ORIGINAL

Colon cancer screening in the balearic islands: current situation and proposals

Cribado del cáncer de colon en las islas baleares: situación actual y propuestas

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Abstract

There is evidence that screening for colorectal cancer (CRC), a cancer whose natural history is well known, is very effective and efficient. The recommendations of Scientific Societies and National and Supra-National Health Institutions for its population application are clear and forceful.
The bases of this evidence, the recommendations made and in force, and the current circumstances of application of the CRC screening in the Balearic Islands are reviewed in the text, establishing at the end recommendations for its improvement, which is much needed.

Keywords: Cancer, colon, screening.

Resumen

Está demostrado que el cribado del cáncer colorrectal (CCR), un cáncer cuya historia natural es bien conocida, es muy eficaz y eficiente. Las recomendaciones de Sociedades Científicas e Instituciones Sanitarias Nacionales y Supranacionales para su aplicación poblacional son claras y contundentes.

Las bases de esta evidencia, las recomendaciones realizadas y vigentes, y las circunstancias actuales de aplicación del cribado de CCR en Baleares se revisan en el texto, estableciendo al final recomendaciones para su mejora, que es muy necesaria.

Palabras clave: Cáncer, colon, cribado.

Introduction

The importance of colorectal cancer (CRC) in our society is very great, although little is known by the general population. In Spain, CRC is the most common cancer, with about 40,000 new cases / year; in the Balearic Islands, over 800 cases are diagnosed annually[1].

Most CRC cancers develop from adenomatous polyps. The probability that a polyp progresses to cancer depends on the histological type, its size, and the degree of cellular dysplasia. The average time required to complete this progression is long, probably 10 years or more, which creates a long period of time that allows preventing or detecting CRC early and improving its prognosis. After the removal of polyps, the incidence of carcinomas decreases by approximately 88-90%, in the following 6 years[2,3,4].

The incidence of CRC clearly increases after the age of 50 5. The progressive aging of the population, exposure to environmental risks and, more recently, screening for CRC, influence the increase in observed cases of CRC.

The main factor associated with the survival of CRC is the degree of extension at the time of diagnosis: 60% of CRC cases are diagnosed when the disease is already advanced at a regional or distant level, that is, with metastases. However, when the diagnosis is made in early stages (stages I and II), overall survival can exceed 90%: this fact highlights the great importance of screening programs (early diagnosis, secondary prevention) of CRC and that in this context most neoplasms are diagnosed in early stages[6,7] (The clinical stages - TNM - of the CRC can be consulted in annex 1).

Given the great importance of CRC and its enormous capacity to be prevented through specific screening programs, as has been demonstrated in the Balearic Islands in areas where the program already operates, we consider it essential to promote the expansion of the program in the Balearic Islands.

This text aims to explain the importance of the CRC and its screening and thus be able to base its implementation in the Balearic Islands.

Epidemiology of colorectal cancer

CRC is one of the most frequent neoplasms in western countries. In Spain, CRC is globally the most frequent cancer, with a total of 39,553 new cases per year, and it occupies the second position among men, behind prostate cancer, and among women, behind breast cancer[1,6]. **Table I** details the incidence of the main types of tumors and their distribution by sex.

The incidence of CRC varies according to age, increasing markedly after the age of 50 5, as can be seen in **figure 1**. The progressive aging of the population, exposure to environmental risks and CRC screening have a very marked influence on the evolution of the number of observed CRC cases.

Figure 1: Colon and rectal cancer incidence rates by age in Spain.
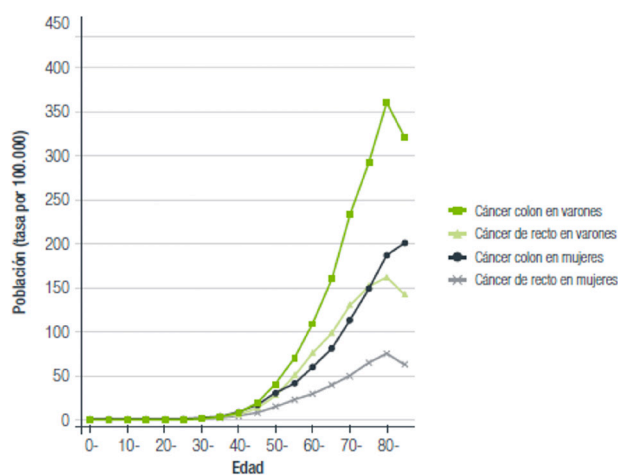
Source: Ref. 5

