UNITED EUROPEAN GASTROENTEROLOGY
ueg journal

Editorial

United European Gastroenterology Journal
2017, Vol. 5(2) 149–152

DOI: 10.1177/2050640616667171
journals.sagepub.com/home/ueg
SAGE

FITting ADR to colonoscopy indication

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The concept of an adenoma detection rate (ADR) first appeared in 2002 from the United States (US) Multi-Society Task Force on Colorectal Cancer.[1] The purpose of ADR was then,[1] and remains today,[2] to measure the detection performance of individual colonoscopists. Thus, in 2002 there was already evidence of dramatically variable colonoscopy performance.[3] The original definition of ADR was the fraction of patients age ≥50 years with one or more conventional adenomas detected during colonoscopy, without reference to the procedure indication, and with the thresholds modified only for gender (≥1 adenoma should be detected in at least 25% of males and 15% of females).[1] In 2006 a joint task force on quality of the American College of Gastroenterology/American Society for Gastrointestinal Endoscopy (ACG/ASGE) restricted the target group for measurement to people undergoing first-time screening colonoscopy.[4] The rationale for the restriction was that the thresholds had been set in 2002 based on screening colonoscopy studies performed on asymptomatic individuals with either negative fecal occult blood tests[5] or with no prior fecal blood testing.[6–8] Subsequent studies have shown that doctors performing surveillance examinations have ADRs that are typically 7%–10% higher than their screening ADRs.[9,10] For unclear reasons, ADRs in populations undergoing colonoscopy for diagnostic indications (generally abdominal pain or altered bowel habit) tend to run lower than ADRs in screening populations.[9] Because ADRs in true screening populations tend to sit near a mid-level between those for surveillance and diagnostic examinations,[9] overall ADRs for all three groups of patients combined tend to run closer to screening ADRs than to either surveillance or diagnostic ADRs, raising the question of whether restricting ADR to screening examinations only is necessary. Anecdotally, many endoscopists express concern that their patient populations are sufficiently different with regard to some factor that is known to affect the prevalence of adenomas (e.g. different average age, fraction of obese patients, diabetics, smokers), that the thresholds recommended for minimum performance should not apply to their ADR, or that some adjustment should be made for their patient populations. Available evidence suggests that adjustment for such factors is entirely unnecessary.[11] Stated differently, colonoscopists rarely have patient populations that are so much thinner or healthier (or vice versa more obese or diabetic) that an adjustment in the threshold for ADR based on such factors is needed. In short, ADR works well in the US and other countries with primary screening colonoscopy when it is adjusted only for gender and using a minimum age cutoff, e.g. age 50 in the US and 55 in Germany. A screening colonoscopy study in Poland found that the original thresholds set for ADR were remarkably good at separating effective from ineffective endoscopists.[12] Subsequently, a much larger study from California found that ADRs above the minimum thresholds provided additional protection against cancer,[13] so that in 2015 the ACG/ASGE quality task force raised the minimum acceptable thresholds for ADR in screening populations to 30% in males and 20% in females.[2] Currently, the US recommendation continues to be that ADR should be measured in the screening population.[2]

In the US and some other countries, colonoscopies performed to evaluate positive fecal blood tests are considered "diagnostic" colonoscopies. Outside the US, colonoscopies performed for positive fecal occult blood tests are sometimes called "screening" colonoscopies because they are an extension of the screening process that began with a fecal immunochemical test (FIT) or a guaiac-based test for fecal blood, and extended to colonoscopy when the fecal test result was positive. In the US, there is currently a trend toward greater interest in FIT screening, primarily in organized screening programs,[14] but colonoscopy still dominates US screening by a substantial margin.[15] What has been clear for some time is that the targets set in the US for primary colonoscopy screening are too low for colonoscopies performed for the indication of

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positive fecal blood tests.[16–23] Indeed, the positive predictive value of fecal blood testing both for early-stage cancers and large adenomas is such that a positive fecal blood test (particularly FIT) is clearly the single highest yield indication for colonoscopy with the possible exception of a positive imaging test (e.g. computed tomography (CT) colonography). This high yield has already led some groups in countries to create minimally acceptable ADR thresholds for the fecal blood-positive patients that are substantially higher than the ADR thresholds set for the $\geq$50 years age group undergoing screening colonoscopy.[24] Thus, colonoscopy for true screening as defined in the US and colonoscopy performed for positive fecal blood tests are two very different undertakings, for which there is wide recognition that different detection targets are appropriate.

In this issue of the *Journal*, Cubiella et al. provide the most direct demonstration yet available that colonoscopists working in populations with positive fecal blood tests have much higher ADRs than when they are performing true primary screening colonoscopy.[25] In a post-hoc analysis of a randomized trial where detection of advanced neoplasia was compared between one round of FIT and primary colonoscopy screening at the population level,[25] the mean ADR in the FIT arm was strictly correlated with the corresponding value in the primary colonoscopy arm, after adjusting for all the possible confounding factors, such as age, sex or geographical distribution.[25] Further, a nearly two-fold difference between the two ADRs was shown, so that the equivalent value for the 25% benchmark adopted for primary colonoscopy screening appeared to be equal to 45% at FIT.[25]

The greatest strength of this post-hoc study is that the same endoscopists performed all procedures in both study arms. This minimizes uncertainty related to possible heterogeneity in diagnostic accuracy among the endoscopists. Clearly any difference in mean ADR between the two arms results from the different disease prevalence in the two arms. This is confirmed by the analogous trend in ADR distribution according to demographic and geographic factors between the two groups.[25]

Initiation of ADR measurements in FIT-based screening programs does not have the same evidence-based support already established for ADR measurement in primary screening colonoscopy. Specifically, higher ADR in the true screening setting is a validated predictor of lower risk of colorectal cancer and cancer-related mortality.[12,13] Nevertheless, we can anticipate that evidence of better detection at colonoscopy resulting in lower cancer risk in the FIT-positive population will be forthcoming. Fecal blood testing has been associated with a lower incidence of colorectal cancer, an effect that can result only from polypectomy.[26,27] It seems certain that better polyp detection and more polypectomy will therefore reduce cancer risk in FIT-positive patients. Measurement of ADR in organized FIT programs should be easier than measuring ADR for primary screening colonoscopy in the opportunistic screening setting, where the burden of manual entry of pathology results into databases often rests on busy colonoscopists.

ADR is the most important measure of the quality of colonoscopy performance. ADR is highly variable between endoscopists,[28,29] can be accurately measured with a few hundred examinations,[30,31] and directly reflects whether the fundamental goal of most colonoscopies (prevention of colorectal cancer and cancer-related death) will be achieved.[12,13] As such, ADR is the constant subject of research, and of very appropriate efforts to refine and improve it.[32] We are now in a position to enumerate most of the elements of procedure indication and patient demographics that should dictate adjustments to ADR calculation and creation of minimum ADR thresholds. An age cutoff is critical, but further adjustments for mean age of patients who are above the set cutoff are not needed.[11] A gender adjustment is important, but only in certain settings such as the US male veteran population, or the largely female patient population of some female endoscopists, where there is a substantial deviation from the typical approximately equal gender distribution of most patient populations. Adjustments for factors such as smoking, obesity and diabetes are not necessary. Very importantly, we have clear confirmation from Cubiella et al. that the thresholds for minimally acceptable performance should be much higher in the FIT-positive population than in a true screening colonoscopy population.[25] The best population to measure ADR in (which in turn determines the right set of minimum ADR thresholds to use) is immediately evident from how screening is conducted locally. In countries with national organized programs based on FIT and in health care systems within the US with organized FIT screening programs, endoscopist performance will be most easily evaluated by measuring ADR in the FIT-positive population. In the opportunistic screening setting in the US and within national organized programs using primary colonoscopy screening (e.g. Germany and Poland), ADR should be measured in the true screening population and evaluated by comparison to the lower minimum thresholds.[2] In some settings perhaps measurement in both populations will be necessary, but clearly the FIT-positive and true screening populations should not be mixed with regard to ADR measurement, unless there is adjustment for indication. ADR is not perfect, but if measured correctly it is very good. The greatest mistake is to not measure ADR, and

to thereby potentially expose patients to ineffective examination and interval colorectal cancer risk.[12,13]

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