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Misclassified and non-detected cancers by colon capsule endoscopy in screening participants: a case series from the CareForColon2015 trial

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Abstract

Background Colon capsule endoscopy (CCE) has emerged as a minimally-invasive alternative to colonoscopy and has in several meta-analyses shown non-inferiority in detection rates of pathology. However, CCE is a reader-dependent technique and pathology can be missed, even though images of the lesions are captured. Furthermore, misclassification of pathology can lead to erroneous conclusions, and possible delays in correct diagnosis and patient management.

Methods We present a series of cancer cases from the Danish trial CareForColon2015. All participants were recruited from the screening program with a positive fecal immunochemical test. The cancers described in this series were detected at subsequent colonoscopy and patients were treated according to the findings.

Results We identified 4 cases of misclassified/misrepresented cancers (reported as non-neoplastic findings, such as inflammation or as a lesion significantly smaller than the actual size, as a result of suboptimal image reporting), and 1 case of a non-detected cancer (not reported by the reader, but captured in images).

Conclusions These cases prompt a discussion of the need for a unified terminology, reader training and implementation of artificial intelligence in the CCE reading process. This is necessary to improve the quality of CCE reporting and minimize the risk of missed pathology and misclassification of findings.

Keywords Colon capsule endoscopy, colorectal cancer, misclassification, gastrointestinal imaging, endoscopy

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Introduction

Although colonoscopy remains the reference standard for colonic investigations, colon capsule endoscopy (CCE) has emerged as a minimally-invasive alternative with non-inferior detection capability for colorectal neoplasia [1-3]. Reports from France, the United Kingdom and Denmark have presented real-life experience with CCE [4-8]. In the Danish population, colorectal cancer (CRC) was detected in 3.5-4.0% of all screening participants who underwent colonoscopy or computed tomography (CT) colonography in 2020-2022 [9,10], when the Danish CareForColon2015 (CFC2015) trial, was enrolling participants. In this trial, CCE was offered as an alternative to colonoscopy in the intervention arm, giving the participants a choice between the 2 investigations in case of a positive fecal immunochemical test (FIT). Results from this trial have recently been published, showing cancer rates similar to those reported in the Danish Colorectal Cancer Screening

program [4]. In the French cohort, adenomas with high-grade dysplasia or CRC were detected in 32 (4.6%) patients who underwent colonoscopy or therapeutic surgery following CCE. Of these 32 patients, 6 (18.8%) had not been diagnosed by CCE, mainly because of technical issues [5]. In a case report from the Scottish cohort, a cancer was reported as missed by CCE, even after a second review of the investigation [11]. In the English study 1 patient presented with a cancer 18 months after having an incomplete colonoscopy followed by CCE. No significant pathology was detected in either investigation, despite thorough reevaluation of the CCE, and the cancer was therefore considered a post-colonoscopy/CCE cancer [8].

CCE remains a reader-dependent technique and pathology can be missed by the reader, even though images of the lesion are captured. This, alongside misclassification of pathology by the reader, can lead to erroneous conclusions and possible delays in correct diagnosis and patient management. We present a series of cases where errors in CCE reporting in the CFC2015 cohort led to CRC near misses.

Patients and methods

This case series was drafted according to the CARE guidelines [12]. The Regional Health Research Ethics Committee (Ref. S-20190100) and the Danish data protection agency (Ref. 19/29858) approved the CFC2015 trial that supplied data for this study. All participants provided oral and written consent.

All participants were referred for colonic investigation as part of the Danish Colorectal Cancer Screening program from August 2020 to December 2022. They were invited to participate through randomization and enrolled in CFC2015 if presenting with a positive FIT (≥100 ng Hb/mL buffer). Participants were between the ages of 50 and 74 years.

An external contractor specializing in capsule endoscopy handled capsule delivery, CCE reading and reporting. Reporting was carried out by a team of readers, but no detailed information (including experience level, reading speed and the degree of supervision) about this group was available to the researchers. The initial reports were checked and approved by physicians with extensive experience in endoscopy who were employed by the external contractor.

As per the CFC2015 study protocol [13], each of the following findings triggered a follow-up colonoscopy:

- Incomplete capsule transit or technical inadequacy
- Inadequate bowel cleansing in 1 or more colonic segments (defined as *poor* on the Leighton-Rex scale [14])
- Detection of at least 1 polyp >9 mm in size, detection of ≥3 polyps or a suspected cancer regardless of size

The 5 cases presented were identified through systematic examination of all CFC2015 participants with a histopathology-confirmed CRC diagnosis after CCE and subsequent colonoscopy. No artificial intelligence tools were applied to the CCE videos in general, or to the 5 cases in this series. Cancers described in this series as misclassified were cases where the lesion was reported as non-neoplastic or having a low risk profile. As all participants were considered to be asymptomatic, based on their referral through the screening program, findings such as inflammation could be considered irrelevant and would not represent an indication for further examination. The cancer described as non-detected was captured in capsule images but not reported by the reader.

