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Colorectal cancer mortality trends in Spain. What shall we do?

Colorectal cancer (CRC) is the third most prevalent cancer worldwide (after lung and breast cancer) and one of the most fatal neoplasms. Nearly 60% of cases are diagnosed in developed countries, and Europe is one of the regions with the highest incidence and mortality rates. The latest data reported show that, in Spain, 28,551 new CRC cases were diagnosed and 14,303 patients died from this cancer in 2008, which represents an age-standardized rate of 32.2 and 13.3 per 100,000 respectively (1).

Over 70% of CRC cases are sporadic and related to life style –a diet poor in fruits and vegetables; excessive red meat, saturated fat, and alcohol consumption; leading a sedentary life; obesity, and smoking are all risk factors for this cancer (2). However, the primary risk factor is older age. CRC is much more common in individuals older than 50 years, and its incidence increases exponentially with age.

Despite being one of the most common cancers in our setting, CRC is also one that may benefit most from prevention via primary and secondary prevention strategies. Estimations show that 66-75% of CRC cases would be prevented with a healthy life style (3). In addition, given its high morbidity, mortality and well known natural history, the availability of diagnostic methods allowing cancer early detection or even precursor lesions, and the existence of therapies that improve survival when used in early stages, CRC meets the key screening criteria established by the World Health Organization (4).

Several strategies are available for CRC screening, including fecal occult blood (FOB) testing once a year or every two years, sigmoidoscopy every 5 years, or colonoscopy every 10 years (5); however, only FOB testing has been effective in reducing the incidence and mortality of this disease in randomized clinical trials (6-9). These studies reveal a reduction in mortality by 15-33% primarily due to a higher percentage of diagnoses in early stages; a reduced incidence is also confirmed from the detection and excision of premalignant lesions (adenomas) to preclude their progression to CRC.

The primary prognostic factor for CRC is known to be CRC stage at the time of diagnosis. CRC survival at 5 years is around 50-55%, much higher for early (75-90%) *versus* advanced (lower than 15%) stages (10). Many CRCs are identified from the presence of signs and symptoms, which usually develop in advanced stages of the disease; in such cases a fast diagnosis does not ensure a better prognosis as symptoms may already reflect the presence of a late-stage CRC. Hence the ultimate importance of early detection and, therefore, the implementation of population-based CRC screening programs. Notwithstanding, not everybody is eligible for screening programs. Target population are those older than 50 years (the age at which CRC development becomes more frequent), with no symptoms and no per-

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sonal or family history of CRC. Specific pathways exist for patients with symptoms or high diagnostic suspicion (rapid diagnosis circuit), as well as for subjects with a family history of CRC (genetic counseling units, clinical high-risk units).

Both the European Commission and the Spanish Health Ministry's Strategic Plan against Cancer (11) include the implementation of screening programs among their goals, and recommend FOB testing as the first-line screening option, leaving each Autonomous Community to decide which specific FOB test should be used (biochemical or immunological).

Catalonia was the first Community to set up a CRC screening program. It was implemented in 2000 as a pilot experience in l'Hospitalet de Llobregat (a town with 239,000 inhabitants in Barcelona metropolitan area). The results from the two first rounds (12) not only demonstrated its feasibility in Catalonia and helped establish a gradual expansion plan for the whole territory, but also served as template for screening programs in other Communities. Thus, in 2005 and 2006 Valencia and Murcia, respectively, started their own programs (13). Spain has today 9 Communities with such programs, and many other Communities are in the recourse assessing phase of programs to be implemented soon. Participation rates in these programs have been quite inferior to those in breast programs, and the minimum standard for effectiveness could not be reached in some cases. Barriers to participation in these programs have been thoroughly studied, and one conclusion stands out –massive diffusion campaigns are needed to inform the general population about the high frequency of CRC in our setting, its primary risk factors and prevention measures, and the risks and benefits of taking part in screening programs (14).

Understanding CRC-related incidence and mortality rates, as well as the projections for future estimates, helps us assess the need to initiate a population-based screening program. While it would be highly unusual in our country, we might find low incidence and mortality rates, which would advise against screening.

In Spain mortality has increased in recent years (1985-2004) with an annual percent change (APC) of 2.4% in men and 0.4% in women, with a trend towards stabilization in the last few years (15). This higher mortality is consistent with a significantly increased incidence in both genders, probably due to improved access to diagnostic modalities and a westernization of some risk factors for CRC, including diet and obesity. Relative 5-year survival in both genders has improved since the 1990s, which may be accounted for by diagnosis in earlier stages, therapy advances primarily for stages II and III, and also a decrease in postoperative mortality. Estimations for the near future by Ribes et al. show a similar pattern to the present day, with an increase in mortality for men and a stable rate for women.

Various theories have been posited to explain the different CRC mortality rates in males and females; one suggests that the use of oral contraceptives in postmenopausal women may be a protective factor (16). Other factors that may explain different mortality patterns include a better access of women to the healthcare system and the adoption of healthier lifestyles.

In the present issue of *Revista Española de Enfermedades Digestivas* Dr. Cayuela et al. (17) review the recent changes in CRC-related mortality rates in Andalusia during the 1980-2008 period. Jointpoint regression models were used, which allow to identify points (years) with significant changes in a time trend, and to estimate such changes' magnitude. As with the rest of Spain, CRC was in Andalusia the second most common cause of cancer deaths both in men and women in 2008. This paper shows that overall during the study period CRC mortality rates increased in both genders, with an APC of 2.6% in men and of 1.1% in women. However, the greatest

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increase in men occurred between 1990 and 1998 (APC of 3.7%) with a smaller growth in subsequent years (0.8%). In women, the greatest increase in mortality began in the 1980-1996 period (APC 2.9%) followed by a significant decrease (-1.0% APC). While these results are consistent with those previously reported at the National and local level (15,18), an increase in overall mortality rates from CRC seems to be confirmed primarily in males.

Current data not only from Andalusia but the whole of Spain support the need to urgently adopt measures to improve the present situation, bearing in mind both the accelerated ageing process in the population and the estimates regarding increased incidence rates. Such measures should aim at improving high-risk behaviors for this cancer, guaranteeing access to appropriate therapies as soon as possible, and initiating population-wide screening programs.

Primary prevention is the best strategy to prevent CRC but health-promoting programs aiming at a change in hygienic-dietary habits offer results in a long-term, and must therefore be supplemented with additional earlier-impact strategies such as secondary prevention measures, that is, screening programs. Importantly, a magnitude analysis (incidence and mortality) followed by a detailed assessment of necessary resources should be performed prior to a screening program implementation, ensuring quality at all levels and perfectly coordinated with both primary and specialist care teams. After completion of these processes, and as suggested in *Plan Integral de Oncología de Andalucía 2007-2012*, pilot experiences should be started (19). Once screening is wide-reaching in our country, different strategies according to both gender and age might be performed.

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