were followed-up to the end of 2008, except for Firenze and Ragusa, for which life status information was, respectively, completely or partially (50%) updated up to the end of 2007.

Age at diagnosis (15–54, 55–64, 65–74, 75–99 years); TNM stage (I, II, III, IV, unknown), chemotherapy, radiotherapy and surgery (done, not done, unknown); type of surgery (hemi-colectomy, Miles’ operation, segmental resection (= any other kind of resection), endoscopic polypectomy, palliative surgery (= any kind of surgery leaving residual tumour), unknown); number of total harvested lymph nodes (1–10, ≥11, unknown); and recurrences in the 5 years following diagnosis (none, local/regional, distant metastases, unknown recurrence or type of recurrence) were obtained by directly accessing clinical/pathological records.

Overall and for each subsite, the distribution of above variables was analysed. Differences in proportions, tested by the two-sided z test, were considered significant for \( P \leq 0.05 \). Five-year RS (Ederer II method3) was age-standardized (where pertinent) by the direct method balanced for year of diagnosis, from cases archived in the Italian Association of Cancer Registries database.
method using the International Cancer Survival Standards age distribution. Differences in age-standardized survival were investigated by generalized linear models assuming a Poisson distribution of deaths.

Analysis of lymph nodes harvested was restricted to 3326 cases undergoing non-polypectomy surgery. Analysis of recurrence was restricted to 2055 cases (excluding stage IV cases, and cases from Firenze and Reggio Emilia for lack of recurrence information for 93% and 28% of cases, respectively). Survival analysis was restricted to 2823 cases (excluding Firenze and Ragusa cases for lack of updated life status, and 16 other cases known by death certificate only or discovered at autopsy). The Stata statistical package was used.

Results

Overall, 11% of 2533 colon and 1220 rectal cases were 15–54 years at diagnosis, and 70% were >65 years. About 40% of cases were stage I or II; 27% were stage IV. Stage I plus II, and stage III plus IV proportions were similar in colon and rectal cases (P > 0.05).

For surgical cases (1231 right colon, 1158 left colon, 1078 rectum), hemi-colectomy was performed in >80% of right colon and 51% of left colon cases; segmental resection was performed in >60% of rectal and 33% of left colon cases. Miles’ operation was limited to 13% of rectal cases, and endoscopic polypectomy to 4% of cases (with no sub-site variation). For the 57% of cases undergoing non-polypectomy surgery, >11 lymph nodes were examined: proportions were higher for right (69%) than left colon (61%) and rectal (49%) cancers. Lymph node information was lacking in 14% of cases, range 10 (right colon) to 18% (rectum).

Overall, 1456 cases received chemotherapy, with small differences between sub-sites, but marked differences according to stage [8% of stage I to 59% of stage III (58% colon, 61% rectum)] and age (78% of stage III cases <75 years, 25% for those ≥75 years). Only 332 cases (302 rectal) received radiotherapy, corresponding to 25% of rectal and 1% of colon cases.

Recurrences within 5 years were more common for rectal than colon cancers (30% vs. 24%, P < 0.05), and were fairly low (9%) for stage I disease, increasing to 25% for stage II and 38% for stage III. Distant metastases were more common than local/regional recurrences for both colon (13% vs. 5%) and rectal (16% vs. 7%) cancers (P < 0.05).

Recurrences were more frequent for rectal than colon cancers (30% vs. 24%, P = 0.03), and were fairly low (9%) for stage I disease, increasing to 25% for stage II and 38% for stage III. Distant metastases were more common than local/regional recurrences for both colon (13% vs. 5%) and rectal (16% vs. 7%) cancers (P < 0.05).

Table 1 Estimates of 5-year relative survival (RS), with 95% confidence intervals (CI), for 2823 colorectal cancer cases, by age, sex and stage

