Non-neoplastic findings in colon capsule endoscopy: Additional yield

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ABSTRACT

Background and study aims Despite the common occurrence of non-neoplastic findings (NNFs) in individuals with a positive fecal immunochemical test (FIT), few studies have reported on these findings. The aim of this cross-sectional study was to determine the prevalence of colonic NNFs in three cohorts of Danish clinical trial participants who underwent colon capsule endoscopy (CCE).

Patients and methods Retrospectively collecting NNFs from CCE reports of three Danish trials, we classified them into five categories: diverticula, vascular abnormalities, inflammation, erosions/ulcerations, and others. The statistical analysis included 516 participants from three trials, with a mean age ranging from 59.2 to 63.9 years. The participants in the three trials were FIT-positive screening or symptomatic individuals.

Results NNFs were reported in more than half of the CCE procedures (50.6% to 77.9%), with colonic diverticula being the most common NNF appearing in 40.9% to 66.9% of the CCE reports. Vascular abnormalities and erosions/ulcerations were also common depending on the specific trial.

Conclusions NNFs are common and may be an indicator of more widespread disease. Furthermore, NNFs may develop into clinically significant conditions despite their benign appearance. This paper expands on the limited literature about prevalence of NNFs and underscores the additional value of CCE video recordings beyond detecting polyps.

Introduction

Colon capsule endoscopy (CCE) is an alternative diagnostic modality for detecting colorectal adenomas and cancers. The first generation of PillCam COLON showed suboptimal sensitivity in detecting colorectal polyps [1]. To address this issue, a second-generation PillCam COLON was released in 2012. The United Kingdom has recently evaluated CCE for application in routine clinical practice and the procedure has been adopted by the local health boards [2, 3]. While CCE is primarily used to detect colorectal neoplasia, other findings are also recorded during the procedure. These non-neoplastic findings (NNFs), such as non-specific inflammation, angiodysplasia, and diverticula, are often seen during CCE investigations. Such findings are also common during optical colonoscopy (OC). Although NNFs may have limited clinical significance compared with neoplastic findings, they represent a diverse group of conditions that may explain gastrointestinal symptoms. Furthermore, NNFs may result in occult bleeding that potentially leads to a false-positive fecal immunochemical (FIT) test.

Vuik et al. reported that colonic abnormalities during CCE appear to be very common in a mostly asymptomatic Western population, with most of the findings lacking clinical relevance and requiring no treatment or observation [3]. Diverticula were reported as the most common colonic NNF, with a prevalence of 71.4%. Similarly, a significant proportion of English Bowel Cancer Screening Programme participants with a positive FIT had at least one NNF in the colon or rectum. However, this population was investigated by OC [5]. Medical or surgical treatment of incidental NNFs in asymptomatic individuals is usually not advocated, but the lesions have the potential to develop into complicated conditions. However, the apparent lack of clinical significance of incidental NNFs has led to a lesser interest in thorough research of these seemingly benign lesions. Evidently unrelated conditions may influence the prevalence of NNFs, which is why these lesions may be of great interest despite their current lack of clinical significance.

Few studies about colorectal NNFs are available in general, and most available material is based on OC results, where NNFs often are reported as secondary findings. Furthermore, the NNF detection rate for CCE may differ from OC because CCE investigations produce images of a non-distended colon. Little is known about the prevalence of NNFs, and even less about NNFs identified by CCE. Currently, diverticula are the best studied NNF, but it is far from the only type of NNF, despite diverticula being the most prevalent. Moreover, most contemporary research reporting the prevalence of NNFs usually only pertains to a few types of NNFs and does not provide a complete overview. Therefore, this cross-sectional paper aimed to investigate prevalence of NNFs in CCE by reviewing CCE reports about 524 patients from a series of three Danish trials, capturing all the NNFs reported [6, 7, 8].