Results

In CFC2015 2031 participants underwent CCE. In 70 participants, cancer was detected in the subsequent colonoscopy; of these participants 2 showed 2 separate cancers, resulting in 72 malignant lesions. Localization of the cancers confirmed by CT-scans and surgery showed 9 (12.5%) in the right colon, 6 (8.3%) in the transverse, 25 (34.7%) in the left colon, 31 (43.1%) in the rectum and 1 (1.4%) in the anal canal, matching the distribution seen in the presented cases, with 1 cancer in the right colon, 2 in the left colon and 2 in the rectum. Forty-nine of the cancers could be matched to lesions detected by the capsule, but only 18 were reported in CCE as suspected of malignancy. In 6 cases neither CCE nor colonoscopy characterized the lesion as malignant, but cancer was found during histopathological examination. Cancers that were not matched to findings in the CCEs could be explained by inadequate bowel preparation (n=6), incomplete colonic transit (n=3), a combination of inadequate bowel preparation and incomplete transit (n=3), cases with multiple similar polyps on CCE, making it impossible to confidently match the polyp-cancer found at colonoscopy to a specific lesion detected on CCE (n=6), misclassification (n=4) or reader error (n=1).

Information on age, FIT and technical aspects of the CCE investigation can be found in Table 1.

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Misclassification as inflammation

Case 1: The CCE report showed 4 sessile polyps in the colon, ranging in size from 4-9 mm. Furthermore, "*a short sequenced retracted sigma-lesion with swollen mucosa and red spots*" was reported. A single CCE frame (Fig. 1A) accompanied this description, and no designation of the finding as "suspect for malignancy" was mentioned. The patient was referred for colonoscopy because polyps were detected, and a semi-circumferential obstructing malignant-looking lesion was found in the sigmoid colon. Histopathology showed mucinous low-differentiated adenocarcinoma. The patient was scheduled for laparoscopic resection, but peritoneal metastasis was found, and the surgery was concluded without resection. In a review of the CCE investigation a 4-min sequence showed the lesion, which was seen with a central depression, a typical sign of malignancy.

Case 2: The main findings reported in CCE were 7 polyps ranging in size from 6-16 mm. Furthermore, "*inflammation in the rectum with erythematous, fibrin-covered mucosa*" was reported, accompanied by a single CCE frame (Fig. 1B). The patient was referred for colonoscopy based on the number of polyps detected, and 7 small polyps were removed. In addition, a semi-circumferential tumor was found in the rectum. Histopathology after resection of the rectum showed a 57-mm adenocarcinoma. When the CCE investigation was reviewed, the finding described as inflammation was clearly a protruding lesion with a central depression.

Case 3: The CCE showed 3 polyps ranging in size from 4-23 mm. Furthermore, bleeding and inflammation in the rectum was described. The patient was referred for colonoscopy because of incomplete capsule transit and the number and size of detected polyps. On colonoscopy, an obstructing tumor was found in the descending colon. Histopathology showed an adenocarcinoma. In view of the disseminated disease, palliative chemotherapy was initiated. When the CCE investigation was reviewed, what was described as inflammation carried the characteristics of an obstructing cancer, and the location was not in the rectum, as reported by CCE, but in the descending colon (Fig. 1C).

Misrepresentation

Case 4: The CCE investigation showed 5 polyps ranging in size from 4-20 mm. The patient was referred for colonoscopy given the number and size of polyps. A 25-mm polyp suspected of malignancy was detected in the rectum during colonoscopy. Pathology after resection of the rectum showed a 20-mm adenocarcinoma. When the CCE investigation was reviewed, the cancerous lesion was captured in the report as a 12-mm polyp. However, the image included in the report presented only the border of the lesion, and therefore gave an inaccurate measurement and overall impression of its character (Fig. 2A). When the capsule progressed, the cancer was clearly visible and was shown to be larger than reported

Table 1 Patient and CCE procedural information

Case no	Age	FIT concentration ng Hb/mL buffer	CCE procedural factors			
			Transit	Colon transit time (h: min)	Technical quality	Bowel cleansing
1	70	791	Complete	0:37	Good	Adequate
2	64	>1000	Complete	0:30	Good	Adequate
3	55	>1000	Incomplete	13:58	Good	Adequate
4	60	689	Complete	1:47	Good	Adequate
5	63	429	Complete	3:54	Good	Adequate

FIT, fecal immunochemical test; CCE, colon capsule endoscopy

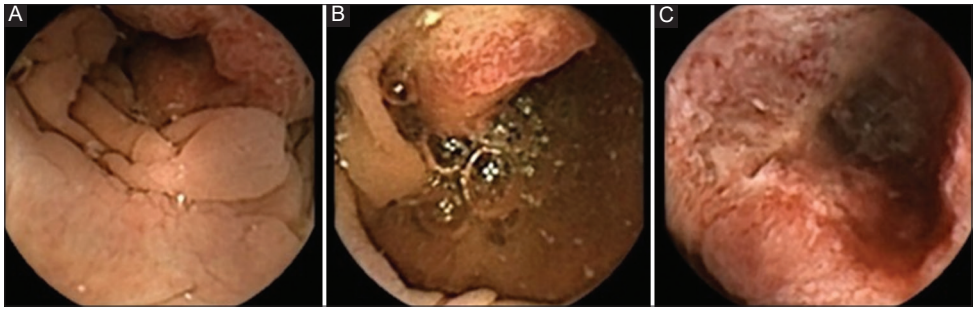

Figure 1 Colon capsule endoscopy images of misclassified cancers in (A) case 1, (B) case 2, (C) case 3

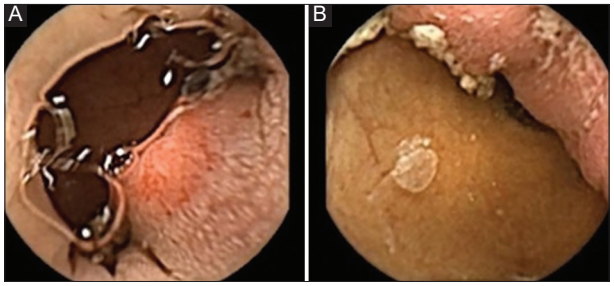

Figure 2 Case 4. Colon capsule endoscopy (CCE) images. (A) Image from the CCE report, lesion described as 12 mm polyp. (B) Image of the same lesion shortly after

(Fig. 2B). Measurement of the lesion size in a representative image was 25 mm.

Non-detected

Case 5: The CCE investigation showed an 11mm polyp and a 7mm polyp. The patient was referred for colonoscopy because a polyp >9 mm was detected. A semi-circumferential malignancy suspect tumor in the right colon was found in colonoscopy. Histopathology showed an adenocarcinoma. Due to several metastases in the liver, chemotherapy was initiated. When reviewing the CCE investigation, the capsule visualized the malignant tumor, although not reported (Fig. 3).

Discussion

In the CFC2015 trial, 72 cancers were detected. In this case series, we demonstrate various reporting errors in CCE that could have led to missed pathology of a serious character. Only in 1 of the 5 cases was the lesion suspected of malignancy missed during CCE, while the remaining 4 cases are examples of misclassification of findings. Misclassification can be considered less severe, but it can be detrimental to patient management and safety. Clinicians may interpret the misclassified findings as benign, hence not warranting urgent or even any further investigation. Inflammation is a good example of a phrase misused in manual reporting to describe everything from light erythema to large malignant tumors, as seen in cases 1-3.

We acknowledge the fact that having the conclusions from colonoscopy and histopathology makes reviewing the CCE investigations easier. In hindsight we can identify reader error, and insist that those errors should not have occurred. We do, however, believe that the cases we present are clear examples of areas where improvements are necessary.

Non-detection represents a perceptual error, where the reader does not identify images with significant lesions, whereas misclassification represents a cognitive error, where the interpretation of the perceived input is flawed. This leaves us with 2 overall issues to consider. The risk of readers making perceptual errors increases with the number of capsules read. In a study on fatigue in small-bowel capsule reading, researchers found that the accuracy declined after the first capsule report for experienced readers [15]. In a practical guide on CCE reporting, readers are encouraged to take breaks to improve their attention and accuracy when reporting on multiple investigations [16]. Furthermore, CCE experts recommend a reading speed of 8-15 frames per sec to maintain optimal pathology detection. A study on the false negative rate for polyp detection in CCE found a polyp miss-rate of 20.6% as a result of reader error, but only 6.2% due to technical errors [17]. This illustrates how useful a second reading of CCE investigations can be.