<table>
<thead>
<tr>
<th></th>
<th>Colon</th>
<th>Rectum</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N cases</strong></td>
<td>RS (%)</td>
<td>95% CI</td>
<td>RS (%)</td>
</tr>
<tr>
<td><strong>Not age-standardized estimates</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cases</td>
<td>1935</td>
<td>58.8</td>
<td>55.9–61.7</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>15–54</td>
<td>199</td>
<td>65.6</td>
<td>57.7–72.5</td>
</tr>
<tr>
<td>55–64</td>
<td>392</td>
<td>68.5</td>
<td>63.2–73.3</td>
</tr>
<tr>
<td>65–74</td>
<td>599</td>
<td>61.3</td>
<td>56.2–66.1</td>
</tr>
<tr>
<td>75–99</td>
<td>745</td>
<td>49.3</td>
<td>43.7–54.9</td>
</tr>
<tr>
<td><strong>Age-standardized estimates</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cases</td>
<td>1930</td>
<td>60.4</td>
<td>57.4–63.2</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>1046</td>
<td>60.7</td>
<td>56.6–64.6</td>
</tr>
<tr>
<td>Female</td>
<td>889</td>
<td>59.4</td>
<td>55.0–63.5</td>
</tr>
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<td>TNM stage</td>
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<td></td>
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</tr>
<tr>
<td>I</td>
<td>296</td>
<td>94.5</td>
<td>85.5–98.0</td>
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<tr>
<td>II</td>
<td>587</td>
<td>87.8</td>
<td>82.8–91.5</td>
</tr>
<tr>
<td>III</td>
<td>489</td>
<td>61.3</td>
<td>55.7–66.4</td>
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<tr>
<td>IV</td>
<td>537</td>
<td>13.6</td>
<td>10.4–17.3</td>
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<tr>
<td>Unknown</td>
<td>26</td>
<td>60.1b</td>
<td>29.9–87.0</td>
</tr>
</tbody>
</table>

Cases from 6 of the 8 participating cancer registries after excluding those known by death certificate and incidentally discovered at autopsy. See text for details.

Age-standardized 5-year RS (table 1) was about 60% overall, for both sexes, with no differences between colon and rectal sites. RS decreased with advancing age and stage.

Discussion

This HR investigation provides an overview of the presentation, treatment and survival of Italian colorectal cancer cases diagnosed in 2003–05. A major finding is that, for both sexes and both sites, 5-year RS was around 60%, in line with estimates for European cases as a whole. Survival was strongly influenced by stage, which remains the most important outcome predictor for these cancers. Notwithstanding increased use of faecal occult blood screening and colonoscopy in Italy, 27% of cases were stage IV at diagnosis.

Right or left hemicolectomy, accompanied by complete removal of associated lymph nodes, was the main treatment for colon cancer, which is considered standard of care; the disabling Miles’ operation was seldom used. Endoscopic polypectomy was not widely used although it is considered the preferred approach for adenomatous and some malignant polyps.

The high proportion of cases with ≥11 lymph nodes harvested is evidence of generally good surgical practice. Although 14% of cases had missing node information, about 60% of these were ≥75 years, and often received palliative surgery only, or neo-adjuvant radiotherapy— which renders nodes difficult to identify.

Fifty-eight percent of stage III colon cases were given chemotherapy, in line with 62% reported for Dutch colon cases, but low compared with the 69% reported for French cases. Strangely, 8% of all cases received chemotherapy for stage I disease although no data support this policy. Perhaps markers of tumour aggressiveness—not available in this study—guided this choice. By contrast only 25% of rectal cancers received radiotherapy compared with 60% in a similar Dutch population. Nevertheless, 90% of all cases given radiotherapy had rectal cancer in line with ESMO guidelines. Of the remaining colon cases, 33% involved the sigmoid colon and 30% were stage IV, providing some rationale for radiotherapy use.

As expected, recurrences were more frequent for rectal than colon cases, and for stage III than earlier stage cases. However stage I and II cases had non-negligible recurrence rates, suggesting that molecular markers should be investigated to predict aggressive behaviour in early-stage disease and select cases for adjuvant therapy (targeted or otherwise).
To conclude, although 5-year survival was relatively high and adherence to treatment guidelines satisfactory, survival can probably be further improved by increased use of faecal occult blood testing, colonoscopy and endoscopic polypectomy to reduce the proportion of cases diagnosed at advanced stage.

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**Conflicts of interest:** None declared.

### Key points

- Five-year relative survival was relatively high in this Italian population and in line with the European average.
- Adherence to treatment guidelines was fairly satisfactory.
- The proportion of cases diagnosed at advanced stage can be reduced by wider use of faecal occult blood testing, colonoscopy and endoscopic polypectomy, which would likely also improve survival.

**References**