

Early diagnosis of colorectal cancer. Diagnostic delay reduction or rather screening programs?

Colorectal adenocarcinoma (CRC) is the second most common and deadly malignancy in Western countries (third worldwide), and had in Spain an incidence of 32/100,000 inhabitants/year for males and 21/100,000 inhabitants/year for females in 2000, with a mortality rate of 17.3 and 11.1/100,000 inhabitants/year—that is, approaching 55%— respectively (1). There has been a sustained increasing trend for the last 15-20 years, while survival improved—average 5-year survival in European countries is now 49.5% for colon cancer and 43% for rectal cancer. CRC is most frequent between the 5th and 7th decades of life, and most cases are sporadic. In a small percentage of total neoplasms, usually in the setting of hereditary forms (polyposis or otherwise), a diagnosis is reached at an age younger than 40 years (2).

A significant number of patients are diagnosed based on the presence of neoplasm-related symptoms and signs, but promptness in the performance of adequate studies, particularly a complete colonoscopy, does not ensure diagnosis in early stages, which are those entailing a much better prognosis. Such is the case even if symptom clustering—particularly combined rectorrhage and recent changes in bowel habits above 55 years of age—rather than an isolated sign or symptom is considered; even more if abdominal pain or an abdominal mass is also present, as these latter conditions reduce specificity whilst not increasing sensitivity (3).

Tumor stage at diagnosis is the most relevant determinant regarding prognosis. While CRC-related 5-year mean survival is 50-55%, it is 75-90% for stages I-II, and smaller than 15% for stage IV. However, an early diagnosis will not ensure an early stage. Slow symptom and sign development may suggest tumor indolence, while a quick presentation is maybe associated with more aggressive tumor biology, particularly in patients younger than 50 years (which is uncommon). The duration of clinical manifestations is unrelated to prognosis (4), and the average 17-week delay between symptom onset and diagnosis is even higher for males under 65 years of age and females older than 80, this being attributable to patients themselves in 60% of cases (5).

Fast diagnosis for any cancer is a priority topic in all oncologic health programs encouraged by WHO guidelines, and represents much more than endoscopy as early as possible. It includes a reduction of time elapsed between diagnosis suspicion, definite diagnosis, and primary and adjuvant therapy, all of which is mostly dependent of healthcare services providers, who should provide adequate diagnostic-therapeutic resources. However, despite the relevance attached to diagnostic procedure celerity, no conclusive data show its influence on disease prognosis, and diagnostic delay has been seen to have no consistent effect on outcome (1), while some patients may actually experience uncertainty and anxiety when faced with delayed diagnosis.

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Hence, it is important that the best coordination possible between caring services –where primary care physicians play a key role as sequence initiators– is achieved, and healthcare continuity as well as, particularly, trust in PC physicians have been pointed out as best predictors for early stage in CRC (6). An adequate management of endoscopy wait lists is also required, which should ultimately lead to close Gastroenterology-Surgery coordination based on the clinical management in coloproctologic units. An interesting Spanish paper convincingly showed a range of individual-related predictors that actually shortened time elapsed between diagnosis and treatment for gastrointestinal cancers (7): lower social class, lack of private vehicle, male gender, age younger than 74 years, two or more symptoms at disease onset, presenting first to secondary or tertiary health care, and being diagnosed outside the vacation period of time.

Obviously, time intervals may also become affected by a number of factors, depending upon the specific condition considered. First comes patient-related delays, when patients do not appropriately interpret the relevance of their clinical manifestations, or simply will not present because of neglect or fear of cancer. Despite this, a good PC-SC correlation may optimize diagnostic times. Second comes the delay until a definite exploration test is found. Treatment accessibility, that is, the time elapsed between diagnosis and CRC therapy should also be as short as possible. While no safety-related maximum wait time can be recommended, as Clinical Practice Guidelines by Sociedad Valenciana de Cirugía recognize (8), it is encouraged that average wait time be shorter than 4 weeks from diagnosis to treatment (grade B recommendation). These same Guidelines advise that CRC be addressed by adequately trained and experienced surgeons in the setting of Coloproctologic Units (grade B recommendation), in order to obtain better perioperative morbidity and mortality rates, shorter postoperative stays, less local relapse, and longer long-term survival.

