

Another brick in the large wall against colorectal cancer: a commentary on effectiveness of screening colonoscopy

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Colorectal cancer (CRC) is the third most commonly diagnosed cancer among both men and women in the United States. Incidence and mortality rates of CRC have been declining for several decades. The recent changes in risk factors (e.g., decreased smoking rates, red meat consumption, increased use of aspirin), the dissemination of screening tests, and the improvements in treatment have been hypothesized to contribute to CRC mortality reduction (1). In Addition, more recent evidence indicates that the increasing use of CRC screening has been a major contributor to the declining incidence and mortality rates in the U.S. from this disease (2,3).

The current study adds to the existing literature two important factors. It shows that screening colonoscopy is associated with a substantial decrease in mortality. Importantly, it demonstrates similar reduction in mortality from left-sided and right-sided CRC in a large community-based analysis. The authors note that there are few on-going randomized trials examining screening colonoscopy, but results are expected in several years.

Unfortunately, in cancer, we do not have the luxury of time. More than 50,000 Americans are expected to die from CRC in 2017, and over 774,000 men and women die of CRC world-wide each year (1). We among others emphasize an analytical approach in order to gain insights from real world, albeit imperfect, clinical data. Actionable clinical knowledge can be derived from well performed

non-randomized studies, such as the one presented here, in a concerted effort to reduce CRC-specific mortality.

The current article and other published reports underscore the fact that evidence supporting the ability of screening colonoscopy to substantially reduce risk of right-sided colon cancer and/or mortality is limited (4-6). Therefore, this study adds an important perspective on screening colonoscopy. It demonstrates that colonoscopy could prevent CRC in right-sided CRC as effectively as left-sided CRC. This is an important, clinically relevant finding, as colonoscopy is the only tool currently in uses, which integrates three important goals: screening for, early detection and prevention of CRC (extirpation of premalignant lesions).

Based on previous studies that showed a reduction in CRC-specific mortality for left-side disease by performing colonoscopy/flexible sigmoidoscopy, it is unreasonable to conclude that there is a similar survival benefit with right-sided disease using the same screening approach. Studies such as this and others, will inform decision makers on standards of practice, potentially bending the CRC survival curves.

The conclusion of the current study was that screening colonoscopy was associated with a substantial and comparably mortality risk reduction for both right-sided and left-sided cancers within a large community-based population. According to trends in mortality and the

aforementioned evidence of other studies, we support the conclusion that screening tests, and exclusively colonoscopy, reduce CRC mortality, but we would like to critically assess the data and methods that led to this study's conclusion.

- (I) Nested control study as a case control study has an inherent bias, as it can only show association and not causation, making it less than ideal evidence on which to base wide spread population-based intervention.
- (II) Few biases could impact the methodology in this study:
 - (i) It is not clear why the authors chose to study patients 55–90 years of age; most evidence-based recommendations state that screening colonoscopy is advised from 50–75 years of age.
 - (ii) According to Figure 1, almost 1,600 cases of the 3,585 cases recruited in the beginning of the study were excluded due to: missing death/diagnosis date (n=404); cause of death not CRC (n=707); and, did not undergo chart audit (n=499). This means that almost 44.6% of cases were excluded without any evidence in the article that this group of excluded cases did not differ from the remaining analytical cases.
 - (iii) The control selection wasn't matched for race/ethnicity, even though it is a well-known fact that there are substantial racial disparities, with CRC incidence rates highest in non-Hispanic blacks (1). According to Table 1, 11.9% of cases compared to 7.1% were non-Hispanic blacks. In the same Table 6.6% of the cases had a family history, which was considered an exclusion criterion.
 - (iv) Table 1 also shows that 17% of patients were from KPSC and accrued from 2011–2012, meaning that a large part of patients were accrued late in the follow-up period.
 - (v) According to Table 2, of the 1,747 cases just 13 cases, and 120 of the 3,460 matched controls, had screening colonoscopy, leaving the conclusion of the article regarding right-sided colon somewhat lacking.

- (vi) This study underscores the challenges in compliance with recommended gold standard CRC screening, which was done in less than 3.5% of the patients studied.

Even though the article is an important step towards improved evidence-based clinical decision making in CRC screening and prevention, a long journey awaits until we reach the destination. But, as once said by a Lao Tzu, even a journey of 10,000 miles starts with one small step.

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Footnote

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

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