Quality in colonoscopic polypectomy

Ina Borgenheim Pedersen

SØRLANDET SYKEHUS

Department of Medicine, Sørlandet Hospital, Kristiansand

University of Oslo

Faculty of Medicine

Department of Health and Society

Series of dissertations submitted to the
Faculty of Medicine, University of Oslo

ISBN 978-82-348-0349-9

Cover: UiO.
Print production: Graphic center, University of Oslo.

Table of contents

Acknowledgments

The work leading to this thesis was conducted at the University of Oslo, Institute of Health and Society, Department of Health Management and Health Economics in cooperation with Sørlandet Hospital Kristiansand. The research has been made possible by grants from the South-East Norway Regional Health Authority.

This thesis and the research behind it would never have been carried out if it weren't for my supervisors, colleagues, collaboration partners at the participating hospitals and my family and friends.

First and foremost, I would like to thank my main supervisor Øyvind Holme for continuous support in both work and life in general. You have taught me all I know in the field of research, and I am so grateful for all the time you have put into my work, and for filling in for me while I was taking care of my youngest daughter. You are one of the most enthusiastic persons I have ever met, you do have a lot of "balls in the air", but still you always manage to find time for answering my questions – whether they are intelligent or not. Despite of your experience and competence, not once have you made me feel stupid or incompetent. Every person should have an Øyvind in their life to build their confidence.

I would also like to thank my great team of co-supervisors, Mette Kalager, Michael Bretthauer, Magnus Løberg and Geir Hoff, for their support and suggestions. It has been very helpful with your views on my work, and I have learnt so much from all of you as well. Thank you for including me in the research group, I have so many nice memories from our trips – especially to Iceland – and I have found the group meetings very interesting, educational and inspiring.

And to the rest of the research group: Thank you! For all the professional discussions, all the laughs, all the nice meals, including eating flowers at a Christmas party, drinking German glühwein that was way too strong for me, for all the "so nice to see you again, Ina"s and for your friendships. You are the best.

I would also like to thank the heads of the medical department in Kristiansand, both the late Ole Rysstad who sadly passed away last year and the new leader Rita Helleren, Thor Kristian Støle, and my clinical supervisor and immediate manager Audun Hasund. You tell me that you believe in me, and that you want research to be a more important part of our department, and your support means a lot to me. The facilitation from Audun and the nurse leader Britt

Tybakken and the rest of the gastroenterological department that have made me able to attend meetings, and the whole departments effort in including patients in my projects have been so helpful and inspiring for me. I feel like we are all one team. Thanks also to my former leader at the gastroenterological department, Asbjørn Stallemo, for investing time and effort to teach me the art of endoscopy.

The research department at Sørlandet hospital, led by Frode Gallefoss, have also been a huge resource and support for me. I would especially like to thank Frode for one of the most meaningful conversations I have had, when I had a rough period in my research and life in general. Inspiring leadership, that I hope one day to be able to perform myself. And to all my co-workers and friends at SSK, both former and present: Thank you for being who you are. I really enjoy working with you, and I look forward to every day at work, much because of you. Some of you have become close and important friends of mine, you know who you are.

All my collaboration partners, both nurses, endoscopists and pathologists, at the different hospitals deserve a huge thank you from me. This would never have been done without you. There is little or no time left in the clinical everyday life, but you still made time to put in extra effort to include patients in these projects. I have met so many kind and inspiring persons while travelling around to our collaborating hospitals, and I tell my colleagues who are struggling with what specialty to choose, that everyone in the gastroenterological departments I have visited are extraordinary nice people.

Last, but not least, I would like to thank my family, and especially my husband Kim, for putting up with me for all these years. You are the most positive person I know, and the way you approach life inspires me. I am so lucky to have a husband who loves me like you. Thank you for taking such good care of our children, Sara, Daniel, and Hanna, when I was out doing my research. And thank you, my three favourites, for giving me hugs almost in your sleep when I come home too late, for writing notes for me to bring on my trips and for living your lives to the fullest even though I have not been around every day. I love you.

Ina B. Pedersen Kristiansand, June 2023

List of abbreviations

ADR	Adenoma detection rate
BMI	Body Mass Index
CI	Confidence interval
CRC	Colorectal cancer
CSP	Cold snare polypectomy
DOPyS	Direct Observation Polypectomy Skills
EMR	Endoscopic mucosal resection
ESGE	European Society of Gastrointestinal Endoscopy
FICE	Fuji intelligent colour enhancement
GEE	Generalized estimating equations
HP	Hyperplastic polyps
HSP	Hot snare polypectomy
IRR	Incomplete resection rate
NBI	Narrow band imaging
OR	Odds ratio
PCCRC	Post colonoscopy colorectal cancer
RR	Relative risk
SD	Standard deviation
SSL	Sessile serrated lesion
SSP	Sessile serrated polyp
TSA	Traditional serrated adenoma

List of papers

Paper 1: Polypectomy techniques among gastroenterologists in Norway – a nationwide survey

Ina B. Pedersen, Magnus Løberg, Geir Hoff, Mette Kalager, Michael Bretthauer, Øyvind Holme

Endosc Int Open. 2018 Jul;6(7):E812-E820. doi: 10.1055/a-0607-0727. Epub 2018 Jul 4. PMID: 29977999

Paper 2: Incomplete endoscopic resection of colorectal polyps: a prospective quality assurance study

Ina B. Pedersen, Michael Bretthauer, Mette Kalager, Magnus Løberg, Geir Hoff, Senaria Matapour, Silje Hugin, Svein O. Frigstad, Britta A. Kleist, Leif Løvdal, Edoardo Botteri, Øyvind Holme

Endoscopy. 2021 Apr;53(4):383-391. doi: 10.1055/a-1243-0379. Epub 2020 Sep 22. PMID: 32961579

Paper 3: Cold snare versus hot snare polypectomy for polyps sized 4-9 mm. A randomized, controlled trial.

Ina B. Pedersen, Anna Rawa-Golebiewska, Audrey Calderwood, Lone D. Brix, Louise B. Grode, Edoardo Botteri, Marek Bugajski, Michal F. Kaminski, Wladyslaw Januszewicz, Johan Holck-Steen, Hjalmar M. Ødegård, Britta A. Kleist, Leif Løvdal, Mette Kalager, Magnus Løberg, Michael Bretthauer, Geir Hoff, Asle W. Medhus, Øyvind Holme

Endoscopy 2022 Oct;54(10):961-969.doi: 10.1055/a-1734-7952. Epub 2022 Jan 10. PMID 35008112

Sammendrag: Kvaliteten på polyppfjerning i tykktarm

Tykk- og endetarmskreft er den tredje vanligste kreftformen i verden, og insidensen av denne kreftformen i Norge er en av verdens høyeste. Insidensen er også stigende, og foreløpig har man ingen forklaring på hvorfor det er slik.

Den senere tiden har det vært økende uro i fagmiljøet grunnet krefttilfeller som oppstår etter gjennomført koloskopi eller før avtalt kontroll-koloskopi, såkalte post-koloskopi kolorektalcancere. Det kan være flere årsaker til dette, bl.a. oversett lesjon, raskt voksende lesjon eller inkomplett fjernet lesjon. Sistnevnte er hovedtema for denne avhandlingen.

Tykk- og endetarmskreft utvikles fra polypper, og ved å fjerne disse kan man både forebygge kreft og også avdekke og fjerne kreft i et tidlig stadium, noe som i sin tur vil senke insidensen og dermed også mortaliteten av kolorektalkreft. De aller fleste polyppene man kan finne i tykk- og endetarmen deles grovt inn i 2 kategorier; adenomer og bredbasede sagtakkede polypper, hvor både adenomer og flere typer bredbasede sagtakkede polypper kan utvikle seg til kreft.

Ved koloskopi kan man fjerne polypper, vanligvis ved hjelp av slyngereseksjon (en slags metallasso som legges rundt polyppen). Det er mulig å bruke strøm i slyngene («varm» polypektomi) eller bruke slyngene uten strøm («kald» polypektomi). Tidligere var det også vanlig å fjerne små polypper kun ved bruk av biopsitang, men det er ikke lenger anbefalt annet enn for polypper under 3 mm.

Første steg i arbeidet med kartlegging av kvalitet på polyppfjerning var å lage en spørreundersøkelse som ble distribuert blant gastroenterologer i Norge, der de fikk 40 spørsmål om forhold rundt polyppfjerning, bl.a. metodevalg, om de brukte definerte retningslinjer for oppfølging av pasienter etter polyppfjerning, og i så fall hvilke, med.mer. 70 av de 119 (59%) av de som mottok spørreskjemaet besvarte dette, og det var overraskende sprikende resultater. Det viste seg at opptil 40% av gastroenterologene brukte en eller flere inadekvate teknikker ved polyppfjerning, eksempelvis at det ble brukt biopsitang eller at man valgte å la være å fjerne små polypper.

Da var et logisk neste steg å gjennomføre en klinisk kvalitetsstudie der målet var å kartlegge hvilke metoder som ble brukt for fjerning av de ulike polyppene, hvor stor andel av disse som ble inkomplett fjernet og forsøke å finne årsaker til inkomplett fjerning, samt registrere

komplikasjoner. Studien ble gjennomført ved at polypper i tykk- og endetarmen ble fjernet etter endoskopørens eget ønske, og tekniske detaljer ved undersøkelsen ble registrert i etterkant. Når polyppen var ansett komplett fjernet ble det tatt 2-4 vevsprøver fra tarmen der polyppen ble fjernet fra (polypptomten) for å se etter polyppvev i disse vevsprøvene. Totalt 246 pasienter med til sammen 339 polypper ble inkludert i studien. Vi fant at hos polypper under 20 mm ble 14,6% inkomplett fjernet, og i regresjonsanalyse fant vi at faktorer assosiert med økt risiko for inkomplett fjerning var hvis polyppen var lokalisert i høyre side av tykktarmen og hvis polyppen var av typen bredbaset sagtakket lesjon. Det var ingen statistisk forskjell i inkomplett reseksjonsrate mellom fjerning med varm eller kald slynge. Inkomplett reseksjonsrate på 14,6% var noe høyere enn i tidligere, sammenlignbare studier. Grunnen til den økte raten i vår studie er ukjent. Vi sammenlignet resultatene for erfarne endoskopører, definert som ferdige spesialister i gastroenterologi med resultatene for uerfarne endoskopører, definert som leger i spesialisering i gastroenterologi. Interessant nok fant vi ingen forskjell mellom disse gruppene, men vi fant stor variasjon i inkomplett polyppreseksjonsrate mellom de ulike enkeltpersonene som deltok i studien som endoskopører, fra 6,7% til 34,6%.

Da polypper under 10 mm i størrelse utgjør rundt 90% av alle polypper som fjernes er dette en viktig gruppe polypper å studere nærmere. Den siste del-studien i denne avhandlingen sammenlignet bruk av varm slynge med bruken av kald slynge for fjerning av polypper mellom fra 4 til 9 mm, først og fremst med tanke på inkomplett polyppfjerning og eventuelle komplikasjoner. Vi valgte å bruke et ikke-underlegenhets design på denne studien for å undersøke om den relativt nye metoden kald slynge var ikke-underlegen den etablerte varm slynge-metoden, med en ikke-underlegenhetsmargin satt til 5%. 425 pasienter med til sammen 601 polypper ble randomisert 1:1 til fjerning med enten varm eller kald slynge. I kald-slynge-gruppen fant vi en inkomplett polyppreseksjonsrate på 10,7% og i varm slynge-gruppen på 7,4%, med en justert risikoforskjell på 3,2% (95% konfidensintervall -1,4-7,8%), altså kunne vi ikke konkludere med at kald slynge var ikke-underlegen varm slynge. Det var ingen forskjeller mellom gruppene når det gjaldt komplikasjoner i form av blødning, tarmperforasjon eller magesmerter i etterkant.

Oppsummert har denne avhandlingen vist at det fremdeles brukes inadekvate teknikker for polyppfjerning og at inkomplett polyppreseksjonsrate forekommer hyppig. Vi kunne ikke vise at kald slynge var ikke-underlegen varm slynge for fjerning av små polypper, men forskjellen mellom gruppene var ikke statistisk signifikant i sekundæranalysene, og kald slynge anses

som et trygt valg for fjerning av polypper under 10 mm. Det er gjort studier hvor endoskopører får intensiv opplæring bl.a. i form av videoer av polyppfjerning før de selv fjerner polypper, og de blir da scoret på ulike parametere før og etter opplæringen, hvor man ser at kvaliteten på polyppfjerningen økes. Opplæring i koloskopi og polyppfjerning er i stor grad en mester/svenn-situasjon, og resultatene fra kvalitetsstudien med stor variasjon mellom de ulike endoskopørene og ingen statistisk signifikant forskjell mellom ferdige spesialister og leger i spesialisering når det gjelder inkomplett polyppfjerning viser at det er behov for økt opplæring og kanskje også en form for resertifisering underveis i karrieren.

Summary: Quality in colonoscopic polypectomy

Colorectal cancer is the third most common cancer in the world, and the incidence rate in Norway is one of the highest in the world.
Recently, there has been increasing awareness on cancer cases that occur after a colonoscopy has been carried out or before an agreed control colonoscopy, so-called post-colonoscopy colorectal cancers. There may be several reasons for this, e.g., overlooked lesions, rapidly growing lesions or incompletely resected polyps/lesions. The latter is the main topic of this thesis.

Colorectal cancer develops from polyps, and by removing these you can both prevent cancer and also detect and remove cancer at an early stage, which in turn will decrease the incidence and thus also the mortality of colorectal cancer. Most polyps found in the colon and rectum are roughly divided into 2 categories; adenomas and sessile serrated lesions, where both adenomas and several types of sessile serrated lesions can develop into cancer.

During a colonoscopy, polyps can be removed, usually using snare resection. It is possible to use electricity in the snare ("hot" polypectomy) or to use the snares without electricity ("cold" polypectomy). Earlier it was also common to remove small polyps only using biopsy forceps, but this is no longer recommended except for polyps under 3 mm.

The first study in this thesis on quality in polypectomy was a survey that was distributed among gastroenterologists in Norway, where the participants were asked 40 questions on

polyp removal, e.g. choice of method for polypectomy, the use of bleeding prevention methods, the use of outdated methods such as hot biopsy forceps for polyp removal, whether they used defined guidelines for follow-up of patients after polyp removal, and if so which guidelines, etc. 70 of the 119 (59%) answered the questionnaire, and there were large variations in polypectomy techniques among the respondents. It turned out that up to 40% of the gastroenterologists used one or more inadequate techniques when removing polyps, for example was hot biopsy forceps still in use, larger polyps than 2 mm were removed by biopsy forceps, and some gastroenterologists chose to not to remove small polyps at all.

