Best Practice & Research Clinical Gastroenterology 31 (2017) 441–446

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology

journal homepage: https://ees.elsevier.com/ybega/default.asp

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Adenoma detection rate and risk of colorectal cancer

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ARTICLE INFO

Article history:
Received 2 June 2017
Received in revised form
27 June 2017
Accepted 5 July 2017

Keywords:
Colonoscopy
Screening
Quality measures

ABSTRACT

Goals: The aim of this paper was to discuss association between adenoma detection rate (ADR) and interval colorectal cancer risk.
Background: Adenoma detection rate is being used as a benchmark quality measure for colonoscopy. There are three studies showing inverse association between ADR and interval colorectal cancer risk. One recent study reports significant impact of increased ADR on decreasing interval colorectal cancer risk.
Study: We discussed evidence for using ADR as a quality measures in colonoscopy and flexible sigmoidoscopy. We revised three studies (Kaminski et al., N Engl J Med 2010; Corley et al., N Engl J Med 2014 and Rogal et al., Clin Gastroenterol Hepatol, 2013) analyzing association between ADR and interval colorectal cancer. We collated strengths and weaknesses of these studies with the perspective of clinical impact of their results.
Results: Kaminski et al. and Corley et al. reported inverse association between ADR at colonoscopy and interval colorectal cancer. Kaminski et al. showed that patients examined by endoscopists with ADR of less than 20% had over 10 times greater risk of interval colorectal cancer during the follow-up time than those examined by endoscopists with ADR $\geq$20%. Additionally, Corley et al. showed that ADR $\geq$28% resulted in a significantly lower risk of colorectal cancer death than ADR of less than 19%. In parallel, Rogal et al. reported similar association for flexible sigmoidoscopy, with 2.4 higher odds of interval colorectal cancer diagnosis during follow-up time in patients examined by endoscopists with distal ADR <7.2% than those with distal ADR $\geq$7.2%.
Apart from inevitable clinical importance of the studies, they are not without disadvantages. In Kaminski et al. study cohort and study endpoint are well defined, but there is lack of statistical power to provide more robust results. In Rogal et al. study cohort is well defined, but approximation of the study endpoint was used. Finally, Corley et al. study has both poorly defined study cohort and study endpoint, but has the highest statistical power of all three to detect the differences for both interval colorectal cancer and colorectal cancer death.
Conclusion: Both, inverse relationship between ADR and ADR improvement and colorectal cancer risk and death reaffirm ADR as a crucial quality control parameter.

1. Introduction

Adenoma detection rate (ADR) is a benchmark quality measure for colonoscopy. It is defined as proportion of patients with at least one colorectal adenoma detected among all patients examined by an endoscopist [1]. Both, the European Society of Gastrointestinal Endoscopy [1] and the American Society for Gastrointestinal Endoscopy jointly with the American College of Gastroenterology [2] in their current guidelines recommend for screening colonoscopy setting a minimum endoscopist's ADR cut-off of 25% (in a male/female population aged 50 or more). It is believed that this standard assures sufficient colorectal mucosa inspection to consider time to surveillance colonoscopy safe.

The aim of this paper is to discuss the available evidence supporting the use of ADR as a quality measure for colonoscopy with special emphasis on its association with interval colorectal cancer

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http://dx.doi.org/10.1016/j.bpg.2017.07.002
1521-6918/

(iCRC) risk.

2. ADR variation

ADR by its definition is highly correlated with adenoma prevalence in a specific cohort. It has been shown that ADR varies between males and females, increases with patients' age [3–12] and differs among geographical regions [4,8,11,13]. ADR depends on indication for colonoscopy with significantly higher values in diagnostic and secondary screening (colonoscopy following positive guaiac fecal occult blood test (gFOBT) or fecal immunochemical test (FIT)) than in primary screening [6,14–16].

Even if the above factors explain the ADR variability between populations, still high variability among endoscopists within one population is observed. Indeed, endoscopist has been shown to be the most powerful predictor of ADR [17]. The studies using primary colonoscopy screening show that ADR ranges between 7% and 44% [5,17–23] with some studies reporting ADR of more than 50% [24,25]. At the same time, polyp miss rate estimated based on tandem colonoscopies varies between 2.1% for adenomas ≥10 mm and 26% for adenomas 1–5 mm [26].

Another study shows that in FIT positive population ADR of 45% is equivalent to ADR of 20% in primary colonoscopy screening and that there is a significant positive correlation between ADR in primary and secondary (following FIT positive) colonoscopy screening (Pearson's coefficient 0.716, $P < 0.001$) [16]. Reported median ADR after positive FIT among subjects aged 50–69 was 55% (range 21%–83%) [16], whereas mean ADR after positive FOBT among subjects aged 60–92 was 46.5% (range 21.9%–59.8%) [14].