Patients and methods

Setting

This retrospective, cross-sectional, descriptive study used all CCE reports from three Danish trials conducted at Odense University Hospital (OUH), Denmark, from 2014 to 2018 [6, 7, 8]. The CCE reports contained information regarding neoplastic findings, NNFs, procedure dates, Leighton-Rex bowel preparation score, investigation completeness, colon transit time (CTT), and patient date of birth and sex. All reported polyps were extracted and sorted into two groups depending on polyp largest diameter: < 6 mm and ≥ 6 mm.

The original CCE reports were accessible through the local GAIA database and thoroughly scrutinized for relevant information. All relevant data were extracted regardless of the technical quality of CCE video evaluation. All NNFs to the end of the investigations were extracted in reports with incomplete transit or technical failure. To ensure all data were collected and documented correctly after data extraction, the data were validated by retroactively cross-checking the entered data with the respective CCE report. All NNFs in the CCE reports were classified into five categories:

- Diverticula
- Vascular abnormalities
- Inflammation (e. g., erythema, edema)
- Erosions/ulcerations
- Other (e. g. bleeding without an obvious source, hemorrhoids)

The manuscript was prepared in accordance with the STROBE initiative [9]. Throughout this paper, “trials” will be used when referring to the three included Danish trials, whereas “studies” will be used when referring to any external research. The study participants gave informed and written consent to participate in the individual prospective Danish trial following local legislation of the Danish National Center of Ethics.

Participants

This study included all participants from the three Danish trials and their respective CCE reports, irrespective of their demographic or clinical circumstances. CCE video reading and reports about all three trials were made by CCE evaluators of an external contractor (CorporateHealth International GmbH, Hamburg, Germany). The three trials differed in inclusion criteria, indication, and some exclusion criteria. Kobaek-Larsen et al. (Trial 1) included FIT-positive screening participants enrolled in the first round of the Danish National Colorectal Screening Programme in 2014, who were aged 50 to 74 years [6]. All participants of the trial underwent CCE one day before the OC. Those who exhibited symptoms of bowel obstruction were excluded from the trial. Deding et al. (Trial 2) included all adult patients from May 2016 to December 2018 who had an incomplete OC and were scheduled for a computed tomography colonography [7]. Patients in this trial were excluded if they had a history of surgically constructed stoma, diabetes, or symptoms suggestive of bowel obstruction. Kroijer et al. (Trial 3) included patients from February 2017 to November 2017, who were aged 18 to 70 years and eligible for post-OC follow-up due to neoplastic findings or family history of colorectal cancer (CRC) [8]. Exclusion criteria for this trial included pregnancy, breastfeeding, and allergy to active substances administered. In all three trials, exclusion criteria were previous bowel surgery (except appendectomy), renal insufficiency/severe kidney disease, cardiac pacemaker, and inflammatory bowel disease (IBD).

All three trials used magnesium-oxide and MoviPrep (Norgine Denmark A/S, Valby, Denmark) for pre-procedure bowel preparation, but different booster regimens. Furthermore, in all trials the patients were prescribed bisacodyl. Kobaek-Larsen et al. used Eziclen (Ipsen Pharma, Paris, France) as boosters, while Deding et al. used MoviPrep. Kroijer et al. used three different booster regimens: MoviPrep, Eziclen, and a combination of MoviPrep and Gastrografin. Further details of the three trials and their respective study population characteristics are published elsewhere [6, 7, 8].

Variables

The primary outcome of this paper was the occurrence of NNFs as a binary category (present, non-present). The NNFs were composed of possible types: diverticula (diverticulum, diverticulosis, and diverticulitis), vascular abnormalities (angiodysplasia, venectasia/phlebectasia, and venous lakes), inflammation, erosions/ulcerations, and other (bleeding without an obvious source, hemorrhoids, fissures, enlarged anal papillae). When no NNFs were reported, the category "none" was used. Additional study population characteristics included age (< 50, 50–59, 60–69, and ≥ 70 years), sex (female, male), polyps < 6 mm (present, non-present), polyps ≥ 6 mm (present, non-present), complete transit (no, yes), Leighton-Rex score (poor, fair, ≥ good), and CTT in minutes. This paper had no secondary outcomes.