A logical next step was to perform a clinical quality study where the aim was to quantify the rate of incomplete polyp resection, and to identify explaining factors for incomplete polyp removal, as well as record complications. The study was carried out by removing polyps in the colon and rectum at the endoscopist's own request, and technical details of the examination were recorded afterwards. When the polyp was considered completely removed, 2-4 biopsies were taken from the polypectomy site to look for residual polyp tissue. A total of 246 patients with 339 polyps were included. We found that 14.6% of polyps under 20 mm were incompletely removed, and in regression analysis we found that only polyp location in the right colon and polyps with sessile serrated histology were associated with an increased risk of incomplete polyp removal. There was no statistical difference in incomplete resection rate between removal with hot or cold snares. Incomplete resection rate of 14.6% was higher than in previous studies. The reason for the increased rate in our study is unknown. We compared the results for experienced endoscopists, defined as board-certified gastroenterologists, with the results for inexperienced endoscopists, defined as gastroenterologists in training. Interestingly, we found no difference between these groups, but we found a large variation in incomplete polyp resection rate between the different endoscopists who participated in the study, ranging from 6.7% to 34.6%.

As polyps under 10 mm in size make up around 90% of all polyps that are removed, this is an important group of polyps to study in more detail. The third study in this thesis compared the use of hot snare polypectomy to cold snare polypectomy for the removal of polyps between 4 and 9 mm, investigating the incomplete resection rate. We chose to use a non-inferiority design for this study to investigate whether the relatively new cold snare method was non-inferior to the established hot snare method, with a non-inferiority margin set at 5%. 425

patients with a total of 601 polyps were randomized 1:1 to either hot or cold snare polypectomy. In the cold snare group, we found an incomplete polyp resection rate of 10.7% and in the hot snare group 7.4%, with an adjusted risk difference of 3.2% (95% confidence interval -1.4-7.8%), so we could not conclude that cold snare was non-inferior to hot snare. There were no differences between the groups in terms of complications such as bleeding, intestinal perforation, or abdominal pain afterwards.

In summary, this thesis has shown that inadequate techniques are still used for polyp removal and that incomplete polyp resection occur frequently. We could not show that cold snare was non-inferior to hot snare for the removal of small polyps, but the difference between the groups was not statistically significant in the secondary analyses. Thus, cold snare polypectomy is considered a safe choice for the removal of polyps smaller than 10 mm. There are few studies that have been conducted in the field of education of endoscopists. A lecture-based training program have been tested, and the endoscopists performance increased after completing the program. The education of endoscopists takes place in the endoscopy suite, with hands-on training and direct feedback. The results from the quality study with great variation between the various endoscopists and no statistically significant difference between qualified specialists and doctors in specialization regarding incomplete polyp removal show that there is a need for increased training and perhaps some form of recertification.

Background

Colorectal cancer epidemiology

Colorectal cancer (CRC) is the third most common cancer in the world [1], and Norway has one of the highest incidence rates of CRC in the world [2]. In Norway, about 4500 persons are diagnosed with CRC each year, and approximately 1600 persons die from the disease [3]. The incidence rates in Norway have been increasing over time, although the mortality rate have been quite stable over the last 60 years [4]. The reason for the increasing incidence rates is unknown.

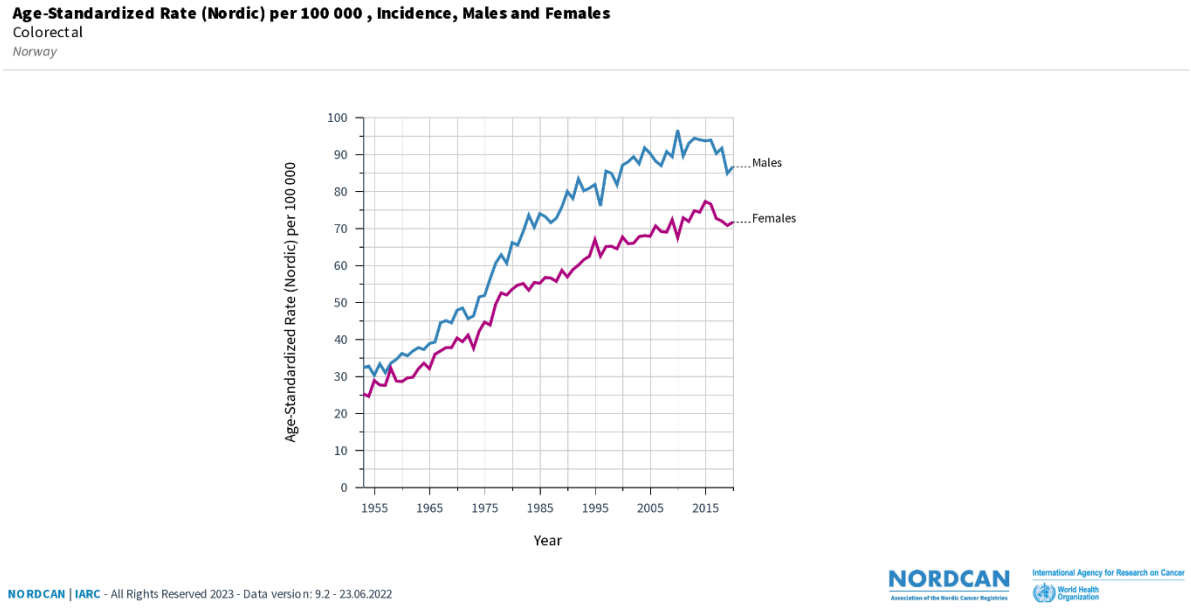


Figure 1: Incidence of colorectal cancer in Norway [5]

Colorectal cancer screening

Principles of screening

The purpose of any screening is to identify asymptomatic persons or groups of persons at high risk of or with an early stage of the disease that is being screened for [6]. For a disease to be

suitable for screening, several prerequisites should be met according to the World Health Organization [7], including:

- The disease should be an important health problem
- The treatment for the disease should be acceptable for the patients
- There should be a suitable test or examination for the disease, including available facilities for diagnosis
- The natural history of the disease should be adequately understood
- The disease should be recognizable in a latent or early stage
- The screening test itself should be acceptable to the population

All the above-mentioned criteria are met for CRC, given the large incidence and mortality, there is available treatment, mostly surgery, and most CRCs are believed to develop from benign precursors that could be discovered during colonoscopy.

For CRC, screening could work in two different ways, either by prevention by removing precancerous lesions or by early detection of cancer. The removal of precancerous lesions may decrease the incidence and hence mortality of cancer, and detection of early cancer may decrease mortality from the cancer in question.

Colorectal polyps

CRC is believed to be developed from colorectal polyps [8-11].

Colorectal polyps could mainly be divided into two categories: adenomas and sessile serrated lesions.

Adenomas

Adenomas are benign tumours derived from glandular tissue of the colonic mucosa, and they have a potential of malignant transformation. They are divided into tubular, villous and tubulovillous adenomas, with tubular adenomas as the most frequent [12]. Adenomas can develop to cancer [13-15]. This is the reason why adenomas should be removed when discovered during colonoscopy. About two thirds of polyps are adenomas, and 30-50% of patients where an adenoma is detected will have at least one other adenoma present [16]. In

USA, adenomas are classified as advanced adenomas if they present one of the following features; >25% villous features, size ≥1.0 cm, high-grade dysplasia or invasive cancer [17], but this classification is not used in Norway or the rest of Europe. The ESGE (European Society of Gastrointestinal Endoscopy) guidelines classifies patients as low or high risk, where high risk patients have removed adenomas with either villous histology, high risk dysplasia, are ≥ 10 mm in size or have had five or more adenomas removed [18].

Risk factors: Age is an important risk factor for developing adenomas, and also for the development of high-grade dysplasia, independent of the size and localisation of the adenoma, with an adjusted OR of 1.8 for patients ≥60 years of age [19,20]. In screening studies, the prevalence of adenomas is reported to be between 25-30% for 50-year-old patients [20-24]. In autopsy studies the prevalence at age 70 is approximately 50%, but only 1-4% in patients under 30 years of age [24,25]. Body mass index (BMI) is also considered to be a risk factor for adenoma development, with a 19% increased risk for every 5-unit increase in BMI, according to a metaanalysis from 2012 [26]. Lack of physical activity is also considered a risk factor, with a reported relative risk (RR) of 0.84 for active persons [27]. It is also found that adenomas are more common in men than in women, with an OR for advanced adenoma of 1.83, and that it may be more common in African-Americans (OR for adenomas >9 mm of 1.16 for men and 1.62 for women, compared to white patients) than in other ethnic groups [23,28,29]. There is also evidence suggesting that high intake of red and processed meat increases the risk of developing colorectal adenomas, with relative risks of 1.27 and 1.29, respectively in one meta-analysis [30] and of 1.24 and 1.19 in another [31]. All of the abovementioned risk factors are also known risk factors for colorectal cancer development, except being African American [32].

Histopathology: The histopathological features of adenomas include nuclear hyperchromatism, crowded, elliptical nuclei and reduction or even total loss of goblet cells. Around 80% of the colonic adenomas are tubular adenomas, and the remaining 20% are villous or tubulovillous. The growth pattern of the adenoma decides if it is defined as tubular, villous or tubulovillous. An adenoma consisting of almost only tubular glands, and no more than 25% of the surface covered with villous structures is a tubular adenoma. If over 75% of the surface is of villous type, the adenoma is named villous adenoma, and if the adenoma consists of both types (tubular and villous) it is defined as a tubulovillous adenoma [12]. The villous adenoma is believed to be of largest cancer risk, probably due to its larger surface

[33]. Adenomas are classified after the extent of dysplasia in the polyp, to either low-grade or high-grade dysplasia. Smaller adenomas have a smaller risk of high-grade dysplasia than the larger adenomas, with an OR of high-grade dysplasia in adenomas ≥1 cm of 10.83 compared to adenomas <1 cm [34] .

Advanced adenomas are believed to be a much larger risk factor for developing colorectal cancer than non-advanced adenoma [35,36]. In a sigmoidoscopy screening study from the US with almost 16.000 colonoscopies, the CRC incidence rate per 10.000 person years after removal of an advanced adenoma at the index colonoscopy was 20 (95% CI 15.3-24.7, n=70), and the OR of developing colorectal cancer compared to patients who had no adenomas removed at the index colonoscopy was 2.7 (1.9-3.7). For patients with removal of a non-advanced adenoma the CRC incidence rate was 9.1 (6.7-11.5) and for patients with no adenomas removed the incidence rate was 7.5 (5.8-9.7) [37]. In another study with 123000 participants, the hazard ratio for colorectal cancer in patients with an advanced adenoma removed at the index colonoscopy compared to patients with no adenomas was 4.07 (2.89-5.72). In comparison, the hazard ratio for CRC in patients with removal of a non-advanced adenoma was 1.21 (0.68-2.16) compared to individuals with no adenomas [38]. In another meta-analysis investigating cancer risk after removal of low-risk adenomas, the standardized incidence ratio for CRC development after a maximum follow up time of 10 years (median 7.7 years) compared to the general population (control group) was 0.68 (0.44-0.99) and an OR for CRC of 0.4 (0.2-0.6) after 3-5 years follow up [39]. The same meta-analysis investigated the risk of development of advanced adenoma after removal of a low-risk adenoma, and the RR for advanced adenoma in the low-risk group compared to the no-adenoma group was 1.55 (1.24-1.94) after 3 to 10 years follow up. For the patients with an advanced adenoma removed at baseline, the 5 year cumulative risk of advanced adenoma was 17.1% (12.0-23.0), compared to 4.9% (3.2-7.0) for patients with non-advanced adenoma at baseline and 3.3% (1.9-5.1) for patients with no adenomas removed.

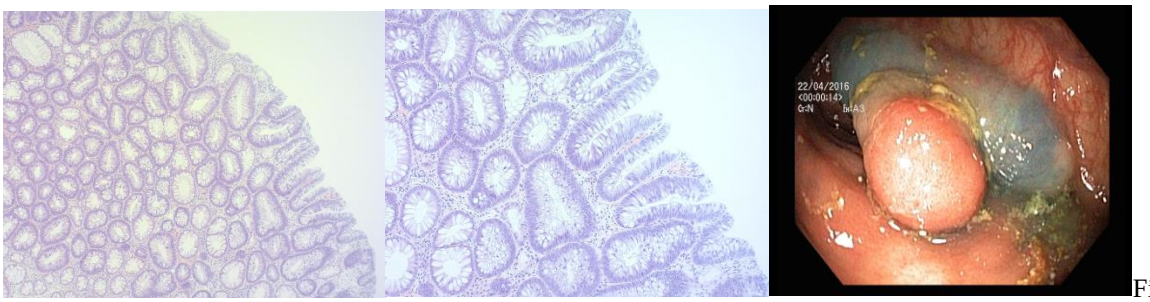


Figure 2: Adenoma seen through the microscope (left and middle picture) and through the colonoscope (right picture) [40,41]

Sessile serrated polyps (SSPs)

Sessile serrated polyps include sessile serrated lesions (SSLs), traditional serrated adenomas (TSA) and hyperplastic polyps (HP). Of these, HPs are most common, and accounts for up to 75% of serrated polyps [42]. A screening study found 15.3% SSPs in unselected patients, of these were 14.7% hyperplastic polyps, 0.5% SSLs and 0.1% TSAs [43]. In a study from Japan in 2021, 64% of the SSPs was found in the distal colon and 36% in the proximal colon [44].

Sessile serrated lesions

These are mostly flat or sessile polyps but can also be pedunculated [44], with serrated histological features such as basal dilatation of crypts, basal serration of crypts, crypt branching and horizontal crypts (the crypts run horizontally to the basal membrane). Unlike adenomas, they normally do not have alterations of the nucleus [45-47]. The prevalence of SSLs ranges from 0.038% to 22.23% [48]. Endoscopically they differ from adenomas in that they have a mucus cap/layer, and they have irregular shape and a “cloud-like” surface [49,50]. SSLs are usually around 5-7 mm in size, and they are mostly found in the right colon [42].