The most obvious evidence of inadequacy –at least partially– for this delay reduction “policy” of shifting the burden onto SC is the English “two weeks” program, which did not fulfill expectations for a number of reasons (poor adherence, wrong protocol usage, use of spurious remission routes, etc.), and which could not reduce time elapsed from initial manifestations to treatment, this being the primary cause of therapeutic delay in the UK (9).

WHO (10) considers that early detection includes both early diagnosis, which is performed on symptom-exhibiting individuals, and screening, which is performed on the non-symptomatic but at-risk population. We already discussed the former; now we shall discuss CRC screening.

Patients where specific cancer types (uterus body or cervix, breast, testicle, colon, melanoma) are detected early, and who receive optimal treatment, have a 5-year survival rate above 75%. In contrast, 5-year survival is usually inferior to 15% in patients with gastric, bronchopulmonary, esophageal, pancreatic or liver cancer. Hence, appropriate designs have to do with prevention strategies, particularly in most efficient instances such as CRC. Primary prevention is impractical in the short-mid term –it only becomes effective in 25-30-year intervals; it is secondary prevention or screening strategies for early CRC – better still “advanced adenoma” – detection that is cost-effective. CRC screening is therefore defined as the testing of asymptomatic individuals to identify benign or malignant colonic neoplasms in their earlier stages. The follow-up of patients already diagnosed with adenoma or CRC (and managed with cure intent) is considered a “monitoring”, rather than a “screening” task. Screening for CRC is cost-effective and reduces mortality in 15-30%, as well as physical and moral suffering in the future (1,2,6).

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CRC is a disease where screening is most appropriate; however, once established, monitoring costs (and risks) should be reasonable. A review of the available evidence suggests that “advanced” adenoma is the most valuable risk marker for current or future CRC (11), this condition being defined as an adenoma that is greater than 1 cm in size, with a villous histology in more than 25%, severe dysplasia or *in situ* carcinoma. Size is the most important aspect, since diameters above 1 cm directly correlate to severe dysplasia. This is why opaque enema explorations, even with dual contrast, are not useful for screening, since their sensitivity is lower than 48% for this sort of colonic adenoma. For several years now MRI colonography has been considered a promising technique (12), but colorectal lesion detection rates above 90% only occur when lesion size is above 10 mm, which, given the advanced adenoma definition, seems rather small, even though MRI colonography is deemed more comfortable than sedation-requiring colonoscopy by patients.

In the current issue of our journal, Elena Gómez et al. –Gastroenterology Department, Hospital de La Princesa, Madrid– demonstrate, using a prospective study with one hundred patients, that more or less diagnostic delay has no influence on tumor spread when examining surgical pieces, with the only variable that significantly influences this parameter being adenocarcinoma differentiation and maybe also a distal localization. Delay between clinical manifestations onset and diagnosis was greater than six months on average, and four of these months were attributable to patient-related delays in visiting a doctor; this means 40% more delay when compared to the aforementioned Finnish paper (5), even though this same team points at a trend towards improvement 25 years after a similar study (reference no. 5 in the published paper). Hence, in order to achieve an effective healthcare policy, these authors decided on investing resources for the development of screening programs regarding CRC, as these are not only cost-effective but also reduce mortality. Screening effectiveness is measured out in quality-of-life-adjusted gained life years, and colonoscopy has been shown to be the test that mostly reduces CRC-related mortality rates (13).

Of course, all things are not that simple. Even in highly aware countries, compliance with screening programs for CRC only reach 55% (14), whatever the screening method, which may result from fear of potential complications. Another suggested reason for poor implementation is inadequate practitioner education on CRC screening (15), this despite the availability of excellent clinical practice guidelines on this topic based on both national (1,2,8) and foreign (16,17) evidence, and the updated BMJ series “Evidence Based Gastroenterology and Hepatology” (18).

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