Figure 2: Survival based on CRC staging .
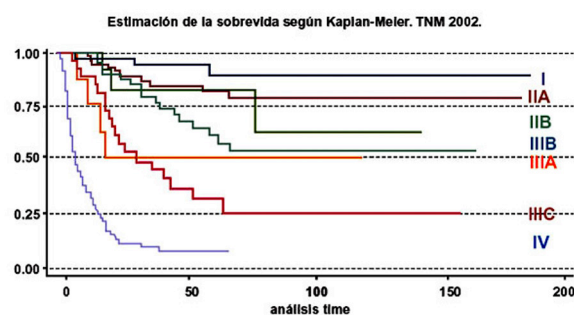
Source: Ref. 7

Table I: Most frequent tumors in Spain according to sex. 2017.

Men			Women			Total		
Cancer	n	%	Cancer	n	%	Cancer	n	%
Prostate	33370	22,42	Breast	27747	28.04	CRC	41441	16,73
CRC	24764	16,63	CRC	16677	16,85	Prostate	33370	13,47
Lung	22430	15,07	Uterus	6160	6,23	Lung	28347	11,44
Bladder	17439	11,71	Lung	5917	5,98	Breast	28047	11,32
Stomach	5150	3,46	Bladder	3654	3,69	Bladder	21093	8,51
Total	148827	100	Total	98944	100	Total	247771	100

Source: Refs 1, 6.

60% of CRC cases are diagnosed when the disease is already advanced at a regional or distant level, that is, with metastasis, and this is the main factor influencing overall survival. However, when the diagnosis is made in early stages (stages I and II), a situation that occurs only in 37% of cases, overall survival can exceed 90%[7].

Most CRC develop from adenomatous polyps. The probability that a polyp progresses to cancer depends on its histological type, its size and the degree of cellular dysplasia it shows[3].
The removal of colon polyps (polypectomy) has two direct consequences, a reduction in the incidence of CRC of 88-90% at 6 years and a decrease in mortality from CRC both after ten and twenty years[3,4].

In recent years, mortality from CRC shows a downward trend, both for colon and rectal cancer and in men and women 8 (**Table II**). This trend observed in Spain since 1995 could be related to the improvement in the diagnosis and treatment of CRC.

Early detection of colon and rectal cancer

CRC is, together with cervical and breast cancer, one of the tumors that can be subjected to a screening program, since all three meet the classically required characteristics of knowledge[9] , namely:

- Constitute a major public health problem
- Have a well-established and identifiable natural history
- Have screening evidence of proven effectiveness and efficiency

The CRC screening tests are grouped into four categories:

1. Stool tests for occult blood (SOB)
2. Endoscopic tests: sigmoidoscopy and colonoscopy
3. Imaging tests: computed tomography (CT), colonography and capsule endoscopy of the colon
4. Biomarkers in peripheral blood: Septin9 methylated DNA and miRNA.

The predominant strategy for population screening in European, Anglo-Saxon and Asian countries is the detection of biennial SOB followed by colonoscopy in positive cases, and annual sigmoidoscopy with or without immunological fecal occult blood test[10,11,12,13]. The ability to measure fecal Hb concentration is the main advantage of the quantitative SOBi tests over the qualitative ones and the guaiac SOB tests (SOBg). It is universally accepted that the ideal test for organized population screening is the quantitative SOBi test, which should replace chemical tests (SOBg test)

The fecal Hb concentration increases as the lesion is more advanced. For this reason, the rate of positive results obtained with the SOBi test varies according to the cut-off point chosen, which makes it possible to select the most appropriate one (best balance between sensitivity and specificity) for a population screening program based on the availability of colonoscopies. The screening programs are aimed at the population at medium risk for developing colon cancer, that is, people aged 50 to 69 years with no symptoms and without the presence of a family or personal history of CRC.