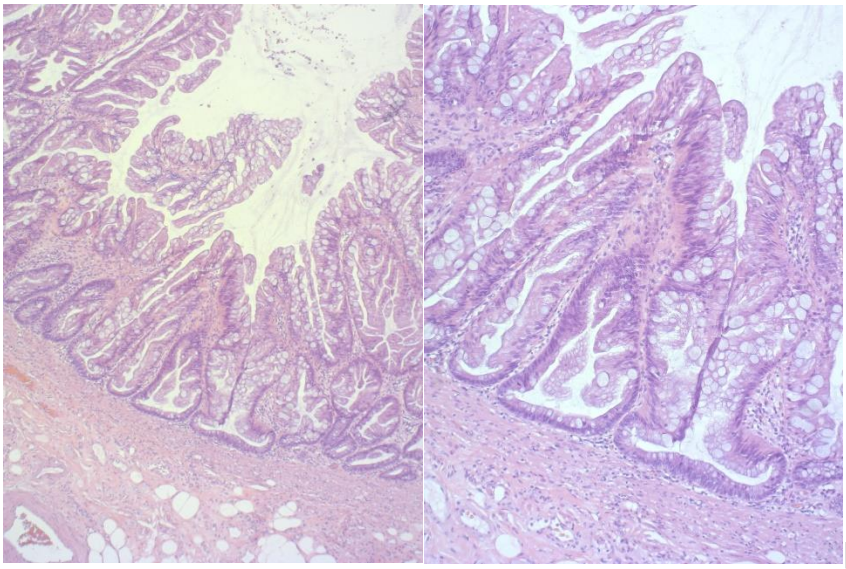
In earlier years, these polyps were considered completely benign, but now it is believed to have substantial cancer risk and to be the cause of up to 30% of colorectal cancers [51,52]. Already in 1983, there was proposed that these polyps could lead to cancer, and in the 90s these polyps were considered to have the potential for cancer development [53] Around 2010 the studies on colorectal polyps paid more attention to the SSLs and TSAs than before [42].

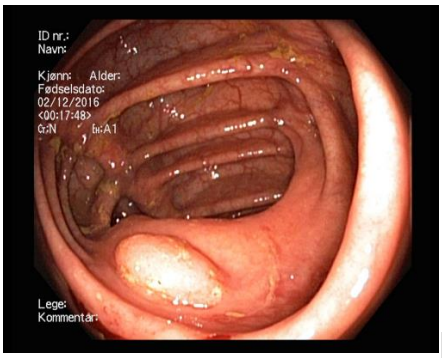
Studies have shown that persons with large SSLs found at screening had up to 4 times higher long-term cancer risk than persons with no SSLs found at screening [54].

Traditional serrated adenomas

These are villous polyps with eosinophilic cytoplasm and almost pencil-shaped nuclei. They have ectopic crypts, which is diagnostic for TSAs. If a lesion has features from both SSL and TSA, they should be classified as TSA [42]. The TSAs are larger than SSLs, with an average size of 15 mm, and they are found in the distal part of the colon and can be pedunculated [55].

Risk factors for SSLs and TSAs are not as established as for adenomas, but includes smoking, alcohol use, age >65 years and diabetes mellitus [56,57].


[41]



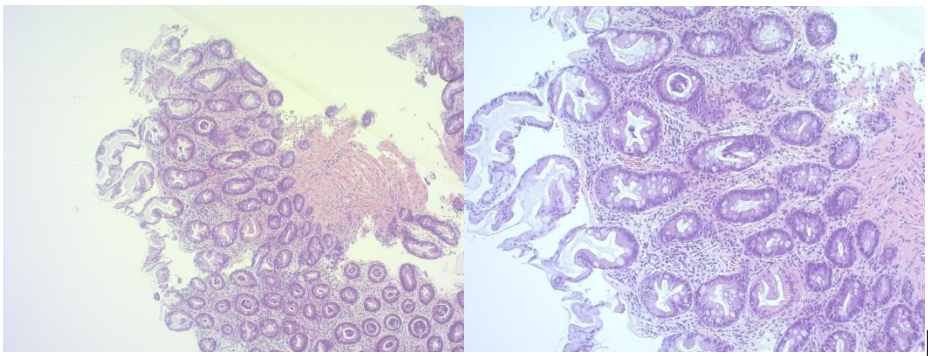
[40]

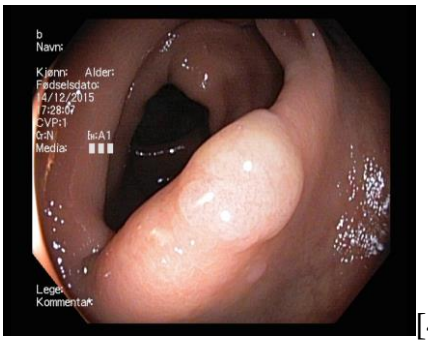
Figure 3: SSL seen through the microscope and through the colonoscope.

Hyperplastic polyps

Hyperplastic polyps are mostly found in the distal colon [58]. They are usually small (<5 mm), pale, and have few or no vessels present, and they flatten when gas is insufflated [59]. Histopathological they have narrow basal crypts, and serrated upper crypts, and there is eosinophilic mucin seen in the cytoplasm [58]. In one study, among patients with hyperplastic

polyps present in the distal colon, the risk of metachronous SSLs or TSAs in the proximal colon increased, with an OR of 2.23 compared to no HPs, and with proximal HP the OR for metachronous SSL was 3.82 [60]. There is also found that larger hyperplastic polyps (5-9mm) found in the proximal colon have an OR of 7.77 for metachronous large SSLs or TSAs [61]. The small hyperplastic polyps in the distal sigmoid and rectal colon are believed not to pose any cancer risk, but it could be discussed if they should still be removed as the ability of endoscopists to separate adenomas from hyperplastic polyps during colonoscopy is not good enough, with a sensitivity of 77% and specificity of 79% for giving the correct diagnose of small polyps [62,63].

 [41]



[40]

Figure 4: Hyperplastic polyp microscopically and endoscopically

Paris classification

Colorectal polyps may be classified according to the Paris classification, a system for the endoscopist to describe the polyps macroscopically [64] and is associated with cancer risk. A study of polyps and Paris classification have shown that Paris Is lesions have a cancer risk of 7,5%, but adenomas categorized as Paris IIa+c had over 30% of having cancer cells [65]. This thesis mainly focuses on polypectomy of polyps classified as Paris Is, IIa and IIb.

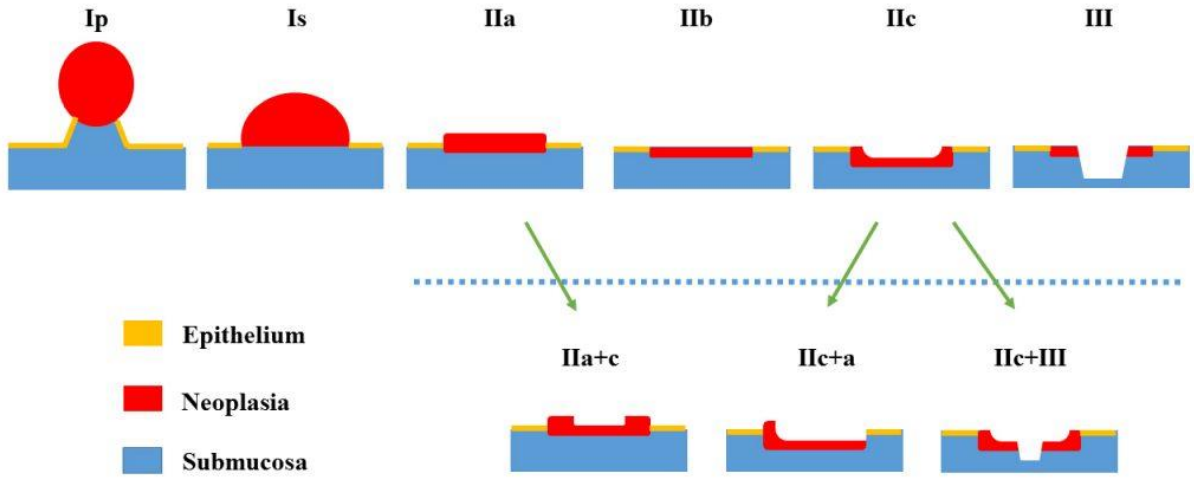


Figure 5: Paris classification of polyps [66]

Development of cancer from colorectal polyps

Both adenomas and sessile serrated lesions may develop to colorectal cancer. Polypectomy of benign polyps may decrease cancer incidence and hence cancer mortality, while early detection may only reduce mortality, not incidence. The progression from adenomatous or serrated polyp to malignant cancer is a result of genetic or epigenetic changes. Inherited gene mutations in CRC are uncommon, and accounts for approximately 5% of CRCs [67]. Three established molecular ways of CRC development from colorectal polyps is defined [13-15]. Any colorectal tumour may have features from more than one of these pathways [13].

- The chromosomal instability pathway (CIN) – the adenoma-carcinoma pathway
- The CpG island methylator phenotype pathway (CIMP) – the serrated pathway
- The microsatellite instability pathway (MSI)

The CIN pathway is associated with adenomas, and accounts for up to 70% of CRCs. The cancer is a result of accumulating mutations, typically within the APC gene, the KRAS oncogene and loss of function in the p53 gene [67].

Serrated polyps develop to cancer through the CIMP pathway, where the mutation of the BRAF gene often is the first mutation [68]. Different epigenetic changes, especially

hypermethylation of gene promoter regions, inhibits gene transcription of many mismatch repair (MMR) genes, and this can cause malignant transformation due to inhibition of growth regulatory genes [67,69].

The MSI pathway causes cancer due to disruption of genes coding for DNA repair, and this pathway is associated with cancer development of both adenomatous and serrated polyps [67].

Post-colonoscopy colorectal cancer

Post-colonoscopy colorectal cancer (PCCRC) is by the World Endoscopy Organization defined as any CRC diagnosed after a screening or surveillance exam in which no cancer is detected, and before the date of the next recommended exam [70,71]. This term was first launched in 2010 by Reabeneck et al [72]. The incidence of PCCRC is about 7% of colorectal cancers [73]. PCCRC could result from missed lesions after colonoscopy, detected lesions that were not resected, incomplete resection of lesions or new CRC [70]. In a study from England, there has been estimated that 89% of PCCRCs could be avoided. The authors have several recommendations for avoiding PCCRCs, where the first is to better identify and review PCCRCs at the local center, to identify factors to explain why the cancers occur. Other recommendations are to identify high risk patients (e.g. IBD patients) and perform regular surveillance and to document the index colonoscopy and the decisions made, e.g. was there adequate bowel preparation or if there was there scheduled any surveillance colonoscopy [74].

A prerequisite for reducing CRC incidence through polypectomy is complete removal of the polyps. There has been growing concern during the last years that incomplete polypectomy can be the cause of up to 27% of CRCs [75-77]. The proportion of incompletely resected polyps vary with size and histology of the polyp, as well as the method used for resection [78-81]. Different techniques may lead to important differences in the ability to remove polyps completely, and the proportion of incompletely removed polyps have been shown to vary more than threefold between endoscopists [78].

Colonoscopy

Colonoscopy with flexible endoscopes was introduced in the 1960s [82]. Colonoscopy is an examination where a flexible endoscope is inserted through the anal canal and all the way

down to coecum, the proximal end of the colon. In the 1980s the video colonoscope was introduced [83]. This has a camera and equipment that allows the video to be displayed on a screen in the examination room, and a working channel, that allows the introduction of instruments through the endoscope. This provides the possibility to visually inspect the mucosa of the colon and rectum, and to do different diagnostic and therapeutic procedures, such as taking biopsies from the mucosa or to remove polyps by polypectomy.

The ability to identify polyps accurately has also improved after the introduction of high definition colonoscopes, with an increase in adenoma detection rate (ADR) from 24.3% to 28.8% (p=0.012) [84].

Chromoendoscopy is used to enhance the imaging quality. The most used technique is to switch from the ordinary white light to another light, (called Narrow Band Imaging (NBI) by Olympus, i-scan by the Hoya group, Image1 by Karl Storz and Fuji intelligent colour enhancement (FICE) by Fuji), which is an imaging technique where light of specific blue and green wavelengths helps enhance the surface of the colon mucosa, and therefore can contribute to more accurate polyp detection and removal [85]. There is also possible to use a dye-based technique for chromoendoscopy. With the dye-based technique the colon mucosa is sprayed with a dyed spray, (mostly containing indigo carmine) before examining the mucosa, and this could enhance the endoscopic imaging quality [86,87].

Chromoendoscopy is shown to improve lesion detection in high-risk patients, such as Lynch syndrome and inflammatory bowel disease, but as of now no meta-analyses have found significant increase in ADR for average risk patients [88]. The adenoma detection rate is influenced by the level of bowel preparation, the withdrawal time, cecal intubation rate and different devices to use during the colonoscopy, e.g. the use of cap-assisted colonoscopy [89,90]. Adenoma detection rate is an important quality measure, as it has been shown to correlate with the rate of post colonoscopy colorectal cancer (PCCRC), where patients examined by endoscopist with ADR below 20% had more than 10 times higher risk of PCCRC than those examined by an endoscopist with ADR ≥20% [91], and there has also been shown that an increase in ADR up to ≥28% significantly reduced the CRC risk compared to an ADR of <19%, and an increase in ADR of 1% resulted in a decrease in CRC risk of 3 % [92].

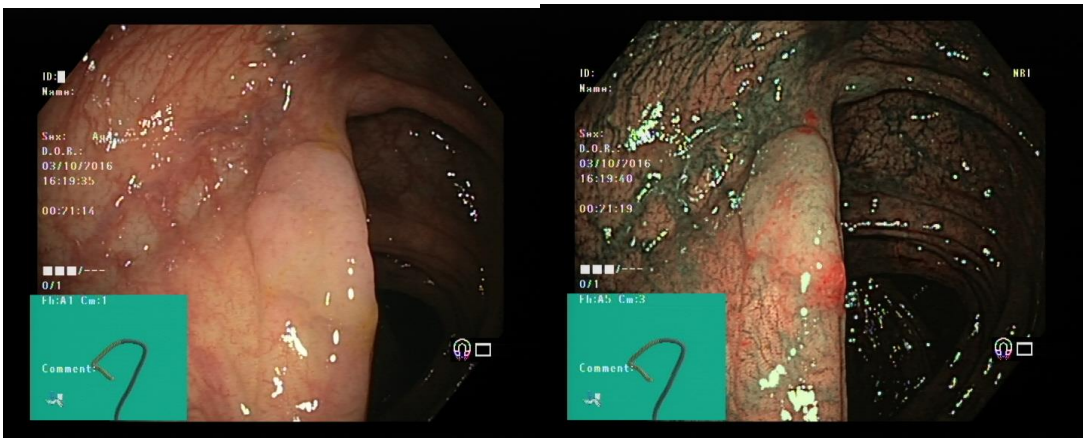


Figure 6: Polyp with (right picture) and without (left picture) NBI [40]

Polypectomy

The removal of a polyp discovered during colonoscopy is called polypectomy.