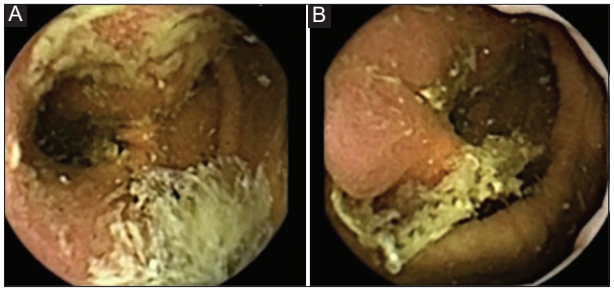

Figure 3 Case 5: Colon capsule endoscopy images of a malignant tumor in the right colon

When turning to the cognitive errors, several focus areas should be addressed to improve reporting and minimize the risk of misclassification. One area of interest is a widely accepted consensus on nomenclature in CCE reporting. In small-bowel capsule endoscopy, this task has been prioritized with Delphi consensus statements on atrophic, vascular, ulcerative and inflammatory lesions [18-20]. The terminology used in colonoscopy should, with minor modifications, be applicable in CCE reporting. CCE reports will be easier for clinicians to interpret and use in patient management if the terminology correlates as far as possible with what is widely used in colonoscopy. A meta-analysis found a suboptimal inter- and intra-observer agreement in capsule endoscopy [21]. The authors suggested the implementation of a unified terminology to improve agreement, which is supported by a recent expert panel publication [22].

Training of CCE readers focusing on rare lesions, and those suspected of malignancy, is another area that should be addressed. Not all CCE readers have extensive endoscopy experience to support their reporting on findings in CCE. Video sequences and images of rare cases should be presented to remedy this. In CFC2015 the reporting was outsourced to an external contractor. Therefore, the research group could not ensure that the learning potential in CCE recordings of rare findings was utilized.

The use of artificial intelligence support is often suggested as a part of the solution to reader error. By applying tailored algorithms for pathology detection and characterization in CCE, the risk of missing and misclassifying pathology, visualized by the capsule, can be reduced. In the large European project AICE a set of 8 artificial intelligence algorithms have been created for CCE reporting [23]. Among these are algorithms for polyp/cancer detection, size estimation and characterization, providing a detailed and objective description of the colorectal pathology found [24].

We believe that CCE is an important addition to the endoscopic field and a valuable supplement to the established colonoscopy pathways. However, continued vigilance and quality assurance regarding cancer detection, classification and miss rates are necessary.

In conclusion, these cases prompt a discussion of the need for a unified terminology, reader training and implementation of artificial intelligence in the CCE reading process. This is necessary to improve the quality of CCE reporting and minimize the risk of missed pathology and misclassification of findings.

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Summary Box

What is already known:

- Colon capsule endoscopy (CCE) has a non-inferior detection capability for colorectal neoplasia compared to conventional colonoscopy
- Few missed cancers have been reported in previous trials investigating the use of CCE
- Reader error in CCE contributes to polyp miss rates to a higher degree than technical errors

What the new findings are:

- This study confirms the low rate of missed cancers in CCE due to non-detection caused by reader error
- Misclassification of cancers is a considerable problem that can delay proper diagnosis and treatment
- A focus on unified terminology, reader training and the implementation of artificial intelligence in the CCE reading process is needed for future improvement, aiming to reduce the rate of missed and misclassified cancers in CCE

References

1. Vuik FER, Nieuwenburg SAV, Moen S, et al. Colon capsule endoscopy in colorectal cancer screening: a systematic review. *Endoscopy* 2021;**53**:815-824.
2. Möllers T, Schwab M, Gildein L, et al. Second-generation colon capsule endoscopy for detection of colorectal polyps: Systematic review and meta-analysis of clinical trials. *Endosc Int Open* 2021;**9**:E562-E571.
3. Sulbaran M, Bustamante-Lopez L, Bernardo W, et al. Systematic review and meta-analysis of colon capsule endoscopy accuracy for colorectal cancer screening. An alternative during the Covid-19 pandemic? *J Med Screen* 2022;**29**:148-155.
4. Baatrup G, Bjørsum-Meyer T, Kaalby L, et al. Choice of colon capsule or colonoscopy versus default colonoscopy in FIT positive patients in the Danish screening programme: a parallel group randomised controlled trial. *Gut* 2025;**74**:1616-1623.
5. Benech N, Vinet O, Gaudin JL, et al; ONECC Study Group. Colon capsule endoscopy in clinical practice: lessons from a national 5-year observational prospective cohort. *Endosc Int Open* 2021;**9**:E1542-E1548.
6. MacLeod C, Hudson J, Brogan M, et al. ScotCap - a large observational cohort study. *Colorectal Dis* 2022;**24**:411-421.
7. MacLeod C, Rajapaksha N, Brown C, Hudson J, Asif Z, Watson AJM. The ScotCap registry: an evaluation of 1000 colon capsule endoscopy procedures carried out in Scotland. *Colorectal Dis* 2025;**27**:e17271.
8. Turvill J, Haritakis M, Pygall S, et al. Multicentre study of 10,369 symptomatic patients comparing the diagnostic accuracy of colon capsule endoscopy, colonoscopy and CT colonography. *Aliment Pharmacol Ther* 2025;**61**:1532-1544.
9. Regionernes Kliniske Kvalitetsudviklingsprogram. Dansk Tarmscreeningsdatabase - Årsrapport for 2022. 2023. Available from: https://www.sundk.dk/media/cd4o5rte/3d004cb1532643f1b6862675bac4973e.pdf [Accessed 2 July 2026].
10. Regionernes Kliniske Kvalitetsudviklingsprogram. Dansk Tarmscreeningsdatabase - Årsrapport for 2023. 2024. Available from: https://www.sundk.dk/media/fgrpkxms/dts-aarsrapport-2023.pdf [Accessed 26 June 2026].
11. MacLeod C, Oliphant R, Docherty JG, Watson AJM. A colorectal cancer missed by colon capsule endoscopy: a case report. *BMC Gastroenterol* 2022;**22**:258.
12. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; CARE Group. The CARE guidelines: consensus-based clinical case report guideline development. *J Clin Epidemiol* 2014;**67**:46-51.
13. Kaalby L, Deding U, Kobaek-Larsen M, et al. Colon capsule endoscopy in colorectal cancer screening: a randomised controlled trial. *BMJ Open Gastroenterol* 2020;**7**:e000411.
14. Leighton JA, Rex DK. A grading scale to evaluate colon cleansing for the PillCam COLON capsule: a reliability study. *Endoscopy* 2011;**43**:123-127.
15. Beg S, Card T, Sidhu R, Wronska E, Ragunath K; UK capsule endoscopy users' group. The impact of reader fatigue on the accuracy of capsule endoscopy interpretation. *Dig Liver Dis* 2021;**53**:1028-1033.
16. Koulaouzidis A, Dabos K, Philipper M, Toth E, Keuchel M. How should we do colon capsule endoscopy reading: a practical guide. *Ther Adv Gastrointest Endosc* 2021;**14**:26317745211001983.
17. Semenov S, Costigan C, Ismail MS, McNamara D. Low colon capsule endoscopy (CCE) false negative rate for polyps excluding reader error. *Diagnostics (Basel)* 2022;**13**:56.
18. Elli L, Marinoni B, Sidhu R, et al. Nomenclature and definition of atrophic lesions in small bowel capsule endoscopy: a Delphi consensus statement of the International CApsule endoscopy REsearch (I-CARE) Group. *Diagnostics (Basel)*

2022;**12**:1704.
19. Leenhardt R, Buisson A, Bourreille A, et al. Nomenclature and semantic descriptions of ulcerative and inflammatory lesions seen in Crohn's disease in small bowel capsule endoscopy: an international Delphi consensus statement. *United European Gastroenterol J* 2020;**8**:99-107.
20. Leenhardt R, Li C, Koulaouzidis A, et al. Nomenclature and semantic description of vascular lesions in small bowel capsule endoscopy: an international Delphi consensus statement. *Endosc Int Open* 2019;**7**:E372-E379.
21. Cortegoso Valdivia P, Deding U, Bjørsum-Meyer T, et al. Inter/intra-observer agreement in video-capsule endoscopy: are we getting it all wrong? A systematic review and meta-analysis. *Diagnostics (Basel)* 2022;**12**:2400.
22. Lei II, Koulaouzidis A, Schelde-Olesen B, et al. Unifying terminology, reporting, and bowel preparation standards in colon capsule endoscopy: Nyborg Consensus. *Endosc Int Open* 2025;**13**:a24955427.
23. AICE. AICE - Simplifying the way we detect colon cancer with the AICE pathway. 2023. Available from: https://aiceproject.eu/ [Accessed 2 July 2026].
24. Nadimi ES, Braun JM, Schelde-Olesen B, et al. Towards full integration of explainable artificial intelligence in colon capsule endoscopy's pathway. *Sci Rep* 2025;**15**:5960.