
Colorectal cancer screening saves lives: The last piece of the puzzle[☆]

There is strong evidence and guidelines that recommend colorectal cancer screening. The benefits of screening are early diagnosis and cancer prevention, through removal of precancerous lesions such as polyps and lateral-spreading tumors. Several countries have established organized or opportunistic screening programs, but there is some debate about the evidence on which screening is based, and some issues are undefined.

At the end of last century, a large amount of evidence was produced, which showed the benefits of screening with fecal occult blood test (FOBT) versus no screening [1–4]. Fecal occult blood test, if positive, is followed by colon examination, preferably with colonoscopy, or with double contrast enema (DCBE) or virtual colonoscopy. An indirect demonstration of the efficacy of colon visualization is given by studies on sigmoidoscopy. In 2010 a good quality study demonstrated that flexible sigmoidoscopy is effective in reducing colorectal cancer incidence by 23% and colorectal cancer mortality by 31% [5]. However, up to now, there are no controlled randomized trials of screening based on colonoscopy alone. Colonoscopy is a part of FOBT-based screening programs, and it is conceivable that colonoscopy itself should contribute to the benefits of screening. In other words, the benefits shown in the FOBT trials should not be attributed only to FOBT *per se*, but subsequent colonoscopy might also have a contributing role.

This is a crucial point since many persons positive to FOBT do not undergo colon examination. Lack of follow up colonoscopy after a positive fecal testing could be due to different reasons, that can be related to the patient, the physician, and the system. It is intuitive that FOBT without follow up colonoscopy is an incomplete procedure with limited benefits. Delay in colonoscopy after a positive FOBT has been shown to be associated with more advanced cancer stage at diagnosis.

A recent systematic review [6] has pooled 8 studies, of which 5 used the fecal immunological test. In that review, colonoscopy performed more than 9 months after fecal testing was associated with higher incidence of stage III and IV cancers compared to colonoscopy performed within one month. A more advanced cancer stage may result in augmented mortality, but this is only a surrogate endpoint for screening efficacy. Only one of the studies included in the systematic review reports data on CRC mortality [7], with confusing results. The Authors examined CRC patients with

interval between FOBT and colonoscopy of 0–3 months (group 1), 4–6 months (group 2), 7–12 (group 3) and more than 12 months (group 4). Mortality in group 4 was higher than in groups 2 and 3, but not significantly higher than in group 1, which was the reference group. The Authors hypothesize that group 1 could also include symptomatic patients, at higher risk of advanced disease. Therefore, it is difficult to accept this study as an evidence of decreased mortality due to screening.

In this issue of Digestive and Liver Disease, Kim [8] and colleagues demonstrate unequivocally the relation between non-compliance to subsequent colon examination, cancer stage at diagnosis and specific mortality. The Authors provide good quality data derived from a population database. In this retrospective study, 258,819 patients with positive FOBT were divided in compliant to colonoscopy or double contrast barium enema within one year (142,269) and non-compliant (116,550). The proportion of non-compliant subjects seems to be remarkably high but is in line with other reported data from Korea [9]. The study shows an augmented number of CRC diagnoses in the compliant group (4.2% vs 2.6%), maybe because indolent cancers were included. At multivariate analysis, non-compliance to follow up was independently associated with an increased risk of CRC mortality, with a hazard ratio of 1.70 and a confidence interval between 1.52 and 1.90. Since this is a population-based study, the Authors were not able to describe how non-compliant patients reached a diagnosis of CRC. We can suppose that many of them became symptomatic, thus getting a CRC diagnosis as “common patients” and not as patients belonging to a screening population. Unfortunately, since patients could choose colonoscopy or DCBE, and the Authors have divided the group into compliant and non-compliant patients, we do not know which type of follow up examination was chosen and therefore if one performed better than the other. In the aforementioned [8] paper about compliance, in 2008, 11.8% of FOBT positive patients had chosen DCBE and 27.6% colonoscopy. Given the similarity of the populations studied, we could assume similar proportions in the present study.

These results should be confirmed in other studies, involving different populations and screening programs, possibly with higher compliance to follow up examinations. However, now it is unequivocally demonstrated that follow up after fecal testing is needed, that direct colon examination is effective in reducing mortality from CRC, and that colon examination is effective even if delayed for up to one year.

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Declaration of Competing Interest

None.

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