There have been developed several techniques and mechanisms to enhance the quality of polypectomy, and they will be presented below. Techniques that are no longer recommended will also be presented, as they are still in use by some endoscopists. The European guidelines for surveillance after polypectomy, will also be presented. Endoscopists use a variety of techniques for polypectomy, and up to 40% uses inadequate techniques, which can lead to increased risk of incomplete polyp resection or higher complication rates [93,94].

Diathermia: Diathermia is used both to cut the polyp and to coagulate the tissue to diminish the risk of bleeding [95]. Pure cutting current provides minimal thermal injury and effective incisions [96,97], but is associated with increased risk for post-polypectomy bleeding [98]. The use of coagulation current gives good haemostasis, but poses an increased risk of thermal injury to the colonic tissue [96], especially when performing polypectomy in the right colon [97]. It is possible to use blended current, either with manual technique where the endoscopist combines the different types of current manually, or with a process controlled by a micro-processor (e.g., Endo Cut), where the cutting and coagulation currents are blended and can be controlled by the endoscopist by using one single foot pedal. The goal is to use the correct amount and type of current to provide haemostasis as well as cutting the polyps, and to minimize the risk of thermal injury [99] The regular blended current and the newer microprocessor-controlled technique has been compared to each other in a controlled trial,

and the microprocessor-controlled technique had a better outcome with less thermal injury (p=0.02) and the resection margins were easier to evaluate for the pathologists (p=0.046) [100]. A survey among British endoscopists showed huge variation in diathermia practice [101], and this is worrying due to the fact that diathermia can cause serious complications after polypectomy [102].

Hot snare polypectomy: The conventional form for polypectomy is performed by using a metal snare that is placed around the polyp. The polyp is then "tented" (pulled into the colon lumen) and electrical current is applied through the snare, so called hot snare polypectomy (HSP)[102]. This cuts off the polyp, and hopefully diminishes the risk of post-polypectomy bleeding, because of coagulation of blood vessels [102]. As mentioned above, there are different types of electrocautery that can be used. For pedunculated polyps (Paris classification 1p) coagulation current is recommended for coagulation of blood vessels in the stalk. Sessile polyps, however, should be removed using cutting or blended current to prevent deep tissue damage of the colonic wall [99,102]. ESGE (European Society of Gastrointestinal Endoscopy) recommends HSP for polyps ≥10 mm in size, and for pedunculated polyps regardless the polyp size [103].

Cold snare polypectomy: There has been developed dedicated polypectomy snares for use without electrical current, so called cold snare polypectomy (CSP). This is also a metal snare, but thinner than the hot snare. The snare is placed around the polyp, and without "tenting" the polyp is cut by the snare [102]. ESGE guidelines from 2017 recommend cold snare polypectomy for removal of diminutive polyps (≤5 mm), and cold snare polypectomy is suggested for polyps from 6-9 mm, due to lacking evidence regarding efficacy compared to hot snare polypectomy [103]. However, there are published studies where the incomplete resection rates between HSP and CSP are comparable [79,80,104], while other studies have shown that HSP is favourable compared to CSP [105,106]. After the ESGE guideline was published, there has been published four meta-analyses on the comparative efficacy of CSP vs HSP regarding completeness of polyp resection and complications to polypectomy , where there is no difference between the groups [107-110]

Biopsy forceps: It is also possible to remove polyps with a biopsy forceps. It is often easier to place a biopsy forceps than a snare on the smallest polyps, and this method is the usual choice

for smaller polyps (<5 mm). However, it is no longer recommended due to risk of incomplete polyp resection, with a proportion of incompletely resected polyps by biopsy forceps of 17% and 48% in two studies. [111,112] The ESGE guidelines recommend snare polypectomy for all types of polyps [103].

Hot biopsy: A technique where electrical current is applied to a biopsy forceps after the polyps is grabbed by the forceps and then pulled into the colon lumen. The electrocautery destroys most of the polyp, besides the part of the polyp inside the forceps, which is taken out and submitted for histological examination. This method is no longer recommended due to high risk of perforation and burned serosa syndrome. In one study there was found necrosis of the muscularis propria in 34% of the polypectomies with hot biopsy, compared to 2 % of polypectomies by cold snare, and full-thickness inflammation of muscularis propria in 32% of hot biopsy polypectomies, and in 12% of cold snare polypectomies [113-116].

Endoscopic mucosal resection (EMR): This technique is the use of fluid injection of in the submucosal space under the polyp before polypectomy. This helps to define the extent of the polyp, and to see if it is adherent to or with growth into the submucosal space, and it helps minimize the risk of colon perforation, with a significant reduction of deep injuries after submucosal injection (p=0.009) [117]. The fluid may contain dye (mostly indigo carmine) and/or epinephrine (to minimize bleeding, with a reduction in post polypectomy bleeding from 16% without injection to 2% with injection [118]). The fluid usually consists of saline or colloid. The latter takes more time before it is dissolved into the colon tissue, and hence provides more time to perform the polypectomy.

Bleeding prevention methods: These methods are mostly used for polypectomy of stalked and large sessile polyps, and include injection of epinephrine in the stalk, detachable snares (metal loops that are placed around the polyp stalk before polypectomy), diathermia of the stalk after polypectomy and metal clips around the stalk [119-122]. The post-polypectomy bleeding risk after polypectomy of pedunculated polyps were reduced from 12.5% after injection of epinephrine in the stalk to 3.1% after the use of detachable snare before and clipping of the residual stalk after polypectomy [119]. Another study showed almost similar results for epinephrine injection and detachable snare (6.7% and 2.7% post-polypectomy bleedings, respectively), and the risk of post-polypectomy bleeding in the control group without any preventive measures was 15.1% [120]. Preventive methods for sessile polyps are not investigated as much as for stalked polyps, but a recent meta-analysis shows that preventive

clipping of the resection field after removal of large, sessile polyps in the proximal colon could decrease the risk of post-polypectomy bleedings with an OR of 0.65 for polyps ≥20 mm, especially in patients using antithrombotic agents where the OR for polyps ≥20 mm was 0.59 [123].

Bleeding treatment methods: These methods include injection of epinephrine, metal clips, coagulation with diathermia equipment, such as argon plasma coagulation (ionized argon gas and diathermia) or regular diathermia using the tip of the snare [95,124].

Surveillance guidelines: ESGE guidelines [125] states that colonoscopies with removal of ≤4 adenomas<10 mm with low-grade dysplasia or any serrated polyp<10 mm without dysplasia indicates no need for surveillance, and the patient can join the regular screening program if present, or be offered a new colonoscopy after 10 years. Surveillance colonoscopy is offered after three years for patients with removal of five or more adenomas, any serrated polyp with dysplasia or size >10 mm, any adenoma ≥10 mm or any adenoma with high-grade dysplasia. The guideline recommends surveillance colonoscopy after three to six months following removal of polyps ≥20 mm. Earlier research show that up to 52% of endoscopists do not adhere to post-polypectomy surveillance guidelines, and in a study of almost 1300 colonoscopies, the guidelines for surveillance were adhered to in only 39% of the cases [18,126-128].

Complications

Diagnostic colonoscopies (i.e. colonoscopies without polypectomy or other interventions) have a low complication risk. The perforation risk of diagnostic colonoscopies is 0.02-0.07% [129,130], and the bleeding risk in diagnostic colonoscopies is very small, but increases substantially when performing polypectomy with an OR of 10.3 for bleeding after polypectomy compared to diagnostic colonoscopy [131]

Complications after polypectomy is more frequent than in diagnostic colonoscopies, but the rate is relatively low, with a bleeding rate of 0.1-0.6% and perforation rate of 0.1% [129,130]

Risk factors for bleeding or perforation after polypectomy includes age (OR 1.72 for bleeding or perforation for patients from 60-75 years compared to 50-59 years), male sex (OR 0.67 for women for bleeding or perforation compared to men), and comorbidity defined as hospital

admissions in the 5 years prior to the colonoscopy (OR 2.29 for patients with comorbidity score ≥3 compared to patients with comorbidity score <3) [131].

Summary

Summarized, polyps in the colorectum should be removed because of potential cancer risk, and studies have shown that sigmoidoscopy screening with polyp removal reduces the incidence and mortality of colorectal cancer. Incomplete polypectomy is believed to be the reason for up to 27% of post-colonoscopy colorectal cancers [75-77]. Snare polypectomy with or without electrocautery is the recommended method for polyp removal [103]. Possible complications to polypectomy are bleedings and perforation, the latter almost always caused by electrocautery damage of the colonic wall [132]. Safe polypectomy requires complex decision-making in what polypectomy technique should be used, what type of electrocautery should be used, if preventive measures should be undertaken or if the polyp should be removed or not.

The perforation risk with cold snare polypectomy for small polyps is almost negligible, but there has been feared that the risk of incomplete polyp resection is higher in cold snare than hot snare polypectomy. Some studies show comparable incomplete resection rates [79,80,104], where others shown that hot snare polypectomy have lower incomplete resection rates than cold snare polypectomy [105,133].

Incomplete polypectomy is one of many risk factors for PCCRC [74] and is the main focus of this thesis.

Aims

The thesis *"Quality in colonoscopic polypectomy"* investigates the quality and efficacy of polypectomy practice.

More specific, the aims are:

1: To investigate whether Norwegian endoscopists use inadequate polypectomy techniques and if they follow the national guidelines for polyp surveillance.

2: To estimate the rate of incomplete polyp removal and to determine risk factors associated with incomplete polyp resection between endoscopists in Norway.

3: To compare hot and cold snare polypectomy regarding the incomplete polyp resection rate and risk of complications.

Material and methods

Paper 1 – Polypectomy survey

Participants: All board-certified gastroenterologists (consultants) in Norway who perform colonoscopic polypectomies were eligible for the study. No trainees or fellows were approached. To identify eligible endoscopists, we approached 30 Norwegian hospitals with gastroenterology departments to obtain e-mail addresses. The identified endoscopists received an electronic questionnaire by email, using commercially available online survey-software (SurveyMonkey). A maximum of two reminders were sent. The survey was conducted between April 2015 and May 2016.

Intervention: The first draft of the questionnaire was made by using the questionnaires from two earlier studies [93,94] as a basis. More questions about polypectomy technique were added to allow further evaluation of this subject. We invited about 360 gastroenterologists, surgeons, and fellows to comment on and suggest additional items to the first draft of the questionnaire. Some questions were removed, other added and some were modified according to these suggestions. Finally, seven experienced gastroenterologists were asked to test the survey. Their comments were taken into account when finalising the questionnaire. The final questionnaire included questions about methodology to assess completeness of polypectomy, complications, and adherence to post-polypectomy surveillance guidelines.

Endpoints: The primary endpoint was the proportion of endoscopists who used one or more inadequate polypectomy techniques and the proportion of endoscopists who adhered to national guidelines for post-polypectomy surveillance. Based on earlier published research and international guidelines inadequate polypectomy was defined as: use of biopsy forceps for polypectomy of polys larger than 3 mm, use of hot biopsy technique (biopsy forceps with electrocautery for polypectomy) and use of the same electrocautery output (power and type of current: cut, coagulation or blend) irrespective of the size and morphology of the polyp to be removed.

Paper 2 – Norpol

Participants: The study was conducted at four hospitals in Norway between January 2015 and June 2017. Patients aged from 50-75 years who were scheduled for outpatient colonoscopy were eligible for the study and included if they had at least one nonpedunculated polyp

≥5mm, and if they signed the informed consent before the colonoscopy. Pedunculated polyps were not included in this study. Patients who had previously undergone biopsy or attempted removal of the detected polyp were excluded, as were patients with an enhanced bleeding risk (defined as use of clopidogrel or other non-acetylsalicylic platelet inhibitor within the last 5 days before the procedure or patients with an international normalized ratio>1.8 or had failed to withdraw other oral anticoagulants before the procedure). Furthermore, patients with severe comorbidity were excluded from the trial.

In total 21 endoscopists participated in the study, of these, 9 were board-certified and 12 were gastroenterologists in training.

Interventions: All patients went through a split-dose bowel preparation of sodium picosulphate/magnesium citrate and 2-4 litres of additional fluid, depending on local procedures prior to the colonoscopy. The colonoscopes were performed using 130cm variable stiffness colonoscopes (Olympus Corp., Hamburg, Germany). The method for polypectomy was upon the discretion of the endoscopist.

After polypectomy, the polypectomy site was rinsed with water, and the endoscopist examined the area with both white light and NBI. If there was suspected residual polyp tissue, additional polyp removal was performed. After visual complete resection was achieved, biopsies were taken from the resection margins (2 biopsies from polyps < 10 mm and 4 (quadrant) from polyps ≥ 10 mm), using a 2.2 mm biopsy forceps. All polyps and corresponding biopsies were sent in separate containers with formaldehyde to the pathology department for histopathological examination. The same pathologist examined both the polyp and the corresponding biopsies, to maximise the likelihood that possible residual polyp tissue was detected, because the pathologist was aware of what type of tissue to look for.

After the polypectomy, the endoscopist recorded the following data on a dedicated paper form: Age and sex of the patient, indication for colonoscopy (screening or symptoms), polyp size (diameter in mm), polyp location (proximal for polyps located proximal to the splenic flexure, distal for polyps located in or distal to the splenic flexure), polypectomy method (with or without electrocautery, with or without submucosal injection (EMR) with contrast agent (e.g. indigocarmine), en bloc or piecemeal resection), complications and endoscopists identification. We also defined different levels of polypectomy difficulty according to the

time needed for complete polypectomy: easy (<2 min), moderate (2-5 min) and difficult (>5 min).

Endpoints: The primary endpoint was the proportion of incompletely removed polyps, defined as the presence of polyp tissue in the corresponding biopsies. Secondary outcomes include differences between endoscopists in complete polyp resection rate and risk factors that could be associated with incomplete polypectomy.

Paper 3 – Cold vs hot snare polypectomy trial

Participants: This randomized trial was conducted at five different hospitals in Norway, one hospital in Poland, one hospital in Denmark and one hospital in the US from August 2015 to January 2020. Patients ≥40 years of age scheduled for outpatient colonoscopy were eligible for the trial. If they had at least one nonpedunculated polyp sized 4-9 mm, they were included. Patients with previous biopsy or attempted polypectomy of the polyp eligible for the trial were excluded, as were patients with an enhanced bleeding risk (defined as use of clopidogrel or other non-acetylsalicylic platelet inhibitor within the last 5 days before the procedure or patients with an international normalized ratio>1.8 or had failed to withdraw other oral anticoagulants before the procedure). Furthermore, patients with severe comorbidity were excluded from the trial.

