COLONOSCOPY SURVEILLANCE FOR DYSPLASIA AND COLORECTAL CANCER IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

Claus Aalykke, Michael Dam Jensen, Jan Fallingborg, Tine Jess, Ebbe Langholz, Søren Meisner, Nynne Nyboe Andersen, Lene Buhl Riis, Ole Østergaard Thomsen, Anders Tøttrup

The guideline has been approved by the Society of Gastroenterology and Hepatology August 28, 2014

Correspondence: Claus Aalykke, Department of Medicine, OUH, Svendborg Sygehus, 5700 Svendborg, Denmark

E-mail: claus.aalykke@rsyd.dk

Dan Med J 2015;62(1):C4995

ABBREVIATION AND DEFINITIONS

CD Crohn's disease
CI Confidence interval
CRC Colorectal cancer
DALM Dysplasia-associated lesion or mass
ECCO European Crohn's and Colitis Organisation
EMR Endoscopic mucosal resection
ESD Endoscopic submucosal dissection
Extensive colitis inflammation proximal to the splenic flexure; identical with pancolitis
IBD Inflammatory bowel disease
iFOBT immunochemical fecal occult blood test
Left-sided colitis Inflammation distal to the to the splenic flexure; identical with 'distal' colitis
NICE National Institute for Health and Care Excellence
Proctitis Inflammation distal to the rectosigmoid junction
PSC Primary sclerosing cholangitis
SIR Standardized incidence ratio
UC Ulcerative colitis

INTRODUCTION

The risk of colorectal cancer (CRC) in Danish patients with ulcerative colitis (UC), followed in an outpatient setting, is similar to that of the background population or slightly increased. However, for a subpopulation of patients with UC, the relative and absolute risk of CRC is augmented. For patients with Crohn's disease (CD) the risk of CRC does not appear to be increased.
No randomized controlled clinical trials, evaluating the potential effect of colonoscopy surveillance in patients with inflammatory bowel disease (IBD), have been published and at present, the benefit of surveillance is uncertain.

Is there an increased risk of colorectal cancer in Danish patients with ulcerative colitis?

- Previous studies of various methodologies have suggested that the prevalence of CRC is increased in patients with UC. However, the magnitude of this risk differs between countries and the risk has likely been overestimated in a comprehensive meta-analysis by Eaden and colleagues, that included studies of varying quality ranging from very selected case series to a few population-based cohort studies[1].

- A meta-analysis solely based on population-based cohort studies including studies from Denmark, Sweden and Canada among others, revealed a more than 2-fold increased relative risk (standardized incidence ratio, SIR, 2.4; 95% CI, 2.1-2.7), whereas the risk was nearly 5-fold increased for the subgroup of patients with extensive disease (SIR 4.8; 95% CI, 3.9-5.9)[2]. The absolute risk was still limited (1.1-5.3% after 20 years).

Colorectal cancer in Danish patients

- A large Danish population-based study including data from the National Patient Registry (NPR) and the Danish Cancer Registry during a 30-year follow-up period (1977-2008) revealed no overall increase in risk of CRC in patients with IBD; however, a slightly increased risk was present for in some subgroups of patients[3].

- Accordingly, the overall risk of CRC in the two former Danish studies included in the meta-analysis of population-based studies[2], found no significantly increased risk of CRC (SIR, 1.05; 95% CI, 0.56-1.79[4] and SIR, 1.67; 95% CI, 0.61-3.62)[5]. A study from Northern Jutland revealed a similar low risk estimate (SIR 0.85; 95% CI, 0.48-1.41)[6]. In absolute numbers, the cumulated risk of CRC after a disease duration of 20 years is 1.1 to 2.5%[7].

- In summary, the risk of CRC in Danish patients with UC, is regarded similar or only slightly increased compared to the background population.

Risk factors for colorectal cancer in patients with ulcerative colitis

Factors associated with an increased risk of CRC in patients with UC[8]:

- Young age at disease onset[2;3]
- Extensive disease[2]
- Male sex[2]
- Severe disease activity[9;10]
- Long disease duration[3]
- Familial aggregation of sporadic colorectal cancer[11]
- Primary sclerosing cholangitis (PSC)[3;12]

Is the risk of colorectal cancer increased in Danish patients with Crohn's disease?

- The aforementioned Danish register-based study did not reveal an increased risk of CRC in patients with CD[3].