Statistical analysis

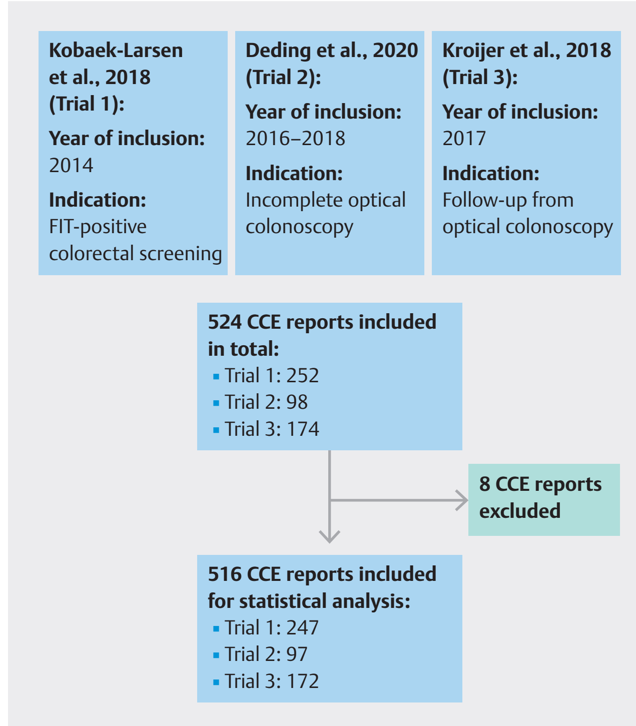
Descriptive statistics were used to describe the main outcome (occurrence of NNFs), stratified by age group and trial. Study population characteristics (age, sex, polyp detection, and CCE performance outcomes) were further described, stratified by trial. The results were stratified by trial due to significant differences in trial indication and study population. All included data were categorical except age, which was numeric but was converted into categorical data. Participant age was calculated as the difference between their date of birth and the respective procedure date. Complete transit and bowel preparation were combined into the "complete CCE investigation" variable, defined as complete transit and ≥ fair on the Leighton-Rex scale. Median and mean CTT were calculated for individuals with a complete CCE transit. Age outliers were checked for all three trials. Statistical analysis of NNFs was stratified by age group. A subgroup analysis for individuals with a complete CCE investigation was performed using the same method as the main analysis. All statistical analyses were performed with StataCorp's Stata/BE ver. 17.0 [10].

Results

Study population

A total of 524 CCE reports were initially included in this study. A single participant from Trial 1 was excluded from the statistical analysis due to data registration errors. Seven additional participants were excluded because of missing CCE reports. Four individuals with obvious wrong procedure dates (e. g., 22–10–1947) in the CCE report were manually reviewed through the Danish eHealth Portal (sundhed.dk), corrected, and included in the statistical analysis. A total of 516 reports were included for statistical analysis. The flow of this paper is presented in ▶ **Fig. 1**.

Across all three trials, the youngest participant was 32.6 years, while the oldest was 83.3 years. The three trial study populations had a comparable mean age of 63.9 years (standard deviation [SD] 7.5), 62.1 (SD 10.5), and 59.2 (SD 9.5) in Trials 1 to 3, respectively. Trials 2 and 3 included participants below 50 years of age, which is reflected in the larger SD and the difference in proportions of the age group, as seen in ▶ **Table 1**. Polyps were common in all three trials, with 71.7%, 67.0%, and 64.0% of the participants having at least one polyp, respectively. All three trials had similar CTTs ranging from 222.3 to 226.7 minutes.



▶ **Fig. 1** Flow diagram summarizing the included Danish trials and the total amount of colon capsule endoscopy (CCE) reports included.

Prevalence of non-neoplastic findings

The proportions of individuals with NNFs are described in ▶ **Table 2**. The most common NNF across the three trials was diverticula. Overall, at least one NNF was observed in 50.6%, 75.3%, and 77.9% of the participants in Trials 1 to 3, respectively. The overall mean number of NNFs was 0.65 (SD 0.73), 1.13 (SD 0.92), and 1.12 (SD 0.80), respectively. An overall total of 159, 105, and 193 NNFs were noted in the three trials, respectively. Reducing the sample to patients with complete CCE investigations increased the NNF proportions in all three trials (**Supplementary Table 1**).