We applied block randomization using varying block sizes (4, 6 and 8). The endoscopist were unaware of the block sizes. The randomization to either hot or cold snare polypectomy was performed 1:1 on the patient level. If there was removed more than one polyp in the same patient, the same method was used.

Bowel cleansing and colonoscopies were performed according to local procedures. All endoscopists had access to instruction videos on how to perform both types of polypectomies before entering the trial.

All patients signed the consent form before start of the colonoscopy, and the signed forms were discarded after the colonoscopy if there were no eligible polyps.

Intervention: When the endoscopist discovered an eligible polyp, the size was measured using a biopsy forceps or a snare as reference. Randomization was performed using sealed, opaque

envelopes opened by a study nurse after signed consent had been obtained and an eligible polyp discovered. All the cold snare polypectomies were performed using the Exacto® cold snare (US Endoscopy, Mentor, Ohio, US), the hot snare polypectomies with the standard hot snare and electrocautery equipment at the different centres.

After polypectomy, the polypectomy site was rinsed with water and thoroughly inspected with white light and NBI (if available), and any remaining polyp tissue was removed. After visual complete polypectomy was achieved, biopsies were taken from the resection margins (2 from polyps 4-6 mm and 3 from polyps 7-9 mm), using a 2.2 mm biopsy forceps. The polyps and the corresponding biopsies were put in separate containers with formaldehyde and sent to the pathologist for histopathological examination.

After the colonoscopies, the endoscopists recorded the following data on a designated paper form: Age and sex of the patient, indication for colonoscopy (screening, symptoms or other), polyp size (diameter in mm), polyp location (colon segment), polypectomy method (with or without electrocautery, en bloc or piecemeal resection), complications and endoscopists identification.

Four weeks after the colonoscopy, all patients received a phone call from a blinded study nurse where they were asked about stomach pain, hospital referrals and bloody stools to assess late complications in terms of perforation and post polypectomy bleedings.

Endpoints: The primary endpoint was the proportion of incomplete polyp resection in each group, defined as polyp tissue present in the margin biopsies. Secondary outcomes include early and late complications (bleeding, perforation, or other complications) and factors explaining the primary outcome.

Statistics

Paper 1: Descriptive statistics for normally distributed data were presented as mean with standard deviation (SD). For assessment of risk factors that could predict inadequate polypectomy techniques, univariable logistic models were used. Explanatory variables used were endoscopists sex, age, experience (years in practice) and hospital category (university versus non-university). The final multivariable model was fitted using backward removal of variables using the Wald test with P-values ≥ 0.05.

Paper 2: The descriptive statistics for normally distributed data in this paper were presented as means. To assess the risk factors that predicted incomplete polyp resection, the unadjusted odds ratio (OR) was firs calculated using univariate logistic regression. The variables of interest were age, sex, histopathology of polyp, level of difficulty of polypectomy (polypectomy duration <2 minutes, 2-5 minutes and >5 minutes), polypectomy method (hot versus cold snare polypectomy, submucosal injection or not, en bloc or piece meal resection), location and size of polyp and the experience of the endoscopists, dichotomized to board-certified gastroenterologists and trainees). Between polyp size and level of difficulty of the polypectomy there was no interaction found, ($P \geq 0.05$). To identify explaining factors for incomplete polypectomy, logistic regression models were fitted, with backward removal of variables with a Wald test of P values ≥ 0.05. Then a multivariable logistic regression model was fitted, using the variables associated with incomplete resection in the univariate analyses. As the study was a quality assurance study, we wanted to estimate the probability of incomplete polyp resection for each endoscopist. Only endoscopists who removed 10 or more polyps in the study were included in this analysis. The variables included in this logistic regression model to adjust for case mix were polyp size, polyp location, level of difficulty of polypectomy, age and sex of patient and histopathology of polyp. In all the multivariable regression models generalized estimating equations models with compound-symmetry covariance structure were used, to take into account that one person may have had more than one polyp removed during the colonoscopy.

Paper 3: In this study, the primary aim was to evaluate whether CSP was non-inferior to HSP regarding complete polyp resection. In earlier studies, the rate of incomplete resection varied, and the studies were performed in different settings [78,105,134]. For the power calculation, there was predicted an incomplete polyp resection rate of 5% in both the CSP and the HSP groups. If there were no difference in incomplete polyp resection (i.e., 5% in both groups), a total of 600 polyps were needed to be 80% sure that the upper limit of the 95% confidence interval (CI) of the difference in incomplete resection rate between the groups would exclude a favour of the HSP group of over 5%. The choice of 5 % as the non-inferiority limit was thoroughly discussed among the investigators in this study, and 5% were considered the upper limit of a clinically acceptable difference. To evaluate non-inferiority, the difference (with 95% CI) in proportions of incomplete polyp resection between the HSP and CSP groups were

calculated for the main analysis, and an upper boundary of the 95% CI <5% would indicate non-inferiority.

We used a modified intention-to-treat approach, where randomized patients with missing pathology reports or non-polyp histology (a total of 4 patients) were excluded from analyses. All patients received a phone call after 30 days to assess complications. The patients we were unable to reach were only excluded from the analyses of late complications and included in all other analyses.

In the secondary analyses, the association between incomplete polyp resection and patient and/or polyp characteristics was calculated, using a univariate logistic regression model. Age, sex, indication for colonoscopy, Boston Bowel Preparation Scale score, polyp morphology, polyp location, polyp histology and dysplasia and polyp resection method were investigated as explaining factors. Then a multivariable logistic regression model was fitted, including randomization arm and the factors in the univariate analysis that were associated with incomplete polyp resection ($P<0.10$). Since one patient could have more than one polyp removed (i.e., clustered data), the generalized estimating equations (GEE) method with a compound symmetry covariance structure were used in all univariate and multivariate analyses, both primary and secondary.

All analyses were conducted with Stata software version 14.2 (StataCorp, College Station, Texas, United States) and SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

Ethics

In the survey (paper 1), the completing of the survey was considered as consent. In both the Norpol trial (paper 2) and the Cold Snare Trial (paper 3), all participants provided written, informed consent before start of the colonoscopy.

The survey and Norpol were both approved by the Norwegian Centre for Research Data and the need for further ethical approval was waived by the regional ethics committee of South-East Norway. The Cold Snare Trial was approved by the regional ethics committee of South-East Norway and the Institutional Review Boards at the individual hospitals. The trial is registered in a clinical trial database (http://www.clinicaltrials.gov, ID: NCT02484079).

Summary of papers

Paper 1

Polypectomy techniques among gastroenterologists in Norway – a nationwide survey

Endoscopy International Open 2018;06:E1-E9

In total 119 board-certified endoscopists (consultants) received the survey, and 70 (59%) responded. Of these, there were 58 (83%) men and 12 (17%) women, with a mean age of 51.5 years. Most of the endoscopists were experienced, 93% had performed over 1000 colonoscopies, and the mean duration of colonoscopy practise was 11,5 years. A total of 52 (74.3) endoscopists worked at non-university hospitals, and 18 (25.7) worked at university hospitals.

Overall, 28 (40%) endoscopists used one or more inadequate methods for polypectomy: Five (7.1%) endoscopists used hot biopsy forceps for polyp removal, 17 (24.3%) endoscopists did not adjust the electrocautery output dependent on type of polyp and 10 (14.3%) endoscopists used biopsy forceps for removal of polyps >3mm. Five endoscopists (7.1%) chose not to remove polyps below 4 cm in size at all. None of the investigated factors (sex, age, experience, and workplace for the endoscopists) were associated with inadequate polypectomy technique.

Twelve (17%) endoscopists stated that they did not have written polyp surveillance guidelines at their hospitals. However, in two hospitals the results were not consistent, as some endoscopists stated that they had written guidelines while other stated they did not. Forty-eight (71%) endoscopists stated that they used the Norwegian guidelines for polyp surveillance, 10% that they used local guidelines, 3 % that they used British guidelines and 15 % that they used other guidelines. One endoscopist stated that surveillance was upon the endoscopist's discretion. In the multivariate analysis, adjusted for sex, age and experience of the endoscopist, working at a university hospital was associated with not adhering to the national guidelines, with an OR of 11.8 (95% CI 3.0-46.2, p=0,001), whereas level of experience, age, sex and years of practice was not associated with not adhering to guidelines.

Interestingly, 30 (43%) of the endoscopists had never performed cold snare polypectomy, and of those who used the technique, 20 (47%) did not use the correct technique but use the same as for the hot snare polypectomy, where the polyp is pulled into the colon lumen before

polypectomy. With the cold snare technique, the polyp should not be pulled into the lumen, to avoid the snare slipping of the polyp.

Paper 2

Incomplete endoscopic resection of colorectal polyps: a prospective quality assurance study

Endoscopy. 2021 Apr;53(4):383-391. doi: 10.1055/a-1243-0379

In total, 246 patients with 339 polyps were included from four different hospitals. After excluding 12 polyps with electrocautery damage in the biopsies that would preclude the histopathological examination of incomplete resection, 327 polyps in 246 patients were eligible for analyses.

Polyp size ranged from 5 mm to 40 mm, with mean polyp size 9.1 mm. A total of 197 (60.2%) had adenomatous histology, and 64.5% of the polyps were located proximal to the splenic flexure. Out of the 21 participating endoscopists, ten contributed with >10 polyps.

Of polyps sized 5-19 mm, 44 (14.6%) polyps were incompletely resected. Increasing polyp size was associated with incomplete resection in the univariate analysis, and the unadjusted OR for incomplete resection was 1.6 (95% CI 1.0-2.5) for every 5-mm increase in polyp size. Sessile serrated polyps were incompletely resected in 24 of 65 (36.9%) of the polypectomies, whereas adenomas were incompletely resected in 11 of 184 (6.0%) of the polypectomies. The adjusted OR for incomplete resection of SSPs was 10.9 (95% CI 3.9-30.1) and for incomplete resection of hyperplastic polyps 4.2 (95% CI 1.7-10.4) compared to adenomas. For polyps ≥20 mm, the incomplete resection rate was 38.5%.

When investigating the factors that could explain incomplete polyp resection, only polyp histology and polyp location in the proximal colon were independent risk factors in the multivariate regression model, whereas polyp size, polyp morphology, resection method, piecemeal vs en bloc resection, the use of EMR or not, the endoscopists experience and the level of difficulty of the polypectomy were not associated with incomplete polyp resection.

There was no difference between experienced and inexperienced endoscopist, with an incomplete resection rate of 14.0% and 14.2%, respectively. For polyps located in the proximal part of the colon, the OR were over twice as high compared to polyps in the distal colon. (OR 2.8, 95% CI 1.0-7.7). The other variables (size, morphology, en bloc or piecemeal

resection, use of EMR, endoscopists experience and level of difficulty) were not associated with incomplete polyp resection in the multivariate logistic regression model.

The incomplete resection rate for each endoscopist varied from 6.7% to 34.6%, adjusted for case-mix, but in the multivariate logistic regression analysis, none of the endoscopists performed statistically worse than the best performing endoscopist.

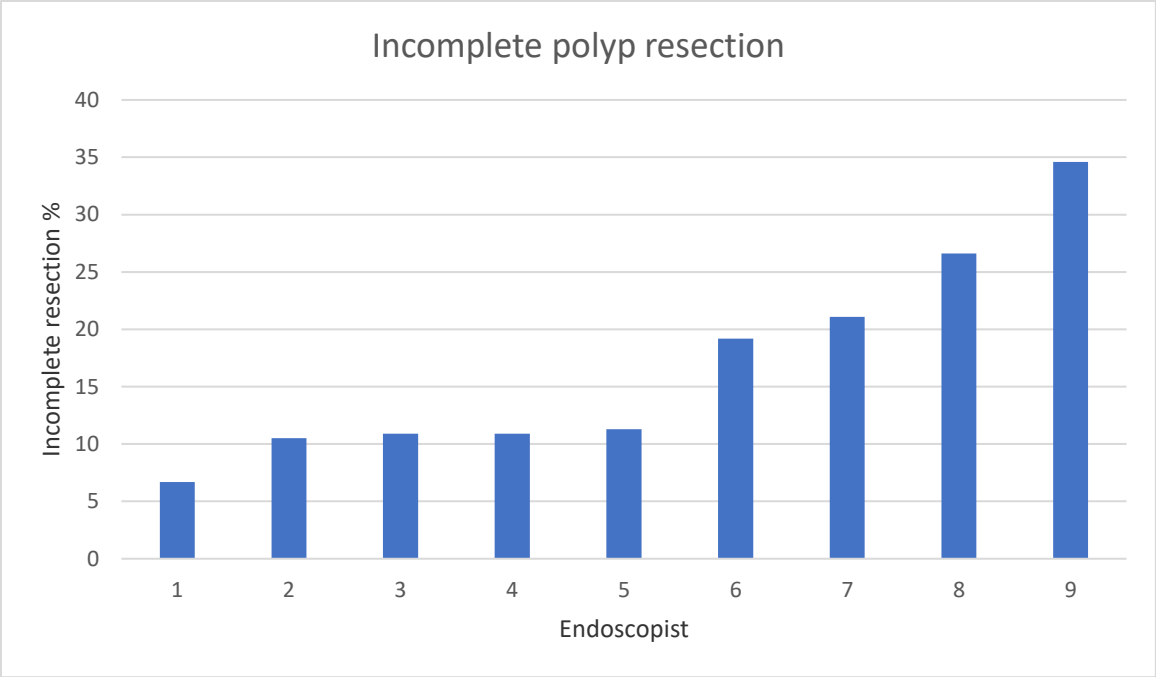


Figure 7: Rate of incompletely resected polyps for individual endoscopists

In one patient, the polypectomy resulted in perforation of the colon. This was after hot snare polypectomy of a 30 mm SSL in the coecum. The patient underwent successful surgery. Altogether eight patients had intraprocedural bleedings that were successfully treated during the same colonoscopy session, three patients after polypectomy and five patients after biopsies from the resection margins.

Paper 3

Cold snare versus hot snare polypectomy for polyps sized 4-9 mm. A randomized, controlled trial.

Endoscopy. 2022 Jan 10. doi: 10.1055/a-1734-7952.

