Editorial Commentary

Programmed colorectal cancer screening decreases incidence and mortality

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Provenance: This is an invited article commissioned by the Section Editor Dr. Qiang Shi, PhD, MD (Zhongshan Hospital, Fudan University, Shanghai, China).

Comment on: Levin TR, Corley DA, Jensen CD, *et al*. Effects of organized colorectal cancer screening on cancer incidence and mortality in a large community-based population. Gastroenterology 2018;155:1383-91.e5.

Received: 14 November 2019; Accepted: 16 December 2019; Published: 26 December 2019.

doi: 10.21037/tgh.2019.12.13

View this article at: http://dx.doi.org/10.21037/tgh.2019.12.13

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second leading cause of cancer-related deaths in the world (1). Detecting and removing precancerous lesions or detecting tumors in early stages through endoscopy decreases CRC mortality (2). Randomized controlled trials (RCTs) have shown that CRC screening based on guaiac fecal occult blood testing (gFOBT) and flexible sigmoidoscopy is effective in reducing incidence and mortality rates of CRC (3).

Nowadays, different tests are available to facilitate detection of CRC or adenomas: indirect techniques such as the gFOBT, or the fecal immunochemical test (FIT). The FIT yields significantly higher detection rates for advanced adenomas, and has greater sensitivity and specificity than gFOBT in detecting CRC (4). Moreover, patient adherence to FIT screening programs appears to be higher than for gFOBT. Based on current evidence, FIT has been recommended as the first option for detection of fecal occult blood in CRC screening (5).

Colonoscopy is more commonly used for screening than flexible sigmoidoscopy, as the former allows full visualization of the colon and reduces both right and left sided cancer. Numerous observational studies have reported that colonoscopy also reduces CRC mortality and incidence (2,6). Despite the evidence, however, adherence to CRC screening programs is still estimated to be only 45%.

Over recent years, many population-based programs have been implemented worldwide, yet few studies have evaluated the role of organized CRC screening in screening uptake, incidence and mortality in community-based populations (7). In Europe, several CRC screening programs have been implemented progressively and in 2015, 24 out of 28 European Union countries had established CRC screening programs. Likewise, in the United States CRC screening rates have been rising during the last 20 years, approaching adherence rates of 65%.

A study by Levin and colleagues explored the implementation and effectiveness of an organized CRC screening program in a Californian population (8), reporting on screening rates before and after introducing the program, CRC incidence, mortality rates and the percentage of fecal test-positives who received a follow-up colonoscopy within 6 months of their positive test.

In this CRC screening program, individuals were continuously enrolled from a Californian region. Screening evolved from an opportunistic sigmoidoscopy and/or FOBT performed by physician request since the year 2000, and involved programmed direct-to-patient annual FIT starting from 2007. In 2008 a population between 51 to 75 years old was targeted. If the FIT test was positive, a colonoscopy was scheduled. Three primary outcomes were analyzed: screening status, CRC incidence and CRC-specific mortality.

This organized CRC screening initiative doubled the percentage of screened patients. The increased screening led to a peak in CRC incidence, followed by a pronounced

descent, falling to below baseline incidence rates in 2015. CRC mortality also decreased by 52.4%. The authors demonstrated that CRC incidence and risk of death can decrease significantly through introduction of an organized CRC screening program.

CRC screening programs are aimed at detection and resection of premalignant lesions and early tumor detection, to facilitate curative-intent surgical treatment and avoid aggressive therapies such as chemo or radiotherapy.

CRC is a good candidate for screening programs due to its elevated incidence, and several screening methods have been shown to decrease incidence and mortality. In Europe, the number of countries implementing screening programs is increasing, as is access to population-based screening in age-eligible populations (9). Opportunistic screening is still the norm in the US, because there is no national screening program, yet compliance with screening has increased, leading to a reduction in both incidence and mortality related to CRC (10). In 2015, a National Colorectal Cancer Roundtable initiative was set up, aiming to raise screening rates in the United States up to 80% by 2018 (11). However, organizing a CRC screening program is a complex process, consisting of several steps and interaction between patients, healthcare providers and health organizations. A successfully organized screening program requires establishing the screening method and interval, defining the target population and inviting them to participate. Furthermore, after the screening tests are performed patients must be notified of the results, and in case of a positive result, referred to a specialist for further treatment. Moreover, implementation of a screening program requires monitoring, regular feedback and periodic reporting to evaluate the impact on society.