It has been suggested that in colorectal cancer (CRC) screening setting endoscopists' ADR does not need to be adjusted for the case mix [14]. However, if ADR is planned to be calculated for endoscopic units providing services only for selected profile of patients the case-mix adjustment would be needed. Currently, this process is not clear yet and needs further studies [27].

With the adenomas being CRC precursors, both low ADR and high adenoma miss rate may have major clinical consequences.

3. ADR vs. colorectal cancer risk

Two studies reported inverse association between ADR and iCRC risk for colonoscopy (Kaminski et al. [28] and Corley et al. [29]) and one study reported inverse association between distal ADR and distal iCRC risk for flexible sigmoidoscopy (Rogal et al. [30]). Below, similarities and differences of these studies are presented.

3.1. Study design

Two of the studies (Kaminski et al. and Rogal et al.) used screening programs' databases for the analysis. In the first study it was an opportunistic colonoscopy screening, in the second study it was a randomized controlled trial comparing sigmoidoscopy screening with the usual care. In the study of Corley et al., integrated databases of insurance companies were used. They covered screening (18.3%), surveillance (24.3%) and diagnostic (57.4%) colonoscopies.

3.2. Study endpoints

Only in Kaminski et al. study final diagnosis of the primary colonoscopy for all subjects were given. This enabled authors to make a fair differentiation between screen detected CRC and iCRC for CRC reported at the beginning of the follow-up time. In this study iCRC was defined as CRC diagnosed between the date of index colonoscopy to the date of scheduled surveillance. Scheduled surveillance was 3 years in subjects with high-risk adenoma removed (adenoma with ≥10 mm in diameter or high-grade dysplasia or villous/tubule-villous or ≥3 adenomas) and 5 years in subjects with low-risk adenoma removed (1–2 tubular adenomas <10 mm in diameter with low-grade dysplasia). Follow-up time for subjects with no adenomas was censored after 5 years of observation.

In the two other studies, the final diagnosis of the primary colonoscopy was not known and distinguish between CRC diagnosed in the index exam and iCRC had to be approximated. In the Corley et al. study, iCRC was defined as CRC diagnosed between 6 months and 10 years after index colonoscopy. All CRCs diagnosed up to 6 months form index colonoscopy were considered to be detected in the index exam. In the Rogal et al. study, iCRC was defined as CRC stage I or II diagnosed between 1 year and 30 months after negative sigmoidoscopy or CRC stage III or IV diagnosed between 1 year and 48 months after negative sigmoidoscopy. All CRC diagnosed after this period of time were considered to be undetectable at the index exam.

In Kaminski et al. and Corley et al. studies data on iCRC were obtained from the cancer registries, whereas in Rogal et al. study iCRC was identified through the annually mailed questionnaire (overall response rate was 93.8%). Corley et al. was the only study where risk of iCRC death was analyzed. Data on causes of death were obtained from cancer registry and state mortality files.

3.3. Inclusion criteria

In Kaminski et al. study only subjects with adequate bowel preparation, with removal of all detected polyps and no detection of CRC at screening were included. In Rogal et al. study all subject that were diagnosed with iCRC and for whom index sigmoidoscopy was found to be low-quality (i.e. with inadequate bowel preparation or inadequate depth of insertion), with delayed follow-up colonoscopy or lesion missed at subsequent colonoscopy were excluded. Moreover, only subjects not undergoing cancer treatment (apart from skin cancer), no history of prostate, lung, colorectal or ovarian cancer and no colonoscopy, sigmoidoscopy or barium enema during last 3 years were eligible to have index colonoscopy (this requirement was not fulfilled during the first 2 years of enrollment period). No data on quality of bowel preparation or depth of insertion were given in Corley et al. study.

Minimum follow up time was 6 months in Corley et al. study, 12 months in Rogal et al. study and was not prespecified in Kaminski et al. study. Minimum number of screening exams performed by endoscopists to be included into the analysis was 30 in Kaminski et al. study, 75 in Corley et al. study and 100 in Rogal et al. study. Additionally, in Corley et al. study endoscopists were also required to perform at least 300 diagnostic exams.

3.4. Study population

Age range and proportion of male sex in the studies population was 40–66 years (55 on average) and 35.7% in Kaminski et al., 50–72 years (64 on average) and 47.7% in Corley et al. and 55–74 years (approx. 62 on average) 52% in Rogal et al. 20% of subjects had 1^0 family history of CRC in Kaminski et al. study and 9.9% had 1^0 family history of CRC in Rogal et al. study. Family history of CRC among subjects in Corley study was not available.

3.5. Adenoma detection rate

Total number of endoscopists was 186 in Kaminski et al. study, 136 in Corley et al. study and 93 in Rogal et al. study. Median non-adjusted ADR in Kaminski et al. study was 12.2% with an interquartile range