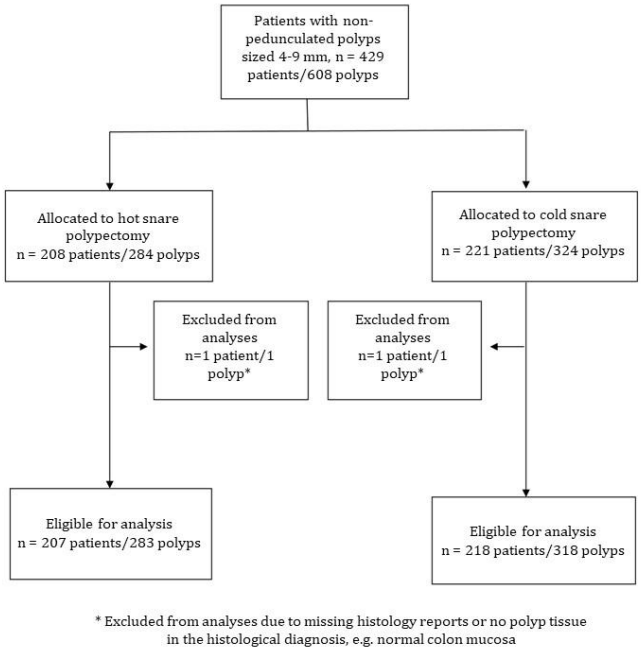


Figure 8: Flowchart Cold vs hot snare polypectomy trial

In total, 429 patients with 608 polyps were eligible and randomized. Out of these, four patients with a total of seven polyps were excluded from analyses due to missing histology report or non-serrated or non-adenomatous histology. 425 patients with 601 polyps were included in the analyses. There were 207 patients with 282 polyps randomized to the hot snare group (HSP), and 218 patients with 318 polyps randomized to the cold snare group (CSP). Mean age was 61.9 and 63.1 years in the HSP and CSP groups, respectively. In the CSP group 34 (10.8%) polyps were incompletely resected, while in the HSP group 21 (7.4) polyps were incompletely resected. The risk difference, after adjusting for clustering, was 3.2 % (95% CI -1.4-7.8), hence we could not claim non-inferiority for cold snare polypectomy compared to hot snare polypectomy, since our pre-defined non-inferiority margin was chosen to be 5 %. In multivariate logistic regression analysis only polyp histology of SSL (OR 3.96, (95% CI 1.63-9.66)) or hyperplastic polyp (OR 2.52 (95% CI 1.30-4.86)) were independent risk factors for incomplete resection. Almost all polyps were removed en bloc, and there was no difference between the groups: in the HSP group 280 (98.9%) polyps were removed en bloc, and in the CSP group 309 (97.2%) polyps were removed en bloc.

Seven patients had a bleeding that needed intervention during colonoscopy, five were related to the polypectomy and two from the margin biopsies. Of the five bleedings after polypectomy, four (1.8%) were after CSP and one (0.5%) after HSP. Four weeks after the

procedure the patients received a phone call asking for late complications. We were able to reach 411 (95%) patients. There were no serious adverse events; eight (1.9%) patients in the CSP group and three (1.5%) in the HSP groups reported visible blood in stool within four seeks, but none were admitted to the hospital. There were two patients, one in each group, who reported abdominal pain after the procedure, but neither of them contacted any health services.

Discussion

This thesis investigates the quality and efficacy of polypectomy in Norway. Our results show that many endoscopists use inadequate polypectomy techniques, and that up to 16% of polyps from 5-40 mm in size are incompletely resected. We also showed that cold snare polypectomy is a safe and effective procedure that can be used for small polyps.

Colorectal cancer is a common malignancy [1], and there are over 100 000 colonoscopies performed each year in Norway [135]. CRC may develop from adenomas and sessile serrated lesions, and endoscopic examination of the colon with polypectomy has been shown to reduce CRC incidence in randomized trials [8-11,136]. Patients examined by an endoscopist who detects adenomas in a high proportion of patients have reduced risk of developing CRC compared to patients examined by endoscopists with low adenoma detection rate [91,92]. It is estimated that up to 27% of CRCs can be caused by incomplete polypectomy [75-77]. This underlines the importance of achieving and maintaining high quality in colonoscopy and polypectomy practise. The two most feared complications of polypectomy are perforation and bleeding [130,132]. Perforation occurs in less than 0.1% of colonoscopies [130], and most of the perforations are due to polypectomy using electrocautery. Cold snare polypectomy does not have the perforation risk as hot snare polypectomy [102,137,138], but it has been feared that CSP poses a larger bleeding risk than HSP. However, post-polypectomy bleeding risk has been comparable to or lower in CSP than HSP in randomized trials [78-80,104,106,107,139,140], so we know that CSP is a safe procedure. In the recent years there have been several studies, including the Cold Snare Trial in this thesis, that have shown that the incomplete resection rate for CSP is comparable to that of HSP [78-80,104,106,107,110,139,140], hence cold snare polypectomy could be used in routine colonoscopy practice for removal of polyps up to 10 mm. Recent studies have also shown that CSP could be safe and effective also for polyps ≥10 mm, with adverse events rate of 0.9 %

and residual SSP rate of 2.9% in a metaanalysis from 2022 [141], and with no significant difference in complication rates for polyps from 10-20 mm compared to HSP [142].

Survey – the use of inadequate polypectomy techniques.

In our survey we found large variation in the choice and use of polypectomy techniques between endoscopists in Norway. This corresponds to the findings of the two earlier surveys on the subject, performed in Israel and in USA [93,94]. One of the more surprising findings was that 7% of endoscopists do not remove polyps smaller than 4 mm at all. There is currently no way to be sure during colonoscopy that a given polyp will not have malignant potential, and therefore all should be removed. A literature review found that 6% of adenomas sized 1-9 mm progressed to advanced adenomas over a two-to-three-year time period [143], and this underlines the importance of removal of also polyps below 1 cm in size. We do not know why some endoscopists choose not to remove the smallest polyps, but it might be because the polyps are believed to be hyperplastic and of little clinical significance. The problem with this approach is that the ability of endoscopists to accurately separate hyperplastic polyps from adenomas is poor, even with imaging enhancing technologies like NBI. In a community setting, the specificity and sensitivity of accurately diagnose small lesions with NBI was 77.0% and 78.8%, respectively [62]. In another study, performed at a tertiary referral center, [63], the negative predictive value for high-confidence characterizations of small polyps in rectum and sigmoideum was 94.7% using NBI. The endoscopists participating in the trial had little or no experience with NBI and were intensively trained before enrolment. The sensitivity and specificity of high-confidence characterization in rectosigmoid was 88.4% and 78.3%, respectively. Under half of the responders to our survey used NBI regularly, and very few used chromoendoscopy, both techniques that could improve diagnostic accuracy.

To achieve reduction in CRC incidence and mortality, all polyp tissue should be removed by polypectomy. It is alarming that 14% of endoscopists used biopsy forceps for removal of polyps larger than 3 mm in diameter. Already before the survey was done, biopsy forceps was considered inadequate for removal of polyps <4mm [111,112], and now the ESGE guidelines recommend snare polypectomy for polyps of all sizes [103]. Earlier studies showed an incomplete resection rate for biopsy forceps polypectomy of 3- and 5-mm polyps of 17% and 47%, respectively [144,145], so the risk of residual polyp tissue are high when using biopsy forceps for removal, and the technique should be abandoned.

As mentioned earlier, the most serious complication to polypectomy is perforation. In our survey, five (7.1%) endoscopists stated that they used hot biopsy technique for polyp removal. This technique is associated with increased risk for perforation and burned serosa syndrome [113,114]. These studies were published already in the 90s, and why some endoscopist still chose to use the technique when this survey was performed in 2016 remains unclear.

In our survey, only 17 (24.3%) used CSP, and of these did 41.7% use the same technique when using the cold snare (pulling the polyp into the colon lumen before snaring) as when using the hot snare. It should be noted that the CSP was a relatively new technique when our survey was made, so this could explain why the numbers were so low. However, there was published good data on the safety of CSP already in 2012 and 2014 [105,146], so it is somewhat surprising that the CSP technique was not more widespread among the endoscopists. We think that the fear of bleeding probably was the main reason for not endorsing the cold snare technique.

Even though all our respondents were experienced, and their mean time of endoscopy practice was 11.5 years, still 25% of our responders did not adjust the electrocautery settings when removing different types of polyps. The use of the different types of electrocautery outputs gives different effects and was believed to reduce the risk of complications in the early 2000s [102], but in 2020 there was published a large, randomized trial studying the effect of blended versus forced coagulation on complications and polyp recurrence, where there was found no difference between the groups. In 7.2% and 7.9% of the polypectomies, respectively, there was registered a serious adverse event, and for the incomplete resection rate the numbers were 96% and 95%. Recurrent polyp tissue at surveillance was found in 17% of patients in both groups [147]. Maybe the categorization of not adjusting the electrocautery outputs as inadequate was in fact inadequate. However, the endoscopists also seemed to be ignoring the possibility to adjust the power output (in watt) of the diathermia equipment.

We also found that almost 1/3 of our responders did not adhere to the national guidelines, which are almost identical to the ESGE guidelines [103] for polyp surveillance. However, the Norwegian guidelines do not recommend colonoscopy after 10 years for low risk patients [148]. The lack of adherence to guidelines is alarming because all responders worked at either public hospitals or hospitals on contract with the health authorities, and one would expect the endoscopists both to be aware of and adhere to the national guidelines. Interestingly, we found that endoscopists working in a university hospital were more likely to be non-adherent

to the national guidelines than endoscopists working in non-university hospitals. The results might be somewhat biased, because some endoscopists from the same hospitals were not consistent in their replies, where some stated they had written guidelines they adhered to, and others denied the existence of written guidelines.

The most important strength of the survey is that all endoscopy units in Norway were invited to reply to the survey. This provided answers from a variety of endoscopists spread over all of Norway, and from different types of hospitals (university and non-university) and from different areas in the country (both cities and more rural areas). Interestingly, the sex distribution among the respondents in the survey was almost the same as in the register of board-certified gastroenterologists in Norway. There were also some limitations to this study. There will always be a risk of selection bias without complete response rate. We had a response rate of 59%, and we cannot know if the respondents are representative of all invited endoscopists. We compared the answers of the early responders (57 endoscopists) to the answers of the late responders (13 endoscopists who replied after the last reminder), and the groups were comparable in their answers. Research show that late responders often are more like non-responders than early responders [149]. Hopefully, this indicates that our results are generalizable to Norwegian endoscopists.

All in all, a substantial number of endoscopists use inadequate techniques for polypectomy, and do not adhere to national guidelines for polyp surveillance.

Norpol – incomplete polyp resection

In our clinical polypectomy quality assurance study, we found that 16.0% of the polyps were incompletely resected. This number is higher than in previous studies, e.g., the CARE-study from 2014 [78], where the incomplete resection rate was 10.1% for polyps between 5 and 20 mm. In addition to the CARE study, two other studies reported polyp recurrence rates of 16% and 31.7% in polyps ≥20 mm [150,151], whereas we in our study found residual polyp tissue in the biopsies in 38.5% of the polyps ≥20 mm. The two latter studies had a different methodology than the CARE study and our study, where they detected recurrence at a second colonoscopy, and they did not take biopsies from the resection margins at the index colonoscopy. In contrast, an Italian study where SSLs were removed by cold snare EMR, the incomplete resection rate for polyps ≥ 10 mm was only 1.2% [81]. This huge discrepancy is difficult to explain. In our study almost all SSLs of larger size was removed by hot snare EMR. After this study was published, there have been more studies on cold snare EMR, with

residual polyp tissue at surveillance colonoscopy after 150 days of 5.5% after cold snare EMR of polyps >20mm [152], another study found recurrent polyp tissue at surveillance colonoscopy in 46% of the cases [153]. In a meta-analysis from 2019 investigating CSP with EMR of polyps ≥10 mm had an incomplete resection rate of 0.7%, and residual polyp tissue at surveillance in 4.1% [154]. There should be performed randomized studies for polyps ≥10 mm to compare hot snare EMR and cold snare EMR.

The most important factor for incomplete polypectomy was serrated polyp histology, almost 40% of the SSLs were incompletely resected in our study. Since SSLs are believed to be associated with up to 30% of CRCs [51], it is important to be vigilant when performing the polypectomies to ensure complete resection [155,156]. There is no doubt that better techniques for polypectomy of SSLs are needed, and the promising results from the Italian cold snare EMR trial [81] shows that maybe cold snare EMR should be the method of choice. In our study, the resection margins were inspected with both white light and NBI after removal, but the incomplete resection rate was still high. One explanation might be that use of electrocautery makes evaluation of the resection margins more difficult during colonoscopy.

In addition to polyp histology of SSL, polyp location in the proximal colon was an independent risk factor for incomplete polyp resection. When we investigated possible correlations, this finding was independent of both polyp histology and polyp size. This implies that polypectomy in the proximal colon is more technically challenging than in the distal colon. The finding of higher incomplete resection rate in the proximal colon is in accordance with previous reports [157,158]. Another important aspect of polypectomy in the proximal colon is that post-colonoscopy cancers are more frequent in the proximal colon [159,160], and polypectomy of proximal polyps is more associated with complications [158]. Post-colonoscopy cancers can be due to new lesions, overlooked lesions or incompletely removed lesions [76,161,162]. The two latter factors are procedural factors that can be modified, and they are the factors that in studies have been shown to explain the majority of post-colonoscopy cancers [77,162].

In our study, size and the level of difficulty scored by the endoscopists were not independent risk factors for incomplete polypectomy. This was surprising, but due to small sample size, this result should be interpreted with caution. However, it is likely to believe that endoscopists are more aware when removing larger and “difficult” polyps, and this might explain the result.

Another interesting result from our study was that being an experienced endoscopist did not influence the rate of incomplete polyp resection. One may argue that these results is not surprising, given that the experienced endoscopists supervised the polypectomies done by the endoscopists in training. However, this is normally not the case in Norway. Endoscopists in training have an introduction to polypectomy and are shown how to do it, and after that they perform polypectomies without direct supervision. There are of course board-certified endoscopists available for help if needed. It might be that the unexperienced endoscopists in our study were extremely skilled, but the finding of no difference between the groups might have other important implications: increasing experience does not necessarily translate into improved clinical practise, and maybe the experienced endoscopists are not as good teachers for trainees as one would expect.

The incomplete resection rate varied substantially between endoscopists as well, from approximately 10% to 30 % in the unadjusted analysis. In the multivariable logistic regression analyses the two endoscopists with statistically significantly poorer performance than the best performing endoscopists had very wide confidence intervals, and the study was not powered to analyse these differences. Hence, these results should be interpreted with caution. However, the difference in incomplete resection rate between endoscopists is interesting and underlines the main point this trial tells us: More education in the field of polypectomy is needed. It might be that our results are not generalizable if trainees are more closely supervised hands-on in other settings. The CARE-study had similar results, with a range from 6.5% to 22.7% incomplete resection rate between endoscopists [78] In a study on simulation-based polypectomy training showed that this type of training improved the polypectomy skills of the participating endoscopists with an improvement from 51% competent endoscopists before training to 71% after training [163] and another study using instruction videos also report an increase in polypectomy skills after watching the videos [164], so it seems that polypectomy technique is improvable.

