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CONSENSUS STATEMENT

World Endoscopy Organization Consensus Statements on Post-Colonoscopy and Post-Imaging Colorectal Cancer

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BACKGROUND & AIMS: Colonoscopy examination does not always detect colorectal cancer (CRC)— some patients develop CRC after negative findings from an examination. When this occurs before the next recommended examination, it is called interval cancer. From a colonoscopy quality assurance perspective, that term is too restrictive, so the term *post-colonoscopy colorectal cancer* (PCCRC) was created in 2010. However, PCCRC definitions and methods for calculating rates vary among studies, making it impossible to compare results. We aimed to standardize the terminology, identification, analysis, and reporting of PCCRCs and CRCs detected after other whole-colon imaging evaluations (post-imaging colorectal cancers [PICRCs]). **METHODS:** A 20-member international team of gastroenterologists, pathologists, and epidemiologists; a radiologist; and a non-medical professional met to formulate a series of recommendations, standardize definitions and categories (to align with interval cancer terminology), develop an algorithm to determine most-plausible etiologies, and develop standardized methodology to calculate rates of PCCRC and PICRC. The team followed the Appraisal of Guidelines for Research and Evaluation II tool. A literature review provided 401 articles to support proposed statements; evidence was rated using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system. The statements were voted on anonymously by team members, using a modified Delphi approach. **RESULTS:** The team produced 21 statements that provide comprehensive guidance on PCCRCs and PICRCs. The statements present standardized definitions and terms, as well as methods for qualitative review, determination of etiology, calculation of PCCRC rates, and non-colonoscopic imaging of the colon. **CONCLUSIONS:** A 20-member international team has provided standardized methods for analysis of etiologies of PCCRCs and PICRCs and defines its use as a quality indicator. The team provides recommendations for clinicians, organizations, researchers, policy makers, and patients.

Keywords: Quality Measures; AGREE II; Colonoscopy; CT Colonography.

Although colonoscopy is pivotal for the diagnosis and prevention of colorectal cancer (CRC), cancers can be diagnosed months or years after a colonoscopy that is negative for CRC or CRC precursor lesions.

To prevent CRC, a colonoscopist must both detect the premalignant polyps and resect them completely.[1,2] Post-colonoscopy CRCs (PCCRCs), that is, cancers diagnosed after a colonoscopy in which no cancer was found, can arise from missed cancers, and missed or incompletely resected benign lesions.[3–11] The proportion of PCCRCs detected shortly after the exam that arise from rapidly progressing

*Authors share co-first authorship.

Abbreviations used in this paper: AA, advanced adenoma; CRC, colorectal cancer; CTC, computed tomographic colonography; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MSI, microsatellite instability; PCCRC, post-colonoscopy colorectal cancer; PICRC, post-imaging colorectal cancer.

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AGA SECTION

precancerous polyps (new cancer or accelerated biology-related cancer), remains to be determined, but is certainly low.[12] Reasons for missed lesions include inadequate bowel preparation and colonoscopist-dependent factors, such as incomplete colonoscopy, short cecal withdrawal time, and suboptimal inspection technique.[6,13,14] Adenoma miss rates and incomplete polypectomy rates vary between colonoscopists,[15–17] and patients of colonoscopists with low adenoma detection rates have higher interval cancer rates.[14,18]

These findings indicate opportunities for improved colonoscopy performance, for using cancer appearing after a negative colonoscopy as an important benchmark for quality, and for standardizing methodologies to allow more direct comparisons between services.[19]

Aim

The literature on PCCRC diagnosed after a colonoscopy in which no cancer was found lacks agreement on terminology, methodology, or analysis of causation. We recently published guidance on the screening term *interval cancer*[7] (which may or may not relate to colonoscopy); however, these 2 terms are not synonymous, as described later, and no standardized performance measure guidelines exist. To address these concerns, the World Endoscopy Organization convened a working group to use an evidence-based consensus process to make recommendations for future investigators, policy makers, clinical services, and patients.

The aims of the PCCRC project were:

1. To standardize terminology and definitions relating to PCCRC
2. To describe the relationship between PCCRC terminology and interval cancer terminology
3. To standardize the categorization of the potential explanations for PCCRC occurrence
4. To create colonoscopy, histology, and radiology minimum data sets to facilitate PCCRC analysis
5. To develop a standardized definition for a PCCRC rate performance measure and a standardized methodology for its calculation, thus allowing benchmarking and comparison between services
6. To recommend appropriate action for services in the monitoring and review of PCCRC cases and PCCRC rates
7. To consider whether the PCCRC concept can be extended to radiological colorectal imaging; and
8. To provide a research manuscript checklist for authors and peer reviewers of PCCRC papers.

Methodology

Our methodology was based on AGREE II (Appraisal of Guidelines for Research and Evaluation) tool.[20] A multidisciplinary team of international experts was selected, including gastroenterologists, pathologists, epidemiologists, a radiologist and a patient representative, to ensure wide range of expertise and broad representation to cover all aspects of our topic.

The approach taken was to:

1. Determine the purpose of having a performance measure of PCCRC to align recommendations with purpose and the rationale for such
2. Develop a series of key questions relating to PCCRC
3. Conduct a systematic literature search of these questions; and
4. Formulate a set of recommendations using a modified Delphi consensus approach.

The Core (initial) group consisted of 14 members (13 voting and 1 non-voting). Members were then allocated to 2 working groups on the etiology of PCCRCs and performance of PCCRC rates in colonoscopy and radiology practice. Key questions were compiled by the project writing group.

Each working group addressed the following key questions:

1. Etiology working group (7 members, 1 of whom participated in both groups):
   a. Which terminology should be used to describe etiology categories?
   b. What are the risk factors and possible explanations of PCCRC?
   c. How should we ascribe possible explanations?
   d. What should be the minimum colonoscopy, histology, and radiology data set to examine PCCRC?
   e. What molecular tests should be performed to examine PCCRC?
   f. How to prevent PCCRC in high-risk groups?
2. Performance working group (8 members, one of whom participated in both groups):
   a. How should PCCRCs be calculated and reported?
   b. How should PCCRC rates be monitored?
   c. How should PCCRC papers be peer-reviewed?
   d. Radiology—Can we, and how do we extend the methodology to post-imaging CRC?

A comprehensive literature search was performed in PubMed and Cochrane databases, for articles published in English language from 2006 until present (see Supplementary Material for details), which ultimately yielded 402 articles providing background and supporting the statements. We limited our search to articles from 2006 and later, aiming for our database to reflect current practice. All members were asked to and added other key references during the consensus process.

Each working group provided initial draft statements, along with supporting text and suggested references, related to their respective sub-topic; each member voted anonymously, via electronic correspondence, on the resulting 33 statements,