Discussion

This paper demonstrates a varying prevalence for the predefined NNFs across a series of three Danish trials. Diverticula was found to be the most common NNF among the participants, with a prevalence of 40.9%, 62.9%, and 66.9% in the three trials. The second most common NNF was vascular abnormalities and erosions/ulcerations, which were found to be tied in the second trial. In contrast, vascular abnormalities were more common in the first trial and erosions/ulcerations

▶ **Table 1** Descriptive characteristics of three Danish trials conducted from 2014 to 2018 including FIT-positive screening or symptomatic study populations.

		Trial 1	Trial 2	Trial 3
Participants	**N**	**247**	**97**	**172**
Age, years	< 50	0 (0.0)	15 (15.5)	31 (18.0)
	50–59	71 (28.7)	26 (26.8)	45 (26.2)
	60–69	115 (46.6)	28 (28.9)	87 (50.6)
	≥ 70	61 (24.7)	28 (28.9)	9 (5.2)
	Mean	63.9 (7.5)	62.1 (10.5)	59.2 (9.5)
Sex	Female	97 (39.3)	72 (74.2)	82 (47.7)
	Male	150 (60.7)	25 (22.7)	90 (52.3)
Polyp	< 6 mm	97 (39.3)	49 (50.5)	84 (48.8)
	≥ 6 mm	146 (59.1)	41 (42.3)	79 (45.9)
	Any	177 (71.7)	65 (67.0)	110 (64.0)
Complete transit	No	104 (42.1)	31 (32.0)	53 (30.8)
	Yes	143 (57.9)	66 (68.0)	119 (69.2)
Leighton-Rex score	Poor	108 (46.4)	23 (24.5)	64 (37.9)
	Fair	92 (39.5)	37 (39.4)	78 (46.2)
	≥ Good	33 (14.2)	34 (36.2)	27 (16.0)
Colon transit time, minutes	Mean	225.9 (127.8)	222.3 (100.7)	226.7 (138.5)
	Median	217 (15–495)	209 (39–416)	237 (14–541)
Complete CCE	No	162 (65.6)	48 (49.5)	94 (54.7)
	Yes	85 (34.4)	49 (50.5)	78 (45.4)

All patients were investigated with colon capsule endoscopy. Variables are presented as frequencies (% of total), mean (SD), and median (IQR) unless otherwise stated.
CCE, colon capsule endoscopy; FIT, fecal immunochemical test; IQR, interquartile range; SD, standard deviation.

in the third. The average number of NNFs per participant ranged from 0.65 (SD 0.73) to 1.13 (SD 0.92) across all three trials, whereas 50.6% to 77.9% of the participants had at least one NNF.

Almost no studies exist that exclusively observe NNFs by CCE, and it was difficult to find an equal comparison. The most comparable study, which uses CCE to observe abnormal findings in the colon, is the study by Vuik et al. The study observed abnormal findings in 93.3% of the included population. However, the study also defined CRCs and polyps as abnormal findings, although the most dominant finding was diverticula in 71.4% of the patients [3]. Alternatively, studies using OC report a NNF prevalence of 21.6% to 39.8% [5, 11, 12, 13]. However, OC findings are not directly comparable to findings observed by CCE due to performance differences between the modalities (e. g. lumen inflation, angle of view, image resolution). When comparing CCE with OC for detecting NNFs, one study shows that CCE has good overall performance in detecting NNFs [14]. The same study showed suboptimal performance for IBD, although this contradicts the results of two other studies [15, 16].