The inclusion of all types of polyps sized above 5 mm, and the multicentre design are strengths of the Norpol trial. The fact that all centres were non-university hospitals increases the external validity of the results. However, the method of using margins biopsies to assess complete polyp resection has not been validated, and the clinical significance of residual polyp tissue is not clear. Some polyps may not increase in size, and some might even regress, and not all polyps progress to cancer [54,143]. We cannot rule out selection bias, as this study

was conducted in busy outpatient clinics with many participating endoscopists, so consecutive inclusion of patients was impossible to achieve. Therefore, it might be that polyps considered "easy to remove" were included in the study. Our results might represent the lower boundary of incompletely resected polyps, but it was still higher than earlier reported in the comparable CARE-trial [78].

The follow-up of the CARE-study published in 2021 showed a risk difference for any metachronous neoplasia between segment with earlier incomplete resection compared to segments without incomplete resection of 28% [165], and it was also shown that incomplete polyp resection was the strongest risk independent risk factor for metachronous neoplasia with an OR of 3.0 in multivariate analysis. This shows that completeness of polypectomy does matter.

Cold snare trial – hot versus cold snare polypectomy of small polyps

The incomplete resection rate for CSP and HSP was 10.8% and 7.4 %, respectively. We could not confirm non-inferiority of CSP, but the incomplete resection rates (IRR) and complications did not differ between the two groups in secondary analyses. The incomplete resection rate difference of 3.2% is in accordance with other studies, reporting rate differences between 0.5% and 7% [79,80,104,106,107,139]. The most recent meta-analysis [110] found a difference in IRR between HSP and CSP for polyps from 1-10mm of 3.1%.

Even if the difference between the groups in IRR is an accordance with other studies, the incomplete resection rates for each group are slightly higher in our study than in earlier trials. A meta-analysis published in 2018 [108] reported an incomplete resection rate for CSP of 5.0% and for HSP 6.0%, but a recent meta-analysis from 2020 [110] found incomplete resection rates of 14.2% for HSP and 17.3% for CSP for polyps from 1-10 mm, which is higher than in our study. In the latter meta-analysis, there was included 32 studies, whereas in the metaanalysis from 2018 only 7 studies were included. The study from 2020 were performed at both academic and non-academic centres, and the incomplete resection rate was determined either by margin biopsies, resection margin of polyp or visually during colonoscopy [110]. Our study was performed in four different countries at altogether eight different centres, in both university and community hospitals. It is difficult to conclude on why the incomplete resection rate was higher in this meta-analysis than in our study, but maybe the different use of assessment of incomplete resection matters.

As in the Norpol trial, hyperplastic and sessile serrated histology were independent risk factors for incomplete resection in multivariate analyses. In the CARE-study from 2013 [78], however, the incomplete resection rate for hyperplastic polyps was only 3.1%. Both the Norpol trial and the CARE study included polyps larger than 9 mm, so the results are not directly comparable to this present trial. The result for SSLs correlates with the Norpol trial, where the OR for incomplete resection of SSLs was 8.5 compared to adenomas, and in this trial the OR for SSLs compared to adenomas was 5.3. There was no difference between the CSP and HSP groups in the complete resection rate for SSLs, and this correlates with other studies [79,104]. As mentioned earlier, SSLs are believed to be precursor of up to 30% of CRCs [143], and it is important to be aware of the potential of incomplete resection. The use of submucosal injection (EMR) before polypectomy might be an important adjunct. In the beforementioned Italian study of cold snare removal with EMR [81], all the included polyps were from ≥10 mm in size and were removed by cold snare polypectomy after submucosal injection of fluid (cold snare EMR). In this study there was an incomplete resection rate of 1.2%. Another study comparing hot snare EMR to cold snare polypectomy in polyps <10 mm found that EMR was superior to CSP for removal of polyps 6-10mm [106]. In a study with 155 patients with 164 polyps by Papastergiou et al [80] cold snare EMR of small polyps is reported to be non-inferior to hot snare EMR, with an incomplete resection rate of 7.2% in the CSP group and 3.7% in the HSP group, and the difference between the two groups was 3.5%. However, the 95% CI for the difference was -4.15 to 11.56, which exceeded the predefined non-inferiority margin of 10%, hence, as in this trial, non-inferiority could not be proven. Unfortunately, we have no data on the use of EMR in our study, so we are not able to compare the incomplete resection rates with or without EMR.

Another interesting finding in this study is that piece meal polypectomy was not correlated with the polypectomy method. We fitted a multivariable model with piece meal resection as outcome variable, and only size from 7-9 mm was an independent risk factor for piece meal resection, and CSP did not increase the risk of piecemeal polypectomy. There were only 12 cases of piece meal polypectomy in this study, so the risk of piecemeal polyp removal in small polyps is very low.

We had very few complications in this study, and this finding is the same as in earlier studies [78-80,104,106,107,140], including our own Norpol trial. The highest reported intraprocedural bleeding risk was 3.6% in the CSP group, and all these bleedings were

successfully treated endoscopically during the same colonoscopy procedure. The lowest reported bleeding risk was 0% in the CSP groups and 0.5% in the HSP group [79]. In this present study, as in the others mentioned above, there was no statistically significant difference in bleeding risk between the CSP and HSP groups.

The randomized design and the inclusion of hospitals from four different countries are the two largest strengths of this study and makes the results generalizable to everyday polypectomy practice in many countries. The inclusion time in this study was quite long due to local circumstances and time-restrictions, and a potential selection cannot be ruled out, as in the Norpol trial. However, the randomized design hindered the selection bias in this trial.

The measure of incomplete resection is not standardized. In this trial we used biopsies from the resection margins. But the gold standard would probably be to perform a surveillance colonoscopy to look for polyp recurrence. However, the timing of the surveillance colonoscopy should also be discussed. Should it be done after six months, one year or even later?

The chosen non-inferiority margin of 5% could also be discussed. In the article on adenoma detection rate (ADR) and post-colonoscopy cancer in 2014, Corley et.al [92] found that each 1% reduction in ADR resulted in 3% increased risk for post-colonoscopy cancer. If we assume that an incompletely removed adenoma has the same risk of developing into CRC as an unremoved adenoma, a difference in incomplete resection rate of 3 % (from 7% to 10%) in a population of 400 persons, would equal a difference in ADR of 0.8%, if the ADR was assumed to be 25% in the first place. This tells us that maybe 5% non-inferiority margin is too high, and we should have chosen an even lower number.

In conclusion, both cold and hot snare polypectomy of small polyps are safe procedures with very low complication rates, but the clinical relevance of incompletely resected polyps should be further investigated in trials using surveillance colonoscopies.

Quality of polypectomy – how can it be improved?

The results from this thesis show that there are need for improvement of the quality of polypectomy. The finding of no difference between experienced endoscopists and endoscopists in training shows that the need for better education in polypectomy technique is not referred to the initial training of new endoscopists but should be a continuous focus during the career. However, it cannot be ruled out that the lack of good education in the beginning of

the endoscopy career propagates throughout the career. In our study only about 60% reported that there had been lectures about polypectomy technique in their internal education program over the last two years, so there is clearly room for improvement. In Norway, gastroenterologists in training and board-certified gastroenterologists both have the opportunity to attend different training courses in hands-on colonoscopy available at "The Endoscopy School", under the supervision of trained instructors.

There have been few studies conducted addressing education of endoscopists in polypectomy techniques. Van Doorn [166] tested a lecture-based polypectomy training program, where endoscopists recorded five polypectomies. After this, they attended three classes with polypectomy technique education, and thereafter they recorded five additional polypectomies. The latter five polypectomies were subject to evaluation by the Direct Observation Polypectomy Skills (DOPyS) method [167]. DOPyS is a set of measures an experienced endoscopists can use to assess the quality of polypectomy (e.g., optimizing polyp position, choosing the correct snare type and size, using appropriate polypectomy technique, uses adequate amount of submucosal injection when needed, ensures adequate haemostasis). In Van Doorns study, there was no statistically significant difference between the before and after polypectomies, and the authors concluded that direct observation and hands-on supervision in the endoscopy suite by experienced endoscopists are the best ways to improve polypectomy skills. This was not tested in their study, though. One study used report cards [164], where the endoscopists recorded their baseline DOPyS score before watching polypectomy instruction videos, and then recorded their DOPyS score after watching the videos. The increase in DOPyS score was only statistically significant for diminutive polyps. In conclusion, the DOPyS method might be a good way to improve polypectomy skills, but it has yet to be fully validated [168].

A way to assess each endoscopists polypectomy technique regarding completeness of polypectomy can be to take biopsies after polypectomy like we did in both the Norpol and the Cold Snare trial. This way the endoscopist could find his/her own incomplete resection rate. The biopsies did not pose any particular problems or complications, so it would be a safe way to ensure complete polypectomy. However, we do not know the polyp recurrence rate in polyps with remaining polyp tissue in the biopsies. Earlier studies have either used the biopsies from the resection margins or a second colonoscopy looking for recurrent polyp tissue to measure the incomplete resection rate, but in 2021 there was published a study

investigating polyp recurrence after incomplete polyp resection [165], that showed an increased risk of recurrence in colonic segments with earlier incomplete polyp resection (risk difference of 28%, 95% CI 9%-47%), but we still do not know if this results in higher cancer incidence. Therefore, the collection of margin biopsies should not be implanted as routine methodology without more studies. As shown in the Norpol trial, case-mix influences the results for the individual endoscopists and must be taken into account if this kind of method should be implemented.

Conclusions

There was great variability in the choice of polypectomy techniques in Norway.

Many endoscopists used outdated methods for polypectomy.

Many endoscopists did not adhere to national guidelines for surveillance after polypectomy.

Incomplete polyp resection was frequent in an unselected, outpatient cohort, with serrated histology and polyp located in proximal colon as independent risk factors for incomplete polyp resection.

Although we could not prove non-inferiority, there was no statistical difference in incomplete resection rate between hot and cold snare for small polyps. Cold snare could be used safely in routine colonoscopy practise.

Improved education of endoscopists and quality assurance are important measures to reduce the risk of incomplete polypectomy.

Future perspectives

The most interesting subject to investigate further is the clinical importance of residual polyp tissue with colorectal cancer incidence and mortality as outcomes. This would require a large prospective trial, with many patients included. As mentioned earlier, it is estimated that incomplete polypectomy is the reason for up to 27% of interval cancers [75-77], but as of now no one has investigated this thoroughly in a prospective trial. Some studies have investigated polyp recurrence at a second colonoscopy [150,151], but without taking biopsies at the first colonoscopy. An interesting trial would be to take biopsies after polypectomy at the index colonoscopy, and tattooing the resection site, and then follow the patients with surveillance colonoscopies to investigate polyp recurrence to see if the biopsy results correspond with the

polyp recurrence results. This trial could be designed as a randomized controlled trial with two arms: hot and cold snare polypectomy.

Whether education of endoscopists improves polypectomy performance should also be investigated further. In Norway we have “the Endoscopy School”, and it would be interesting to look at polypectomies performed before and after attending polypectomy classes here, and the DOPyS-method could also be further evaluated and investigated in larger trials, preferably multicentre and multinational studies to increase generalizability.

References

1. Favoriti P, Carbone G, Greco M et al. Worldwide burden of colorectal cancer: a review. Updates in surgery 2016; 68: 7-11
2. Cardoso R, Guo F, Heisser T et al. Colorectal cancer incidence, mortality, and stage distribution in European countries in the colorectal cancer screening era: an international population-based study. Lancet Oncol 2021; 22: 1002-1013
3. Health NIoP. Kreft i Norge. In; 2022
4. [Anonymous]. Cancer Registry of Norway, Cancer insidence, mortality, survival and prevalence. In; 2020
5. Registries N-AotNC. Prediction - Trends. 2022, DOI:
6. Raffle A.E MA, Gray JAM. . Screening: Evidence and Practice. 2nd ed. Oxford, UK: Oxford University Press 2019. 2019, DOI:
7. Organization WH WJ, Jungner G. The principles and practice og screening for disease. Geneva: World Health Organization. 1966, DOI:
8. Holme O, Loberg M, Kalager M et al. Effect of flexible sigmoidoscopy screening on colorectal cancer incidence and mortality: a randomized clinical trial. Jama 2014; 312: 606-615
9. Atkin WS, Edwards R, Kralj-Hans I et al. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. Lancet (London, England) 2010; 375: 1624-1633
10. Holme O, Schoen RE, Senore C et al. Effectiveness of flexible sigmoidoscopy screening in men and women and different age groups: pooled analysis of randomised trials. BMJ (Clinical research ed) 2017; 356: i6673
11. Lin JS, Piper MA, Perdue LA et al. Screening for Colorectal Cancer: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. Jama 2016; 315: 2576-2594

12. Myers DJ, Arora K. Villous Adenoma. In, StatPearls. Treasure Island (FL): StatPearls Publishing

13. Pino MS, Chung DC. The chromosomal instability pathway in colon cancer. Gastroenterology 2010; 138: 2059-2072
14. Boland CR, Goel A. Microsatellite instability in colorectal cancer. Gastroenterology 2010; 138: 2073-2087.e2073
15. Leggett B, Whitehall V. Role of the serrated pathway in colorectal cancer pathogenesis. Gastroenterology 2010; 138: 2088-2100
16. Carlsson G, Petrelli NJ, Nava H et al. The value of colonoscopic surveillance after curative resection for colorectal cancer or synchronous adenomatous polyps. Arch Surg 1987; 122: 1261-1263
17. Winawer SJ, Zauber AG. The advanced adenoma as the primary target of screening. Gastrointestinal endoscopy clinics of North America 2002; 12: 1-9, v
18. Hassan C, Antonelli G, Dumonceau JM et al. Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2020. Endoscopy 2020; 52: 687-700
19. O'Brien MJ, Winawer SJ, Zauber AG et al. The National Polyp Study. Patient and polyp characteristics associated with high-grade dysplasia in colorectal adenomas. Gastroenterology 1990; 98: 371-379
20. Heitman SJ, Ronksley PE, Hilsden RJ et al. Prevalence of adenomas and colorectal cancer in average risk individuals: a systematic review and meta-analysis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2009; 7: 1272-1278
21. Rex DK, Lehman GA, Hawes RH et al. Screening colonoscopy in asymptomatic average-risk persons with negative fecal occult blood tests. Gastroenterology 1991; 100: 64-67
22. Rex DK, Lehman GA, Ulbright TM et al. Colonic neoplasia in asymptomatic persons with negative fecal occult blood tests: influence of age, gender, and family history. The American journal of gastroenterology 1993; 88: 825-831
23. Rex DK. Colonoscopy: a review of its yield for cancers and adenomas by indication. The American journal of gastroenterology 1995; 90: 353-365
24. Pendergrass CJ, Edelstein DL, Hylind LM et al. Occurrence of colorectal adenomas in younger adults: an epidemiologic necropsy study. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2008; 6: 1011-1015
25. Williams AR, Balasooriya BA, Day DW. Polyps and cancer of the large bowel: a necropsy study in Liverpool. Gut 1982; 23: 835-842
26. Ben Q, An W, Jiang Y et al. Body mass index increases risk for colorectal adenomas based on meta-analysis. Gastroenterology 2012; 142: 762-772
27. Wolin KY, Yan Y, Colditz GA. Physical activity and risk of colon adenoma: a meta-analysis. Br J Cancer 2011; 104: 882-885
28. Nguyen SP, Bent S, Chen YH et al. Gender as a risk factor for advanced neoplasia and colorectal cancer: a systematic review and meta-analysis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2009; 7: 676-681.e671-673
29. Lieberman DA, Holub JL, Moravec MD et al. Prevalence of colon polyps detected by colonoscopy screening in asymptomatic black and white patients. Jama 2008; 300: 1417-1422
30. Aune D, Chan DS, Vieira AR et al. Red and processed meat intake and risk of colorectal adenomas: a systematic review and meta-analysis of epidemiological studies. Cancer Causes Control 2013; 24: 611-627