Levin's study confirms the feasibility of implementing a successful screening program in a real population setting. Adherence to the screening program increased progressively over the years, reaching almost 90% of the target population. FIT tests have the advantage of needing only one feces sample, as opposed to gFOTB where dietary restrictions are generally required to perform the test, and more than one sample is needed (12). Adherence to FIT test has been shown to be greater than gFOBT in five population-based RCTs, showing an absolute increase in participation ranging from 5.4% to 16.2% with FIT (5).

This screening program showed an initial rise in CRC diagnosis, followed by a progressive decrease in incidence of the disease, partly due to early detection and resection of premalignant lesions. These findings are consistent with other related studies (13).

A reduction in CRC mortality rates was confirmed in Levin and colleagues' study, though it should not be attributed exclusively to the screening process. Trends in CRC incidence and mortality have been downward since 1975, and screening has been used since 20 years ago, suggesting that other factors must have played a role in this decrease, such as improved therapies, earlier detection of symptomatic disease or change in dietary habits (14).

Although implementing a CRC screening program has demonstrated a positive impact on incidence and mortality, it must be weighed up against potential harm. Despite being considered a more cost-effective technique, at the manufacturer-recommended cut-off FIT tends to have a higher positivity rate than gFOBT and thus twice as many colonoscopies are required with FIT screening (15). Disadvantages of colonoscopy include the need for thorough bowel cleansing and a low risk of perforation or postprocedural bleeding (4,13), although if performed in experienced centers with high-volume endoscopists, perforation and bleeding rates are significantly lower (16). Another possibility to consider regarding screening is the psychological harm caused by false positive results. Psychological distress was evaluated as part of a systematic medical literature review on morbidity attributed to CRC screening. Five out of seven prospective studies reported an adverse effect on psychological well-being, with the greatest effect observed before the screening test and shortly after receiving a positive test result (17). However, this reaction declined post-colonoscopy and disappeared later on. On the other hand, a RCT in a Norwegian population found that screened populations with a positive screening result (from FIT or flexible sigmoidoscopy) showed no increase in anxiety or depression levels compared with a control group with no screening (18). Nevertheless, only 35% of invited individuals completed the questionnaire, which could have biased these results.

The target population is another important factor in any screening procedure. The US Preventive Services Task Force (USPSTF) recommends screening for CRC from age 50 until 75 (19). There is a lack of RCTs exploring screening interventions in elderly people (20). Despite their increased risk of developing CRC, early CRC detection may have no impact on their life expectancy. It is also important to weigh up potential injury caused during screening procedures, particularly invasive endoscopic techniques, against expected benefits in this subgroup. According to USPSTF recommendations, the decision to screen for

CRC in adults aged 76 to 85 years should be individualized, taking into account the patient's overall health and prior screening history, as the expected benefit is higher in those who have never been screened for CRC. On the other hand, more people under 50 years old are being diagnosed with CRC, a leading cause of cancer incidence and mortality among young adults relative to other cancers (21). Recently, a Microsimulation Screening Analysis-Colon (MISCAN-Colon) model was performed to evaluate the optimal age to start CRC screening, resulting in the USPSTF recommendation to initiate this procedure at age 50 (22). In light of the increased incidence of CRC in the under fifties, a new microsimulation analysis was performed, adjusting the model to reflect increased CRC incidence in more recent birth cohorts (23). In this analysis, screening initiation at age 45 showed a favorable balance between screening benefits and burden based on the increase in CRC incidence in young adults, suggesting that future guidelines could recommend beginning CRC screening earlier.

In conclusion, implementing organized CRC screening with FIT and colonoscopy has proved effective in reducing CRC burden and mortality. Healthcare providers and governments should prioritize starting CRC screening programs, and should also employ strategies to improve adherence in the target population.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/tgh.2019.12.13
Cite this article as: Roselló S, Simón S, Cervantes A. Programmed colorectal cancer screening decreases incidence and mortality. Transl Gastroenterol Hepatol 2019;4:84.