Table II: Evolution of adjusted mortality rates from colon and rectal cancer in Spain during the 1975-2018 period for men and women.
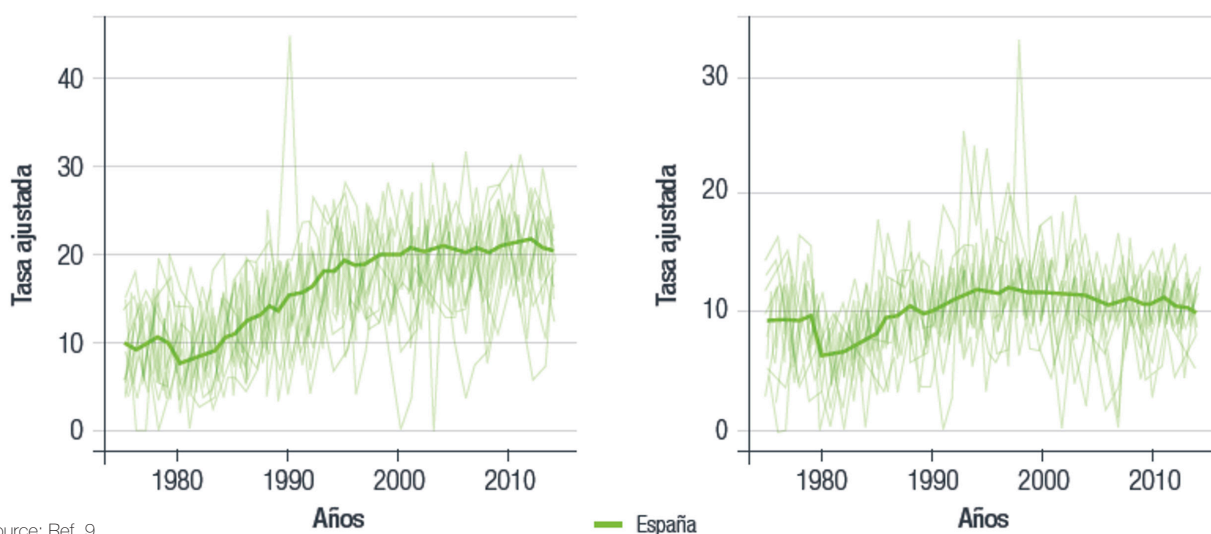
Source: Ref. 9.

In the first round of screening of the COLONPREV Randomized Clinical Trial[14] the effect on CRC detection and its impact on saving colonoscopies of increasing the cut-off point from 15 to 40 μg Hb / g of stool was analyzed. In women under 60 years of age, increasing the cut-off point to 40 μg Hb / g reduced the detection of advanced adenoma by 35% without altering the detection of CRC, which would mean a saving of 44.5% in colonoscopies. Likewise, increasing the cut-off point to 30 μg Hb / g of stool in men under 60 years of age and up to 25 μg Hb / g of stool in women over 60 years of age did not modify the CRC detection rate, assuming savings in colonoscopies 28.6 and 32.9%, respectively. However, in men older than 60 years, any increase in the cut-off point above 15 μg Hb / g of stool leads to a loss of CRC diagnosis, which reaches up to 25% with the cut-off point of 40 μg Hb / g of feces. This study suggests that the cut-off point for the SOHi test can be optimized based on age, sex, and existing resources for colonoscopy. Ultimately, in groups selected by age and sex, the cut-off point for SOBi could be increased, which would result in savings in endoscopy resources without loss of diagnosis of CRC cases.

The COLONPREV study has provided fundamental data for the justification of SOB-based screening in medium-risk populations, since it has shown that in the long term in two overlapping cohorts, the effect in terms of diagnosis and prevention of colon cancer was equivalent if compared doing an initial colonoscopy with doing SOBi every 2 years with colonoscopy when the result was positive.

Of the different types of tests to detect occult blood in feces, the immunological (OC-Sensor®) is used in the colorectal cancer prevention program of most Autonomous Communities. The sensitivity of immunological PDSOH to detect cancer varies between 85% and 95%; specificity, between 39% and 94%. The sensitivity to detect polyps with a higher probability of malignancy (>1cm) is 10-20%. With non-rehydrated tests, the positive predictive value varies between 10% and 15% for CRC, and between 30% and 40% for adenomas[15].

There is extensive experience in previous programs both at a Spanish and international level that show the high efficiency (cost / benefit) of CRC screening programs[16] based on the fact that the diagnosis of pre-cancerous lesions (adenomas) or cancers in very early stages of their development represents a great cost saving in health and social terms compared to those generated by the treatment of advanced invasive cancer, with, in addition the great improvement in the vital prognosis of the disease.

A clear example is found in France[17], where it is expected that with the application of the population screening program for CRC in a medium-risk population, the number of deaths from CRC will decrease from 15,000 / year to 12,000 / year. Furthermore, in population-based studies the reduction in mortality from CRC has been 15-18%, although it is estimated that this reduction may reach 30%[18,19].