Diverticula

In comparing the results of this study with similar studies, it is observed that the overall prevalence of diverticula is significantly lower, ranging from 40.9% to 66.9% than the 82.7% and 79.3% reported by another study among female and male participants, respectively, whose mean age was 67.4 years (SD 4.9) [3]. A study conducted on an American population with a mean age of 54 years (SD 7.0) reported a diverticular prevalence of 42%, which is more comparable to the first trial of the series included herein [17]. Last, another study conducted on a Western asymptomatic population older than age 60 years reported a diverticular prevalence of 34.9% [18]. It is important to note that the age of the study population plays a significant role in prevalence of diverticula, making it difficult to compare studies because the incidence of diverticula is associated with increasing age [19]. In contrast, our study found a higher prevalence of diverticula in the trial that had the cohort with the lowest mean age.

▶ **Table 2** Prevalence of non-neoplastic findings (NNFs) in three Danish trials conducted from 2014 to 2018 including either FIT-positive screening or symptomatic study populations.

		Trial 1	Trial 2	Trial 3
Partici-pants	**N**	**247**	**97**	**172**
NNFs	**None**			
	< 50	–	6 (40.0)	8 (25.8)
	50–59	40 (56.3)	5 (19.2)	9 (20.0)
	60–69	57 (49.6)	6 (21.4)	18 (20.7)
	≥ 70	25 (41.0)	7 (25.0)	3 (33.3)
	Overall	122 (49.4)	24 (24.7)	38 (22.1)
	Diverticula			
	< 50	–	6 (40.0)	22 (71.0)
	50–59	24 (33.8)	18 (69.2)	32 (71.1)
	60–69	49 (42.6)	22 (78.6)	56 (64.4)
	≥ 70	28 (45.9)	15 (53.6)	5 (55.6)
	Overall	101 (40.9)	61 (62.9)	115 (66.9)
	Vascular abnormalities			
	< 50	–	3 (20.0)	1 (3.2)
	50–59	6 (8.5)	5 (19.2)	7 (15.6)
	60–69	10 (8.7)	3 (10.7)	15 (17.2)
	≥ 70	13 (21.3)	7 (25.0)	1 (11.1)
	Overall	29 (11.7)	18 (18.6)	24 (14.0)
	Erosions/ulcerations			
	< 50	–	1 (6.7)	7 (22.6)
	50–59	4 (5.6)	10 (38.5)	9 (20.0)
	60–69	3 (2.6)	5 (17.9)	22 (25.3)
	≥ 70	0 (0.0)	2 (7.1)	0 (0.0)
	Overall	7 (2.8)	18 (18.6)	38 (22.1)
	Inflammation			
	< 50	–	0 (0.0)	1 (3.2)
	50–59	1 (1.4)	0 (0.0)	1 (2.2)
	60–69	4 (3.5)	1 (3.6)	4 (4.6)
	≥ 70	0 (0.0)	1 (3.6)	0 (0.0)
	Overall	5 (2.0)	2 (2.0)	6 (3.5)
	Other			
	< 50	–	4 (26.7)	1 (3.2)
	50–59	2 (2.8)	2 (7.7)	3 (6.7)
	60–69	8 (7.0)	2 (7.1)	4 (4.6)
	≥ 70	8 (13.1)	3 (10.7)	2 (22.2)
	Overall	18 (7.3)	11 (11.3)	10 (5.8)
	Total NNFs			
	< 50	–	14	32
	50 – 59	37	35	52
	60 – 69	74	33	101
	≥ 70	49	28	8
	Overall	160	110	193
	Mean NNFs			
	< 50	–	0.93 (0.96)	1.03 (0.84)
	50–59	0.52 (0.65)	1.35 (0.89)	1.16 (0.77)
	60–69	0.64 (0.73)	1.18 (0.98)	1.16 (0.82)
	≥ 70	0.80 (0.81)	1.00 (0.86)	0.89 (0.78)
	Overall	0.65 (0.73)	1.13 (0.92)	1.12 (0.80)
	Any NNFs			
	< 50	–	9 (60.0)	23 (74.2)
	50–59	31 (43.7)	21 (80.8)	36 (80.0)
	60–69	58 (50.4)	22 (78.6)	69 (79.3)
	≥ 70	36 (59.0)	21 (75.0)	6 (66.7)
	Overall	125 (50.6)	73 (75.3)	134 (77.9)

NNFs are stratified by age groups. All patients were investigated with colon capsule endoscopy. Age-stratified variables are presented as frequencies (% of stratum) and mean (SD) of the respective age group. Overall variables are presented as frequencies (% of total) and mean (SD) of the respective age group of the total population (N).
FIT, fecal immunochemical test; NNF, non-neoplastic finding.

Vascular abnormalities

There have been different reports about prevalence of vascular abnormalities in the colon. Two studies that included an asymptomatic population reported prevalence ranging from 0.83% to 7.8%/12.0% for females and males, respectively [3, 20]. Meanwhile, three other studies that included symptomatic patients reported a prevalence ranging from 5% to 26.7% [21, 22, 23]. Our study observed a prevalence of 11.7% to 18.6%. It is important to note that variations in findings across studies could be due to differences in population ages, nomenclature, and definition. For instance, formation of vascular abnormalities in the colon may be linked to increasing age [21]. Also, differences in definitions of vascular abnormalities may affect reported prevalence [24]. For example, Vuik et al. described it as aberrant blood vessels, whereas Boley et al. defined it as mucosal ectasia. In addition, variation in the investigation indication could also account for differences in reported prevalence. For instance, Wilcox et al. included patients with acute lower gastrointestinal bleeding, whereas Boley et al. studied post-CRC resection patients with no bleeding history. Therefore, comparing the current literature investigating vascular abnormalities with the three trials is not ideal.

Inflammation and erosions/ulcerations

A study conducted on a Western asymptomatic population reported that the prevalence of erosions was 17.7% for females and 15.9% for males, whereas inflammation was 0.0% for females and 2.4% for males [3]. Another study reported that prevalence of colonic ulcers was 10% [23]. These findings are similar to results from our study, which found a prevalence of 2.8% to 22.1% for erosions/ulcerations and 2.0% to 3.5% for inflammation. However, there was a discrepancy in prevalence of erosion/ulcerations across the three Danish trials, possibly due to differences in classification or technical difficulties. A review investigating usability of CCE in monitoring IBD concluded that CCE has good potential for observing the extent and severity of erosive and ulcerative colitis [25]. Therefore, the discrepancy due to lack of performance is unlikely but cannot be ruled out. Although re-reading the CCE video footage would have been ideal, it was not feasible because of time constraints and concerns about introducing bias.

Bowel preparation and completion rate

The three Danish trials found that adequate bowel preparation (defined as ≥ fair on the Leighton-Rex scale) was achieved in 53.7%, 75.6%, and 62.2% of participants, respectively. These results are somewhat similar to the 76.8% adequate bowel preparation (defined as ≥ good on the Leighton-Rex scale) from a recent meta-analysis [26]. Although the Leighton-Rex scale was used in the meta-analysis and the three Danish trials, the definition of adequate bowel preparation differed from the usual definition in the three trials. The three trials used relatively old CCE reports, which were often evaluated as simply "adequate bowel preparation" instead of a specific score from the scale. This made it difficult to determine if preparation was adequate based on technical quality or subjective cleanliness rather than an objective scale. Nevertheless, bowel preparation in the three trials was in accordance with guidelines from the European Society of Gastrointestinal Endoscopy, which recommends cleansing with a total of four liters of polyethylene glycol (PEG) solution in combination with boosters based on sodium phosphate [27]. The CCE completion rates (CRs) in the three trials were 34.4%, 50.5% and 45.5%, respectively. This is much lower than the overall CR of 79.8%, as concluded in the meta-analysis [26].

The relatively big proportion of inadequate bowel preparation and lower CCE CR potentially introduces an underreporting of NNFs. Polyp detection rates (PDRs) of 71.7%, 67.0%, and 64.0% in the three Danish trials, respectively, suggest an overestimation of colonic findings when comparing the PDR in OC of 27% to 55%, depending on OC indication and study population [28, 29, 30]. However, a systematic review reported the PDR of CCE as 24% to 75% in an average-risk population [31]. Also, CCE has been reported to have a higher PDR than OC [6]. Therefore, the high PDR of CCE, as observed in the three Danish trials, has previously been reported despite the three trials having relatively low adequate bowel preparation and low CCE CR. This further suggests that the observed prevalence of NNFs could be accurate despite the observed bowel preparation and CCE CR. However, it is worth noting that PDR is not directly comparable to detecting NNFs.

Limitations

The main limitation of this paper is that the data were obtained from various studies with different settings and inclusion criteria, making it difficult to pool the results and limiting generalizability of the findings. The three Danish trials were biased toward screening and symptomatic populations. Furthermore, the comparability with OC is limited to a small subgroup of patients, which limits the reliability of the reported NNF prevalences. This also means that the estimated prevalences are the lower limits. This becomes obvious when comparing the lower number of NNFs observed in Trial 1 compared with Trials 2 and 3. Suspicion of underreporting is further amplified when comparing the results of the three Danish trials with the results of Vuik et al., which observed a very high number of NNFs even compared with OC [17]. Another limitation is that the trained staff evaluating the CCE video recordings may have had different reporting approaches, resulting in observer bias. The primary objective of the CCE recordings was identification of polyps, which introduces additional observer bias and further limits the reliability of the findings. In addition, the observed low CCE CR also limits reliability of the results and an attempt at adjustment for that is shown in **Supplementary Table 1**. Furthermore, there was a risk of misclassification because there was unclear consensus on nomenclature in CCE procedures across the trials. Last, none of the three Danish trials had NNFs as their primary or secondary aim. Covariates such as ethnicity, economic and social status, and education are all potential confounders of this study. However, this information was unavailable and not corrected for or examined in the statistical analysis.

Interpretation

Incidental NNFs may have clinical relevance that is yet to be elucidated. However, no literature investigating clinical administration of incidental NNFs was identified, and potential treatment of NNFs is usually based on expert opinion. For example, 5% of patients with diverticulosis will develop acute diverticulitis, whereas increased prevalence of angiodysplasia has been observed in patients with end-stage kidney disease [32, 33]. In addition, some literature suggests that aortic valve replacement clinically significantly reduces gastrointestinal bleeding from angiodysplasia [34, 35]. True cases of nonspecific colonic ulcerations are rare because solitary erosions and ulcerations usually have a known etiology, frequently use of nonsteroidal anti-inflammatory drugs. However, these ulcerations can be life-threatening if not treated correctly [36, 37]. Last, colonic inflammation with no clinical manifestation is hypothesized to be related to a systemic inflammatory condition, which is considered important in early-stage chronic disease and multimorbidity [38]. Therefore, the diagnosis of NNFs could be an additional yield, even though they usually are determined to be clinically irrelevant. Although of strong interest, a clinical evaluation of the included patients to investigate the need for further OC or other clinical outcomes related to the NNFs was not possible due to practical and legislative constraints.

Conclusions

This paper presents prevalence of NNFs in a series of three Danish trials. Most participants had at least one NNF, with diverticula being the most common. The study's main limitation was the data sourcing, which originated from three unrelated studies with different indications, study populations, and aims. To establish better evidence about the prevalence and incidence of NNFs in the colon, future prospective studies with more systematic study design and systematic nomenclature for evaluating CCE investigations are needed. In addition, further studies are needed elucidating the clinical relevance of incidental NNFs. However, this paper is an important reference about prevalence of NNFs in samples of FIT-positive screening or symptomatic individuals from the Danish population investigated by CCE.

Conflict of Interest

Sebastian Radic Eskemose, Lasse Kaalby Møller, and Ulrik Deding have no conflicts of interest or financial ties to disclose. Anastasios Koulaouzidis has received consultancy fees from Jinshan Science and Technology (Group) Co. Ltd. (Jinshan Group) and Corporate Health International, received honoraria from Jinshan Group and Medtronic, received travel support by Jinshan Group, has issued a patent with AJM Med-i-Caps Ltd., and has equity interest in iCERV Ltd. and AJM Med-i-Caps Ltd. Thomas Bjørsum-Meyer has received consulting fees from Medtronic. The funders had no role in the design of the paper; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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