31. Xu X, Yu E, Gao X et al. Red and processed meat intake and risk of colorectal adenomas: a meta-analysis of observational studies. Int J Cancer 2013; 132: 437-448
32. Sninsky JA, Shore BM, Lupu GV et al. Risk Factors for Colorectal Polyps and Cancer. Gastrointestinal endoscopy clinics of North America 2022; 32: 195-213
33. Bujanda L, Cosme A, Gil I et al. Malignant colorectal polyps. World journal of gastroenterology 2010; 16: 3103-3111
34. Kurome M, Kato J, Nawa T et al. Risk factors for high-grade dysplasia or carcinoma in colorectal adenoma cases treated with endoscopic polypectomy. European journal of gastroenterology & hepatology 2008; 20: 111-117
35. Winawer SJ, Zauber AG, O'Brien MJ et al. Randomized comparison of surveillance intervals after colonoscopic removal of newly diagnosed adenomatous polyps. The National Polyp Study Workgroup. The New England journal of medicine 1993; 328: 901-906
36. Atkin WS, Morson BC, Cuzick J. Long-term risk of colorectal cancer after excision of rectosigmoid adenomas. The New England journal of medicine 1992; 326: 658-662
37. Click B, Pinsky PF, Hickey T et al. Association of Colonoscopy Adenoma Findings With Long-term Colorectal Cancer Incidence. Jama 2018; 319: 2021-2031
38. He X, Hang D, Wu K et al. Long-term Risk of Colorectal Cancer After Removal of Conventional Adenomas and Serrated Polyps. Gastroenterology 2020; 158: 852-861.e854
39. Dubé C, Yakubu M, McCurdy BR et al. Risk of Advanced Adenoma, Colorectal Cancer, and Colorectal Cancer Mortality in People With Low-Risk Adenomas at Baseline Colonoscopy: A Systematic Review and Meta-Analysis. The American journal of gastroenterology 2017; 112: 1790-1801
40. Pedersen IB. Pictures of polyps from the Norpol Trial. In: Sorlandet Hospital; 2018
41. Kleist B. Pictures of polyps. In; 2021
42. Crockett SD, Nagtegaal ID. Terminology, Molecular Features, Epidemiology, and Management of Serrated Colorectal Neoplasia. Gastroenterology 2019; 157: 949-966.e944
43. Kim HY, Kim SM, Seo JH et al. Age-specific prevalence of serrated lesions and their subtypes by screening colonoscopy: a retrospective study. BMC Gastroenterol 2014; 14: 82
44. Zhao X, Dou LZ, Zhang YM et al. [Clinicopathological features of the colorectal serrated adenoma and analysis on influencing factors of malignancy]. Zhonghua Wei Chang Wai Ke Za Zhi 2021; 24: 75-80
45. Torlakovic E, Skovlund E, Snover DC et al. Morphologic reappraisal of serrated colorectal polyps. Am J Surg Pathol 2003; 27: 65-81
46. Torlakovic E, Snover DC. Sessile serrated adenoma: a brief history and current status. Crit Rev Oncog 2006; 12: 27-39
47. Torlakovic EE, Gomez JD, Driman DK et al. Sessile serrated adenoma (SSA) vs. traditional serrated adenoma (TSA). Am J Surg Pathol 2008; 32: 21-29
48. Shiu SI, Kashida H, Komeda Y. The prevalence of sessile serrated lesion in the colorectum and its relationship to synchronous colorectal advanced neoplasia: a systemic review and meta-analysis. European journal of gastroenterology & hepatology 2021; 33: 1495-1504
49. Pereyra L, Gómez EJ, González R et al. Finding sessile serrated adenomas: is it possible to identify them during conventional colonoscopy? Digestive diseases and sciences 2014; 59: 3021-3026
50. Hazewinkel Y, López-Cerón M, East JE et al. Endoscopic features of sessile serrated adenomas: validation by international experts using high-resolution white-light endoscopy and narrow-band imaging. Gastrointestinal endoscopy 2013; 77: 916-924
51. Singh R, Zorron Cheng Tao Pu L, Koay D et al. Sessile serrated adenoma/polyps: Where are we at in 2016? World journal of gastroenterology 2016; 22: 7754-7759
52. Erichsen R, Baron JA, Hamilton-Dutoit SJ et al. Increased Risk of Colorectal Cancer Development Among Patients With Serrated Polyps. Gastroenterology 2016; 150: 895-902.e895

53. Orlowska J. Serrated lesions and hyperplastic (serrated) polyposis relationship with colorectal cancer: classification and surveillance recommendations. Gastrointestinal endoscopy 2013; 77: 858-871
54. Holme O, Bretthauer M, Eide TJ et al. Long-term risk of colorectal cancer in individuals with serrated polyps. Gut 2015; 64: 929-936
55. Bettington ML, Walker NI, Rosty C et al. A clinicopathological and molecular analysis of 200 traditional serrated adenomas. Mod Pathol 2015; 28: 414-427
56. Lui RN, Kyaw MH, Lam TYT et al. Prevalence and risk factors for sessile serrated lesions in an average risk colorectal cancer screening population. Journal of gastroenterology and hepatology 2021; 36: 1656-1662
57. Bailie L, Loughrey MB, Coleman HG. Lifestyle Risk Factors for Serrated Colorectal Polyps: A Systematic Review and Meta-analysis. Gastroenterology 2017; 152: 92-104
58. Li SC, Burgart L. Histopathology of serrated adenoma, its variants, and differentiation from conventional adenomatous and hyperplastic polyps. Arch Pathol Lab Med 2007; 131: 440-445
59. Bertoni G, Sassatelli R, Conigliaro R et al. Visual "disappearing phenomenon" can reliably predict the nonadenomatous nature of rectal and rectosigmoid diminutive polyps at endoscopy. Gastrointestinal endoscopy 1994; 40: 588-591
60. Monachese M, Mankaney G, El-Khider F et al. Association between baseline hyperplastic polyps and metachronous serrated lesions. Gastrointestinal endoscopy 2021; 93: 1401-1407.e1401
61. Anderson JC, Robinson CM, Butterly LF. Increased risk of metachronous large serrated polyps in individuals with 5- to 9-mm proximal hyperplastic polyps: data from the New Hampshire Colonoscopy Registry. Gastrointestinal endoscopy 2020; 92: 387-393
62. Kuiper T, Marsman WA, Jansen JM et al. Accuracy for optical diagnosis of small colorectal polyps in nonacademic settings. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2012; 10: 1016-1020; quiz e1079
63. Patel SG, Schoenfeld P, Kim HM et al. Real-Time Characterization of Diminutive Colorectal Polyp Histology Using Narrow-Band Imaging: Implications for the Resect and Discard Strategy. Gastroenterology 2016; 150: 406-418
64. [Anonymous]. Update on the paris classification of superficial neoplastic lesions in the digestive tract. Endoscopy 2005; 37: 570-578
65. Moss A, Bourke MJ, Williams SJ et al. Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. Gastroenterology 2011; 140: 1909-1918
66. Rösch AMaT. Paris Classification Early Cancer. In
67. Simon K. Colorectal cancer development and advances in screening. Clin Interv Aging 2016; 11: 967-976
68. Hinoue T, Weisenberger DJ, Pan F et al. Analysis of the association between CIMP and BRAF in colorectal cancer by DNA methylation profiling. PLoS One 2009; 4: e8357
69. Thompson BA, Martins A, Spurdle AB. A review of mismatch repair gene transcripts: issues for interpretation of mRNA splicing assays. Clin Genet 2015; 87: 100-108
70. Rutter MD, Beintaris I, Valori R et al. World Endoscopy Organization Consensus Statements on Post-Colonoscopy and Post-Imaging Colorectal Cancer. Gastroenterology 2018; 155: 909-925.e903
71. Sanduleanu S, le Clercq CM, Dekker E et al. Definition and taxonomy of interval colorectal cancers: a proposal for standardising nomenclature. Gut 2015; 64: 1257-1267
72. Rabeneck L, Paszat LF. Circumstances in which colonoscopy misses cancer. Frontline Gastroenterol 2010; 1: 52-58

73. Burr NE, Derbyshire E, Taylor J et al. Variation in post-colonoscopy colorectal cancer across colonoscopy providers in English National Health Service: population based cohort study. BMJ (Clinical research ed) 2019; 367: l6090
74. Anderson R, Burr NE, Valori R. Causes of Post-Colonoscopy Colorectal Cancers Based on World Endoscopy Organization System of Analysis. Gastroenterology 2020; 158: 1287-1299.e1282
75. Farrar WD, Sawhney MS, Nelson DB et al. Colorectal cancers found after a complete colonoscopy. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2006; 4: 1259-1264
76. Robertson DJ, Lieberman DA, Winawer SJ et al. Colorectal cancers soon after colonoscopy: a pooled multicohort analysis. Gut 2014; 63: 949-956
77. le Clercq CM, Bouwens MW, Rondagh EJ et al. Postcolonoscopy colorectal cancers are preventable: a population-based study. Gut 2014; 63: 957-963
78. Pohl H, Srivastava A, Bensen SP et al. Incomplete polyp resection during colonoscopy-results of the complete adenoma resection (CARE) study. Gastroenterology 2013; 144: 74-80.e71
79. Kawamura T, Takeuchi Y, Asai S et al. A comparison of the resection rate for cold and hot snare polypectomy for 4-9 mm colorectal polyps: a multicentre randomised controlled trial (CRESCENT study). Gut 2018; 67: 1950-1957
80. Papastergiou V, Paraskeva KD, Fragaki M et al. Cold versus hot endoscopic mucosal resection for nonpedunculated colorectal polyps sized 6-10 mm: a randomized trial. Endoscopy 2018; 50: 403-411
81. Tutticci NJ, Hewett DG. Cold EMR of large sessile serrated polyps at colonoscopy (with video). Gastrointestinal endoscopy 2018; 87: 837-842
82. Williams C, Teague R. Colonoscopy. Gut 1973; 14: 990-1003
83. Berci G, Forde KA. History of endoscopy: what lessons have we learned from the past? Surg Endosc 2000; 14: 5-15
84. Buchner AM, Shahid MW, Heckman MG et al. High-definition colonoscopy detects colorectal polyps at a higher rate than standard white-light colonoscopy. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2010; 8: 364-370
85. Lahiff C, East JE. Endoscopic approach to polyp recognition. Frontline Gastroenterol 2017; 8: 98-103
86. Wong Kee Song LM, Adler DG, Chand B et al. Chromoendoscopy. Gastrointestinal endoscopy 2007; 66: 639-649
87. Longcroft-Wheaton G, Bhandari P. Electronic chromoendoscopy. Gastrointestinal endoscopy 2015; 82: 765
88. Bisschops R, East JE, Hassan C et al. Advanced imaging for detection and differentiation of colorectal neoplasia: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2019. Endoscopy 2019; 51: 1155-1179
89. Gubbiotti A, Spadaccini M, Badalamenti M et al. Key factors for improving adenoma detection rate. Expert review of gastroenterology & hepatology 2022; 16: 819-833
90. Nutalapati V, Kanakadandi V, Desai M et al. Cap-assisted colonoscopy: a meta-analysis of high-quality randomized controlled trials. Endoscopy international open 2018; 6: E1214-e1223
91. Kaminski MF, Regula J, Kraszewska E et al. Quality indicators for colonoscopy and the risk of interval cancer. The New England journal of medicine 2010; 362: 1795-1803
92. Corley DA, Jensen CD, Marks AR et al. Adenoma detection rate and risk of colorectal cancer and death. The New England journal of medicine 2014; 370: 1298-1306
93. Carter D, Beer-Gabel M, Zbar A et al. A survey of colonoscopic polypectomy practice amongst Israeli gastroenterologists. Annals of gastroenterology 2013; 26: 135-140

94. Singh N, Harrison M, Rex DK. A survey of colonoscopic polypectomy practices among clinical gastroenterologists. Gastrointestinal endoscopy 2004; 60: 414-418
95. Rex DK, Lewis BS, Waye JD. Colonoscopy and endoscopic therapy for delayed post-polypectomy hemorrhage. Gastrointestinal endoscopy 1992; 38: 127-129
96. Chino A, Karasawa T, Uragami N et al. A comparison of depth of tissue injury caused by different modes of electrosurgical current in a pig colon model. Gastrointestinal endoscopy 2004; 59: 374-379
97. Parra-Blanco A, Kaminaga N, Kojima T et al. Colonoscopic polypectomy with cutting current: is it safe? Gastrointestinal endoscopy 2000; 51: 676-681
98. Kim HS, Kim TI, Kim WH et al. Risk factors for immediate postpolypectomy bleeding of the colon: a multicenter study. The American journal of gastroenterology 2006; 101: 1333-1341
99. Tokar JL, Barth BA, Banerjee S et al. Electrosurgical generators. Gastrointestinal endoscopy 2013; 78: 197-208
100. Fry LC, Lazenby AJ, Mikolaenko I et al. Diagnostic quality of: polyps resected by snare polypectomy: does the type of electrosurgical current used matter? The American journal of gastroenterology 2006; 101: 2123-2127
101. Verma AM, