

Equivalence between low adenoma detection and high miss rates: Is AI the ultimate response?



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Bibliography

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Most post-colonoscopy colorectal cancers (CRC) have been exclusively attributed to missed lesions, marginalizing the role of de novo or incompletely removed lesions [1]. What may be called a simple lack of efficacy could represent one of the most unique opportunities for endoscopic innovation.

The definition of a “missed” lesion is apparently straightforward. Anytime an overlooked lesion is detected by the same or a different operator, it accounts for a “miss.” Thus, it is a lesion—rather than patient-based analysis, indicating that in the same patient, we can miss more than one lesion. There are several reasons to explain why we miss lesions, and these are broadly referred to as polyp- and technique-based factors. The former is represented by lesions too subtle to be recognized by community-based endoscopists as well as by those located in spots not accessible, i.e. behind the folds or in the flexures. How much do we miss? Despite doing our best to slow down the withdrawal phase or to widen the angle of view of our scope, one in every four lesions is still missed, according to a very recent meta-analysis [2]. Disappointingly, this is likely to represent an underestimation, as the reference standard in these studies is represented by the same somewhat suboptimal technique we are assessing. In addition, the miss rate for community-based endoscopy is likely to be much higher than that generally measured in referral centers, which represent the more common setting for these kinds of studies.

If miss rate is the most reasonable candidate for post-colonoscopy CRC, the sooner that we – as an endoscopy community – can measure our individual miss rate, the sooner we can provide the strongest guarantee our patients that they can avoid a dismal oncological outcome. Along this line, once we are aware of our miss rate, we can try to reduce it with interventions such as retraining, imaging, and mechanical innovations

that have been shown to be effective for this purpose [3]. There is a logic to all of this!

That premise, however, is simply impossible! To measure the actual miss rate implies a tandem repetition of two consecutive colonoscopies that is clearly unethical in a clinical setting. In addition, it has been argued that to “miss” a lesion is not always so clinically relevant. It is implausible that “missing” a diminutive “low-risk” adenoma can result in an interval cancer, as much as “missing” one of several adenomas in a high-risk patient undergoing intensive surveillance is also unlikely to affect the outcome of that patient.

These pitfalls have been addressed by replacing the “miss” rate with its exact opposite: the adenoma detection rate (ADR) [4]. The main assumption is that a low rate of detection is inversely proportional to a high “miss” rate, so that a high-detector will characterize the competent endoscopist who misses a few lesions. Such a quality indicator gained immediate approval by the endoscopic community. First, the ADR is relatively easy to measure and only requires already available endoscopic and histological data. Second, it is clinically-oriented as strictly associated with the risk of post-colonoscopy CRC. Third, it can be improved by the same innovation that has been related to reduction of the “miss” rate.

Is ADR completely equivalent to its opposite, that is, the “miss” rate? Unlike the “miss” rate, ADR represents a per patient rather than per polyp analysis. That indicates that only in the hypothetical case of a patient with a single adenoma will ADR and “miss” rate will refer to the same amount of clinical information. On the other hand, if a patient has two or more adenomas, ADR and “miss” rate can give different results any time that one or multiple lesions are missed. The result can potentially be an imbalance between ADR and “miss” rate. Let’s as-

sume that a patient has three small adenomas and that two of them are missed. In that case, the patient will neglect to follow the required “intensive” surveillance, despite the appearance of proper classification from the ADR perspective. Second, we should consider the combination of disease prevalence and natural history. Non-polypoid lesions – especially those that are depressed – are much less frequent than polypoid lesions, especially in fecal immunochemical test-based programs. Thus, it is unlikely that the “miss” of such lesions, which are the most difficult to detect, would meaningfully affect the nominator of the ADR, largely dominated by small to large polypoid lesions. That is a potential major limitation of ADR, as flat depressed lesions have an accelerated carcinogenesis that has been related to lack of right-sided CRC protection by colonoscopy [5].

Replacement of the “miss” rate with ADR may have additional detrimental effects on the psychology of the endoscopist. ADR generates the irrational feeling that it is only the first adenoma detected that discriminates between a positive and a negative colonoscopy. This gap in motivation may result in an optimal quality of mucosa exploration until we find the stigmatizing lesion, immediately followed by a drop in attention and dedication in the subsequent part of the colonoscopy. Because it is more likely that the first lesion was “easy” to detect (i. e., large or polypoid), the risk of missing one or more subsequent subtle non-polypoid lesions is theoretically increased.

This has been extensively addressed in a large United States-based series of over 25,000 primary screening colonoscopies by 69 endoscopists in which both ADR and the mean number of adenomas in positive colonoscopes (ADR-*plus*) was measured [6]. The clinically relevant correlation between the two parameters supports a theoretical equivalence between detection and miss rates [6]. Unlike ADR, ADR-*plus* is indeed a per polyp real-life measure mimicking the equally per polyp “miss” rate assessed in the artificial studies. This also indicates that the association between ADR and post-colonoscopy CRC is amplified, as endoscopists who miss the initial adenoma are also more likely to miss subsequent adenomas in the same patient. Such ADR-ADR-*plus* correlation represents a plausible reason for which a high-ADR – despite being driven mainly by diminutive low-risk adenomas – minimizes risk of CRC. It is not that the endoscopist detects meaningless lesions, but that such detection is associated with detection of additional, presumably more advanced lesions.

Once we agree, as seems logical, that ADR is just a per patient surrogate of the possibility of missing multiple adenomas in the same patient, is it possible to return to a more direct measure of the “miss rate” at per polyp level? In the future, artificial intelligence (AI) may be of substantial help in computer-assisted detection of polyps. Its main advantage is intra-procedural assessment of the “miss” rate in a single procedure. Unlike in the tandem colonoscopy setting, such an AI-based “miss” rate will be highly precise as both the human and the computer raters are exposed to exactly the same pool of polyps. In addition, “miss” rates will be stratified according to

clinical relevance of a lesion, with higher emphasis placed on flat and depressed lesions.

More importantly, AI may be expected to fully address the unfavorable effects of the combination of a low-ADR and a low-ADR-*plus*. There is no apparent reason to believe that AI would have different degrees of benefit in assist detection of first versus subsequent lesions actually missed by a low-detector endoscopist. The only residual pitfall is the natural tendency of AI to measure only perception errors, i. e., polyps visualized by the monitor but undetected by the operator. However, that may be offset by use of alternative AI functions that would allow evaluation of coverage of the total colorectal mucosa exposed to the endoscopic lens or the quality of colonoscopy withdrawal based on quantification of scope slippage near the lumen in cases in which images are blurred images.

Conclusion

In conclusion, implementation of ADR as a more feasible and clinically orientated proxy for “miss” rate at colonoscopy had a tremendous impact on reducing inter-endoscopist variability in diagnostic performance. However, the next implementation of AI may be expected to replace ADR with real-time assessment of the “miss” rate, which would inescapably represent the most direct and comprehensive indicator of colonoscopy quality.

Competing interests

None

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