During the period 2005-2008, after carrying out and evaluating a pilot CRC screening test carried out by the Catalan Institute of Oncology in order to determine the acceptance and viability of a program on a population scale, the Master Catalunya Oncology Plan, determined that colorectal cancer screening should be extended to the entire population. For this reason, it was implemented at the population level in Barcelona city[20].

A recent Spanish cooperative study[21], shows how the development of screening programs reduces the incidence and mortality from colon cancer 7 years after their introduction. This work is of great importance since it is developed on the Spanish population of different territories and not selected, that is, the population of the colon cancer screening programs.

There are recommendations made by the European Commission urging all member countries to develop screening programs since 2003, as well as a European guide for the development of screening programs[22]. There is also an order from the Ministry of Health of Spain in 2014 establishing the CRC screening program as part of the portfolio of common services of the National Health System[23].

Consequently, and based on these solid evidence of effectiveness and efficiency, there are currently CRC screening programs in activity in all the Spanish Autonomous Communities with the endorsement and legal and administrative support of both the European Commission and the Spanish Ministry of Health .

Current situation of the CRC screening program in the balearic islands

In view of the enormous potential benefits, the current situation of the program in the Balearic Islands is not acceptable based on the results published in the last day of the Alliance against colon cancer of the year 2019[24].

The CRC screening program in the Balearic Islands began in January 2015, in the form of biannual rounds, using the quantitative immunological SOH (OC-Sensor) as a screening test. At present, the program covers the areas of Ibiza-Formentera and the Inca District Hospital in Mallorca.

We have the general results of the first two rounds of the program (January 2015-December 2018). They can be consulted in **table III**.

The results of the endoscopic activity are detailed in the following **table IV**.

It should be noted that 77% of the colonoscopies performed found lesions directly related to CRC, while only 23% of the colonoscopies were negative for CRC or colon polyps.

That is, summarizing:

- Detection of 116 cases of CRC, 80% in stages I and II: that is, less therapeutic aggressiveness with better prognosis and lower personal and social cost.
- Detection of 472 people with high-risk adenomas, which implies a clear task of preventing CRC cases in the future

These excellent results are those of a program that covers 29% of the population of the Balearic Islands. The estimate in the case of 100% coverage of the population would produce the following results:

- Detection of 400 cases of CRC in 4 years
- Detection of 1,628 high-risk adenomas

If we do the calculation by doubling the participation rate to 50% then the estimated results are even more relevant:

• Detection of 689 cases of CRC in 4 years
• Detection of 2806 high-risk adenomas

In the whole of Spain, other Autonomous Communities have already reached 100% coverage of the program or have a clear objective on when to achieve it, while in the case of the Balearic Islands, from the Spanish Association against Cancer with the Balearic Government, we are finally working on planning to achieve a total population coverage, or at least greater than 85% as neighboring Communities and with a similar socio-sanitary structure have already achieved.

Participation is another synergistic objective to cover. The global participation rate of the population in the areas of the Balearic Islands where the program has been carried out is 28.8%, clearly lower than the national average of 48% and the participation rate recommended by the European Union 45%[22]. **Table V** details the coverage achieved by the program in the Spanish Autonomous Communities. It can be seen that the Community of the Balearic Islands has the penultimate worst participation rate.

The collaboration of Civil Society has been fundamental during the current development of the screening program. This is due to the clear perception that the population has of the benefit of the diagnosis of cancer in the asymptomatic phase and the fact that almost everyone has a family member or friend who has benefited from the program. Volunteers from the Spanish Cancer Association (SCA) carried out a work of personalized phone calls at the beginning of the second round of the program that was very effective in almost doubling the very low initial participation rate.

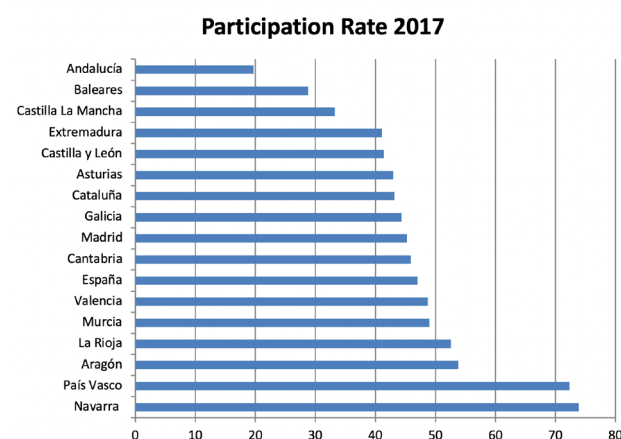**Table V:** Participation rates by Autonomous Communities.

Participation Rate 2017

Table III: General results of the January 2015- December 2018 Program.

	INCA		IBIZA-FORM		MENORCA	TOTAL
	1st Round	2nd Round	1st Round	2nd Round	1st Round	
Letters sent	25,352	25,498	25,090	26,267	19,871	122,078
Total SOB	8,362	8,991	5,363	6,618	5,826	35,160
SOBi (+)	616	533	388	379	373	2289
Exclusions	50	39	18	19	27	153
Waivers	17	15	11	10	17	70
Colonoscopias	539	478	359	350	329	2055
Participation rate	32,98	35,26	21,37	25,19	29,31	28,80

Table IV: Endoscopic activity of the Program January 2015- December 2018.

	FIRST ROUND	SECOND ROUND	TOTAL (%)
Colonoscopies performed	1233	816	2049
High-risk polyps	276	196	472 (23,03%)
Medium risk polyps	325	181	506 (24,7%)
Low risk polyps	283	200	483 (23,6%)
Normal colonoscopies	275	197	472 (23,03%)
CRC	74	42	116 (5,66%)
Stage I	53	22	75
Stage II	8	5	13
Stage III	12	5	17
Stage IV	1	4	5

Impact of the Covid19 pandemic on the program

The impact of the Covid-19 pandemic on all screening programs in Europe has been enormous. In this sense, it should be considered that the Balearic Islands have not been an exception: the CRC screening program was stopped in March 2020 and restarted in October 2020. A national survey conducted in December 2020 and directed by the SCA with the strategic collaboration of the Spanish Societies of Medical Oncology, Radiotherapy Oncology, Pathology, Hematology and Hemotherapy and Oncology Nursing[25] showed that between March / June 2019 and March / June 2020 34% fewer cytologies and 24% fewer biopsies had been performed nationwide, in addition to objectifying the very strong impact that the pandemic had caused on job stability and the psychological balance of cancer patients and their families. It is legitimate to assume and hope that this activity stoppage will have a harsh impact in the coming years in the form of an increase in cancer cases diagnosed in more advanced stages.

Conclusions

1. It is urgent to complete the implementation of the Screening Program in all health areas of the Balearic Islands 26. At the present time, the program covers only 20% of the population of the Balearic Islands. The lack of extension to the population as a whole, generates a situation of inequity within the population that, although in the initial phases of the development of the program can be acceptable, at this time they are very difficult to justify before the population.

2. Through preventive education programs, the population should be made aware of the benefits of participating in the Screening Program, to avoid rejection of the invitation and thus achieve high coverage.

3. The diagnostic results obtained in the Balearic Islands in the first rounds of the program are equivalent to those obtained in other Autonomous Communities, in line with those required by good practice, demonstrating the quality of the Program and the technical preparation of all the team that It is carried out, which makes it possible to ensure that a population expansion of the Program, with adequate organizational planning, can and should –extremely high efficiency– be assumed.

ANNEX 1. Tumor stages of colon cancer.

Stage I: The cancer has grown, crossed the mucosa, and invaded the muscle layer of the colon or rectum. It has not spread to nearby tissues or lymph nodes (T1 or T2, N0, M0).

Stage II
A: The cancer has grown through the wall of the colon or rectum, but has not spread to nearby tissues or lymph nodes (T3, N0, M0).
B: The cancer has grown through the muscle layers to the lining of the abdomen, called the visceral peritoneum. It has not spread to nearby lymph nodes or elsewhere (T4a, N0, M0).

Stage III
A: The cancer has grown through the inner lining or into the muscular layers of the intestine. It has spread to 1 to 3 lymph nodes, or to a tumor node in tissues around the colon or rectum that do not appear to be lymph nodes, but has not spread to other parts of the body (T1 or T2, N1 or N1c, M0; or T1, N2a, M0).
B: The cancer has grown through the intestinal wall or into surrounding organs and into 1 to 3 lymph nodes, or into a tumor node in tissues surrounding the colon or rectum that do not appear to be lymph nodes. It has not spread to other parts of the body (T3 or T4a, N1 or N1c, M0; T2 or T3, N2a, M0; or T1 or T2, N2b, M0).
C: Regardless of how deep it has spread, the cancer has spread to 4 or more lymph nodes, but not to other distant parts of the body (T4a, N2a, M0; T3 or T4a, N2b, M0; or T4b, N1 or N2, M0).

Stage IV: The cancer has spread to one or more distant organs of the body.

Interests conflict
The authors declare no conflict of interest.

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