- Only one patient was diagnosed with CD, PSC and CRC, hence this study was not able to conclude on any potential risk of cancer related to this comorbidity. A Swedish study on CD and PSC found an increased risk of CRC in these patients[13].

Does surveillance with colonoscopy decrease the mortality of colorectal cancer in patients with inflammatory bowel disease?

- No randomized controlled trials have examined the potential effect of surveillance colonoscopy on CRC related mortality in patients with IBD.

- A Cochrane review based on case-control studies concluded that there is no clear evidence that surveillance colonoscopy prolongs survival in patients with extensive colitis[14]. In a subsequent case-control study from a tertiary center in the US, a significant 62% reduction in risk of CRC was found in patients with extensive UC undergoing surveillance colonoscopy[10].

- From the St. Marks Hospital, UK, the hitherto largest evaluation of a surveillance program revealed 30 cases of CRC after 2627 colonoscopies in 600 patients followed for a period of 30 years; 14 of the CRC cases were diagnosed by surveillance colonoscopy[15]. The number of colonoscopies required to diagnose one CRC was 88, and in order to diagnose a resectable cancer this number was 188. These results can be compared with the "Funen-investigation" in which 31.000 healthy individuals aged 45-75 years underwent screening with Hemoccult and subsequent colonoscopy if the test was positive. In this study, the number of colonoscopies required to diagnose one CRC was 8, and 10 in order to diagnose a resectable cancer[16].

- On the other hand, another case-control study suggested a potential effect of colonoscopy surveillance[17]. Among 149 patients with IBD-associated CRC followed from 1990 to 2006, a total of 23 patients had participated in a surveillance program with colonoscopy. The mortality related to CRC was significantly lower in the group of patients undergoing surveillance (5-year survival 100% and 65%, respectively). Unfortunately, no randomization was performed and the criteria for the patient selection were not given, hence results may be due to selection bias.

Which patients with inflammatory bowel disease should undergo surveillance colonoscopy, when, and how often?

Based on Danish data it is recommended to initiate surveillance colonoscopy after a disease duration of 10-13 years, unless the patient has PSC. The recommended time intervals between colonoscopies in the present guideline are in accordance with the recommendations from ECCO[18] (European Crohn's and Colitis Organization) and NICE[19] (National Institute for Health and Care Excellence).

Based on information about the principles and benefit of the surveillance program, the following patients with UC may decide to participate in a colonoscopy surveillance program:

- Patients with extensive disease (inflammation proximal to the splenic flexure). Surveillance colonoscopy should be offered after a disease duration of 10-13 years.

- Patients with early onset (less than 19 years of age) and a minimum of left-sided colitis (inflammation distal to the splenic flexure). Surveillance colonoscopy should be offered after disease duration of 10-13 years.

- Patients with UC and PSC. Surveillance colonoscopy should be offered at diagnosis of PSC.

Based on information about the principles and benefit of the surveillance program, the following patients with *CD* may decide to participate in a colonoscopy surveillance:

- Patients with CD and PSC. Surveillance colonoscopy should be offered at diagnosis of PSC.

The surveillance program includes:

- Colonoscopy every 5th year:
  - Patients with extensive ulcerative colitis
  - Early onset patients (<19 years of age) with a minimum of left-sided colitis.

- Colonoscopy every 3rd year:
  - Patients with post-inflammatory polyps in colon or rectum

- Colonoscopy every year:
  - Patients with both UC and PSC
  - Patients with both CD and PSC

- Colonoscopy every 3-6 months:
    - Patients with UC and strictures in colon or rectum
    - Patients with dysplasia in colon or rectum

How should the surveillance colonoscopy be carried out?

- In patients with UC, the detection rate for dysplasia is significantly higher when a chromoendoscopy with targeted biopsies is performed compared to a conventional colonoscopy with random biopsies[20-23].

- Surveillance colonoscopy should be performed during clinical remission[24]. However, colonoscopy should not be unnecessarily postponed if imminent remission is unlikely. It is recommended that chromoendoscopy is done with high definition colonoscopy

Recommendations for chromoendoscopy

- Optimal bowel preparation is pivotal. A new colonoscopy is recommended in case of incomplete bowel cleansing.
- Consider anti-peristaltic medication.
- The endoscope is advanced to the terminal ileum.
- Photo documentation of:
    - Ileum or caecum/ileocaecal valve
    - All visible lesions prior to biopsy
- During evacuation of the endoscope, secretion and fluid should be aspired.
- Chromoendoscopy is performed with a 0.03% Indigocarmine solution injected through the working channel with a 50 cc syringe. Two 5 cc ampoules with Indigocarmine 8 mg per cc is dissolved in 250 cc water. With this technique, the visibility of discrete lesions in the mucosa are enhanced.
- If chromoendoscopy is not available, white-light endoscopy can be performed.
- Mucosal lesions suspicious of dysplasia are examined with a 0.13% Indigocarmine solution (1 ampoule of 5 cc Indigocarmine 8 mg per cc dissolved in 25 cc water). Prepare the two Indigocarmine solutions prior to the procedure.
- Describe any visible lesions of the mucosa.
- Obtain targeted biopsies of all mucosal lesions.
- Routine biopsies from or removal of pseudopolyps is not recommended.
- The diagnostic value of random biopsies is questionable and is not recommended.

An informative video on how to conduct a chromoendoscopy is available online at:
http://www.gastrojournal.org/article/S0016-5085(13)00509-X/fulltext

How to diagnose dysplasia?

- Dysplasia is classified as low- or high-grade dysplasia, or indefinite for dysplasia[25]. The inter-observer variation associated with diagnosing dysplasia in patients with IBD is significant. It is recommended that the diagnosis of dysplasia is confirmed by another pathologist with expertise in gastrointestinal pathology (second opinion)[26]. Likewise, a second opinion is worth considering in case of a diagnosis of indefinite for dysplasia. The treating physician should act as the coordinator during this process.

- The term DALM (dysplasia-associated lesion or mass) is no longer recommended and should be replaced with a more operational terminology for the endoscopist, focusing on whether or not the lesion is endoscopically resectable (figure 1)[23].

- If the lesion is resectable, it is removed *en bloc* – optimally at a specialised unit mastering endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) at the highest level. It is recommended that the surrounding mucosa is examined by four-quadrant biopsies. The subsequent treatment depends on the pathology of the lesion.

- If the lesion is not endoscopically resectable, it is recommended to take biopsies in order to diagnose dysplasia or cancer. If it is not possible to confirm the suspicion of dysplasia or cancer the patients should be referred to a highly specialised unit.

How is dysplasia treated? (See algorithm, figure 1)

- All patients with dysplasia should be discussed at a multidisciplinary team conference including a gastroenterologist, surgeon, and pathologist. It is recommended to use the 2013-published algorithm (figure 1) for diagnosing and treating superficial colorectal lesions[23].

- High-grade dysplasia: several studies performed with white light colonoscopy have revealed an increased risk of synchronous CRC when plane high-grade dysplasia is present which has led to the recommendation of colectomy in most cases[15;27-29]. After the introduction of chromoendoscopy, EMR and ESD are the recommended procedures in case of a resectable high-grade dysplastic lesion without dysplasia in the surrounding mucosa. The area is marked with ink to facilitate localization of the affected area at subsequent colonoscopy[23].

- Low-grade dysplasia: the evidence regarding plain low-grade dysplasia is uncertain and controversial, however the associated risk of CRC or progression to CRC appear to be smaller than for high-grade dysplasia. If the lesion is resectable and no dysplasia is present in the surrounding mucosa, an EMR or ESD is recommended with subsequent ink marking and a control colonoscopy after 3-6 months.

- If it is not possible to remove an elevated lesion completely or if the dysplasia is detected in the surrounding mucosa (regardless of degree of dysplasia), a colectomy is recommended due to a substantial risk of synchronous CRC[30-34].

- If the resection is considered radical after histological evaluation and dysplasia is not detected in the surrounding mucosa, a surveillance colonoscopy is performed after 3-6 months[35-39]. If no residual lesion is detected at the control colonoscopy, the patient should follow an annual colonoscopy surveillance program. If a residual lesion is found, it is recommended that the patient undergo colectomy. However, if the resectable lesions are small it is worth considering a renewed EMR or ESD.

Indefinite for dysplasia

- Only few studies have dealt with the presence of indefinite for dysplasia and the risk of progression to CRC. One study found a lower progression rate compared with low-grade dysplasia but a higher risk than for no dysplasia[40]. When indefinite for dysplasia is observed, the diagnosis should be consulted with another pathologist with expertise in gastroenterology. If the diagnosis of indefinite for dysplasia is sustained a new endoscopy should be performed within 3-6 months and preceded by intensified treatment.

Special patients groups

Patients with ulcerative colitis, colectomy, and a left residue of the rectum

- After colectomy for UC there is still a risk of cancer in the rectal stump[41-44].
- The risk of cancer in the rectal stump tend to increase with disease duration[41].
- Patients with a rectal stump should be informed about the presumed risk of cancer and that surveillance does not eliminate the risk of cancer[42].
- In patients who do not wish an ileo-anal reservoir, a rectum extirpation should be considered.

Patients with ulcerative colitis and ileo-anal reservoir (pouch)

- Only few cases of cancer in the pouch or anal tract have been described in patients with an ileo-anal reservoir[45;46].
- Pre-operative occurrence of cancer or dysplasia are risk factors for later malignancy in the pouch[47].
- However, the rare occurrence of malignant transformation does not support a routine surveillance program for patients with an ileo-anal reservoir.

National screening for sporadic colorectal cancer in patients with IBD above 50 years of age

- From 1st of March 2014, Danish persons aged 50-74 years are offered screening every second year for CRC with iFOBT (immunochemical fecal occult blood test) and a subsequent colonoscopy in case of a positive test. If no polyps or cancer are detected an eight-year deferred period is commenced, hence the consecutive three screenings are skipped[48].
- IBD patients are invited to participate in the CRC screening program.
- In order to implement the CRC screening program for patients with IBD in an expedient manner and further to lower the risk of undue colonoscopies and increasing health care cost, the current guideline has been presented to the National CRC Screening Committee.

Recommendations for patients with IBD aged 50-74 years regarding participation in the national screening program for colorectal cancer

- Patients with IBD are recommended to take contact to their outpatient clinic and discuss whether to participate in the national CRC screening program.
- IBD patients participating in a colonoscopy surveillance program should not participate in the national CRC screening program. It is the responsibility of the patient to unregister to the national CRC screening program either at www.sundhed.dk or through direct contact to the nearest screening center.
- As IBD patients with active disease often have blood in the stool and thus a positive iFOBT, they should not participate in the CRC screening program.
- Those patients with IBD who have underwent a complete colonoscopy within the last year should not participate in the current screening round. If the iFOBT is positive at the next screening round, the patient is offered a renewed colonoscopy. Thus, the next colonoscopy will be 2-3 years after the last colonoscopy.

Patients with IBD and a positive iFOBT

- There is no current consensus on who should perform the colonoscopy in patients with IBD and a positive iFOBT. The Danish Society of Gastroenterology and Hepatology guideline committee recommends that a gastroenterologist with IBD expertice performs the colonoscopy, either as a chromoendoscopy or a white-light colonoscopy. In contrary, the National CRC Screening Committee recommends a surgeon-performed colonoscopy as for the rest of the population.

Patient information

- Following information, it is up to the patient to decide whether to participate in a colonoscopy surveillance program.
- Thorough information of patients prior to participation is essential as international studies indicate that patients overestimate the risk of CRC and additionally overestimate the effect of surveillance[49;50].

The evidence levels for the above described clinical recommendations are summarised in Table 1.

SUMMARY

The risk of colorectal cancer (CRC) and dysplasia in patients with inflammatory bowel disease (IBD) has been highly debated as risk estimates from different studies vary greatly. The present national Danish guideline on colonoscopy surveillance for dysplasia and colorectal cancer in patients with IBD is based on a thorough review of existing literature with particular focus on recent studies from Denmark revealing a lower risk of CRC than previously assumed.

The overall risk of CRC in the Danish IBD population does not appear to be different from that of the background population; however, in some subgroups of patients the risk is increased. These subgroups of patients, who should be offered colonoscopy surveillance, includes patients with ulcerative colitis having extensive disease and a long disease duration (10-13 years); early age at onset (less than 19 years of age) of ulcerative colitis; and patients with ulcerative colitis as well as Crohn´s disease with a concomitant diagnosis of primary sclerosing cholangitis. A colonoscopy surveillance program is recommended in these subgroups with intervals ranging from every 3-6 months to every 5 years, using chromoendoscopy with targeted biopsies of the lesion and adjacent mucosa, instead of conventional colonoscopy with random biopsies. Preferably, the colonoscopy should be performed during clinical remission. If a lesion is detected the endoscopical resectability together with the pathology of the lesion and the adjacent mucosa determine how the lesion should be treated.

References

(1) Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. *Gut* 2001;48:526-535.
(2) Jess T, Rungoe C, Peyrin-Biroulet L. Risk of colorectal cancer in patients with ulcerative colitis: a meta-analysis of population-based cohort studies. *Clin Gastroenterol Hepatol* 2012;10:639-645.
(3) Jess T, Simonsen J, Jorgensen KT, et al. Decreasing risk of colorectal cancer in patients with inflammatory bowel disease over 30 years. *Gastroenterology* 2012;143:375-381.
(4) Winther KV, Jess T, Langholz E, et al. Long-term risk of cancer in ulcerative colitis: a population-based cohort study from Copenhagen County. *Clin Gastroenterol Hepatol* 2004;2:1088-1095.
(5) Wandall EP, Damkier P, Moller PF, Wilson B, et al. Survival and incidence of colorectal cancer in patients with ulcerative colitis in Funen county diagnosed between 1973 and 1993. *Scand J Gastroenterol* 2000;35:312-317.
(6) Jess T, Horvath-Puho E, Fallingborg J, et al. Cancer risk in inflammatory bowel disease according to patient phenotype and treatment: a Danish population-based cohort study. *Am J Gastroenterol* 2013;108:1869-1876.
(7) Langholz E. Relative or relevant risk? *Gastroenterology* 2012;143:e20-e21.
(8) Baumgart DC. Endoscopic surveillance in Crohn's disease and ulcerative colitis: who needs what and when? *Dig Dis* 2011;29 Suppl 1:32-35.
(9) Rutter MD, Saunders BP, Wilkinson KH, et al. Cancer surveillance in longstanding ulcerative colitis: endoscopic appearances help predict cancer risk. *Gut* 2004;53:1813-1816.
(10) Velayos FS, Loftus EV, Jr., Jess T, et al. Predictive and protective factors associated with colorectal cancer in ulcerative colitis: A case-control study. *Gastroenterology* 2006;130:1941-1949.
(11) Askling J, Dickman PW, Karlen P, et al. Family history as a risk factor for colorectal cancer in inflammatory bowel disease. *Gastroenterology* 2001;120:1356-1362.
(12) Soetikno RM, Lin OS, Heidenreich PA, et al. Increased risk of colorectal neoplasia in patients with primary sclerosing cholangitis and ulcerative colitis: a meta-analysis. *Gastrointest Endosc* 2002;56:48-54.
(13) Lindstrom L, Lapidus A, Ost A, et al. Increased risk of colorectal cancer and dysplasia in patients with Crohn's colitis and primary sclerosing cholangitis. *Dis Colon Rectum* 2011;54:1392-1397.
(14) Collins PD, Mpofu C, Watson AJ, et al. Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease. *Cochrane Database Syst Rev* 2006;CD000279.
(15) Rutter MD, Saunders BP, Wilkinson KH, et al. Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. *Gastroenterology* 2006;130:1030-1038.
(16) Kronborg O, Fenger C, Olsen J, et al. Randomised study of screening for colorectal cancer with faecal-occult-blood test. *Lancet* 1996;348:1467-1471.
(17) Lutgens MW, Oldenburg B, Siersema PD, et al. Colonoscopic surveillance improves survival after colorectal cancer diagnosis in inflammatory bowel disease. *Br J Cancer* 2009;101:1671-1675.
(18) Van AG, Dignass A, Bokemeyer B, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 3: special situations. *J Crohns Colitis* 2013;7:1-33.
(19) Colonoscopic Surveillance for Prevention of Colorectal CAncer in People with Ulcerative Colitis, Crohn's Disease or Adenomas. Centre for CLinical Practice at NICE (UK) 2011
(20) Hurlstone DP, Sanders DS, Lobo AJ, et al. Indigo carmine-assisted high-magnification chromoscopic colonoscopy for the detection and characterisation of intraepithelial neoplasia in ulcerative colitis: a prospective evaluation. *Endoscopy* 2005;37:1186-1192.
(21) Kiesslich R, Fritsch J, Holtmann M, et al. Methylene blue-aided chromoendoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. *Gastroenterology* 2003;124:880-888.
(22) Rutter MD, Saunders BP, Schofield G, et al. Pancolonic indigo carmine dye spraying for the detection of dysplasia in ulcerative colitis. *Gut* 2004;53:256-260.
(23) Soetikno R, Subramanian V, Kaltenbach T, et al. The detection of nonpolypoid (flat and depressed) colorectal neoplasms in patients with inflammatory bowel disease. *Gastroenterology* 2013;144:1349-52, 1352.
(24) Rutter M, Bernstein C, Matsumoto T, et al. Endoscopic appearance of dysplasia in ulcerative colitis and the role of staining. *Endoscopy* 2004;36:1109-1114.
(25) Riddell RH, Goldman H, Ransohoff DF et al. Dysplasia in inflammatory bowel disease: standardized classification

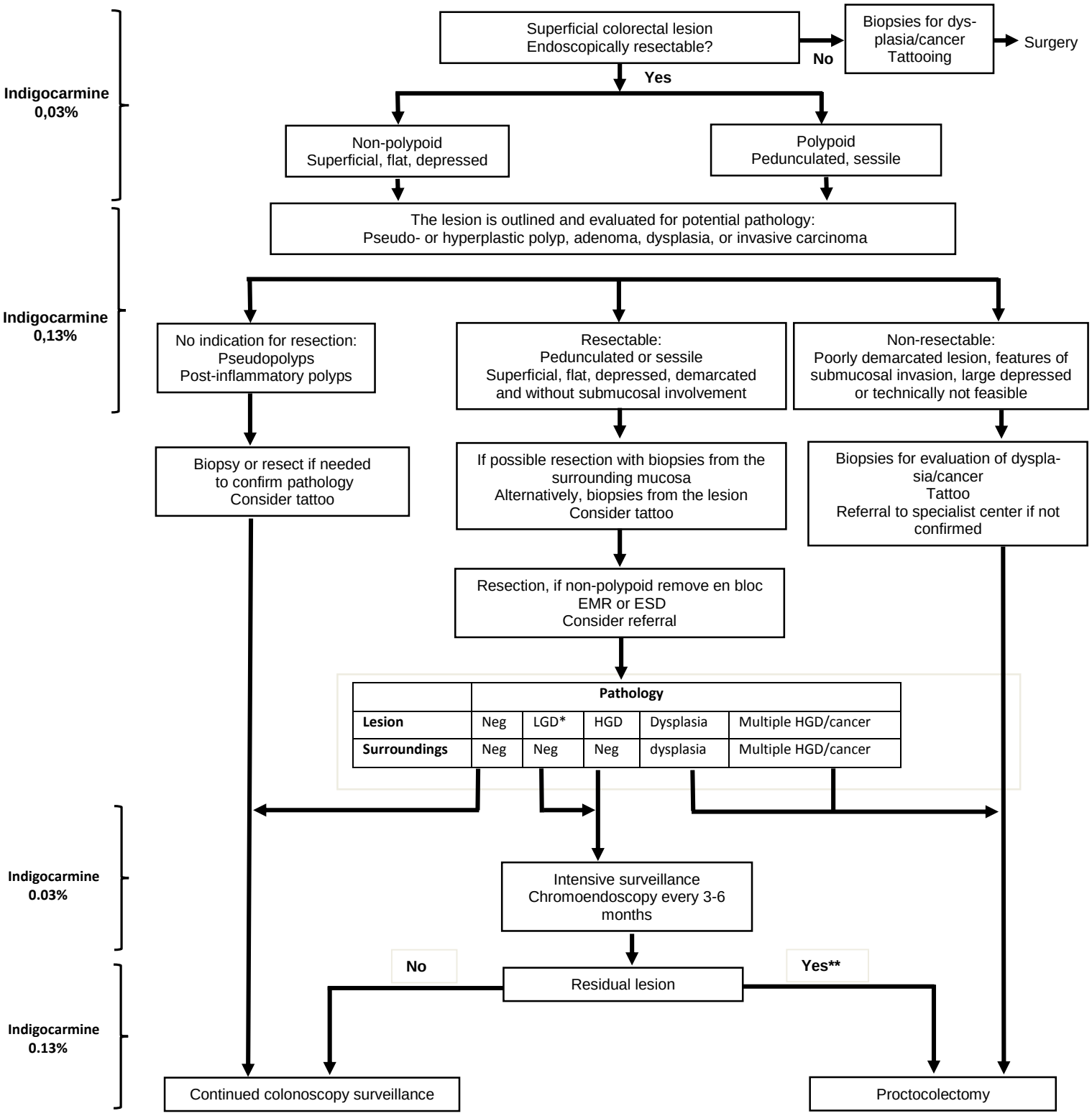
with provisional clinical applications. *Hum Pathol* 1983;14:931-968.
(26) Odze RD, Goldblum J, Noffsinger A, et al. Interobserver variability in the diagnosis of ulcerative colitis-associated dysplasia by telepathology. *Mod Pathol* 2002;15:379-386.
(27) Bernstein CN, Shanahan F, Weinstein WM. Are we telling patients the truth about surveillance colonoscopy in ulcerative colitis? *Lancet* 1994;343:71-74.
(28) Connell WR, Lennard-Jones JE, Williams CB, et al. Factors affecting the outcome of endoscopic surveillance for cancer in ulcerative colitis. *Gastroenterology* 1994;107:934-944.
(29) Hata K, Watanabe T, Kazama S et al. Earlier surveillance colonoscopy programme improves survival in patients with ulcerative colitis associated colorectal cancer: results of a 23-year surveillance programme in the Japanese population. *Br J Cancer* 2003;89:1232-1236.
(30) Blackstone MO, Riddell RH, et al. Dysplasia-associated lesion or mass (DALM) detected by colonoscopy in long-standing ulcerative colitis: an indication for colectomy. *Gastroenterology* 1981;80:366-374.
(31) Butt JH, Konishi F, Morson BC, et al. Macroscopic lesions in dysplasia and carcinoma complicating ulcerative colitis. *Dig Dis Sci* 1983;28:18-26.
(32) Itzkowitz SH, Harpaz N. Diagnosis and management of dysplasia in patients with inflammatory bowel diseases. *Gastroenterology* 2004;126:1634-1648.
(33) Lennard-Jones JE, Melville DM, Morson BC, et al. Precancer and cancer in extensive ulcerative colitis: findings among 401 patients over 22 years. *Gut* 1990;31:800-806.
(34) Rosenstock E, Farmer RG, Petras R, et al. Surveillance for colonic carcinoma in ulcerative colitis. *Gastroenterology* 1985;89:1342-1346.
(35) Blonski W, Kundu R, Lewis J, et al. Is dysplasia visible during surveillance colonoscopy in patients with ulcerative colitis? *Scand J Gastroenterol* 2008;43:698-703.
(36) Engelsgjerd M, Farraye FA, Odze RD. Polypectomy may be adequate treatment for adenoma-like dysplastic lesions in chronic ulcerative colitis. *Gastroenterology* 1999;117:1288-1294.
(37) Odze RD, Farraye FA, Hecht JL, et al. Long-term follow-up after polypectomy treatment for adenoma-like dysplastic lesions in ulcerative colitis. *Clin Gastroenterol Hepatol* 2004;2:534-541.
(38) Rubin PH, Friedman S, Harpaz N et al. Colonoscopic polypectomy in chronic colitis: conservative management after endoscopic resection of dysplastic polyps. *Gastroenterology* 1999;117:1295-1300.
(39) Vieth M, Behrens H, Stolte M. [Sporadic adenoma and colitis-associated intraepithelial neoplasia: a difficult differential diagnosis]. *Pathologe* 2003;24:36-43.
(40) Ullman T, Croog V, Harpaz N et al. Progression to colorectal neoplasia in ulcerative colitis: effect of mesalamine. *Clin Gastroenterol Hepatol* 2008;6:1225-1230.
(41) Baker WN, Glass RE, Ritchie JK, et al. Cancer of the rectum following colectomy and ileorectal anastomosis for ulcerative colitis. *Br J Surg* 1978;65:862-868.
(42) Filipe MI, Edwards MR, Ehsanullah M. A prospective study of dysplasia and carcinoma in the rectal biopsies and rectal stump of eight patients following ileorectal anastomosis in ulcerative colitis. *Histopathology* 1985;9:1139-1153.
(43) Lutgens MW, van Oijen MG, Vleggaar FP, et al. Risk factors for rectal stump cancer in inflammatory bowel disease. *Dis Colon Rectum* 2012;55:191-196.
(44) Oakley JR, Lavery IC, Fazio VW, et al. The fate of the rectal stump after subtotal colectomy for ulcerative colitis. *Dis Colon Rectum* 1985;28:394-396.
(45) Das P, Johnson MW, Tekkis PP, et al. Risk of dysplasia and adenocarcinoma following restorative proctocolectomy for ulcerative colitis. *Colorectal Dis* 2007;9:15-27.
(46) Kariv R, Remzi FH, Lian L et al. Preoperative colorectal neoplasia increases risk for pouch neoplasia in patients with restorative proctocolectomy. *Gastroenterology* 2010;139:806-12, 812.
(47) Veress B, Reinholt FP, Lindquist K, et al. Long-term histomorphological surveillance of the pelvic ileal pouch: dysplasia develops in a subgroup of patients. *Gastroenterology* 1995;109:1090-1097.
(48) Sundhedsstyrelsen. Anbefalinger vedrørende screening for tyk- og endetarmskræft. 2010
(49) Siegel CA, Schwartz LM, Woloshin S et al. When should ulcerative colitis patients undergo colectomy for dysplasia? Mismatch between patient preferences and physician recommendations. *Inflamm Bowel Dis* 2010;16:1658-1662.
(50) Baars JE, Siegel CA, van't Spijker A, et al. Inflammatory bowel disease-patients are insufficiently educated about the basic characteristics of their disease and the associated risk of colorectal cancer. *Dig Liver Dis* 2010;42:777-784.
(51) Owford Centre for Evidence-based Medicine - Levels of Evidence (March 2009). http://www.cebm.net/?o=1025

Table 1: Evidence level for clinical recommendations

	Evidence level[51] Ia,b.IIa,b-V	Recommendation A-D
Risk of CRC in patients with IBD:		
The overall risk of CRC in Danish patients with IBD does not appear to be increased	**Ib**	
However, the following factors may increase the risk for CRC in patients with UC:		
• Disease duration > 13 years	**IIa**	
• Early age at onset (less than 19 years of age)	**IIa**	
• Extensive UC	**IIa**	
• Patients with UC and PSC	**IIa**	
The risk of CRC in Danish patients with CD does not appear to be increased but,	**IIb**	
• Patients with CD and PSC may have an increased risk of CRC	**IIIb**	
Risk factors for sporadic CRC in patients with IBD:		
• Patients with a first degree relative with CRC are at increased risk of CRC	**IIb**	
The surveillance program includes:		
Colonoscopy every 5th year:		
• Patients with extensive UC and a disease duration of more than 10-13 years	**V**	**D**
• Young age at onset (less than 19 years of age) with a minimum of left-sided colitis and disease duration of more than 10-13 years	**V**	**D**
Colonoscopy every 3rd year:		
• Patients with colorectal post-inflammatory polyps	**V**	**D**
Colonoscopy annually:		
• Patients with UC and PSC	**V**	**D**
• Patients with CD and PSC	**V**	**D**
Colonoscopy every 3-6 months:		
• Patients with UC and colonic or rectal strictures	**V**	**D**
• Patients with any degree of colonic or rectal dysplasia	**V**	**D**
How is colonic dysplasia classified?		
• Lesions are divided into indefinite for dysplasia, low-grade and high-grade dysplasia	**II**	**B**
• If dysplasia, including indefinite for dysplasia, is diagnosed, a second opinion from a gastroenterology-specialised pathologist is recommended	**IIb**	**B**
How is colorectal dysplasia treated?		
• Total colectomy is recommended for non-resectable high-grade dysplasia	**IIb**	**B**
• A total colectomy is recommended for a dysplastic lesion (high-grade and low-grade) if dysplasia (regardless of the grade) is found in the surrounding mucosa	**IIb/III**	**B/C**
• Resectable lesions are removed with EMR or ESD	**IIb**	**B**
• If polypectomy is performed due to *high*- or *low-grade* dysplasia, a control colonoscopy should be performed after 3 to 6 months	**IIb**	**B**
IBD subgroups		
Patients with UC and a left residue of the rectum following subtotal colectomy (potentially with an ileo-rectal anastomosis)		
• Cancer may develop in the rectal stump	**IIb**	
• For patients who refuse an ileo-anal reservoir, extirpation of the rectum should be considered.	**V**	**D**
Patients with UC and an ileo-anal reservoir (pouch)		
• Routine surveillance for malignancy is not recommended.	**V**	**D**

Abbreviations: CD, Crohn's disease; CRC, colorectal cancer; EMR endoscopic mucosal resection; ESD, endoscopic submu cosal dissection, IBD, inflammatory bowel disease; UC, ulcerative colitis; PSC, Primary sclerosing cholangitis;

Figure 1. Algorithm for pancolonic chromoendoscopy with targeted biopsies and management of superficial lesions in patients with inflammatory bowel disease



*Including multiple LGD; **Consider renewed resection in case of small residual lesions

The figure is slightly modified from the original algorithm by Soetikno et al[12] by excluding random biopsies in case of multiple pseudo polyps are present.

Abbreviations: EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; LGD, low-grade dysplasia, Neg, Negative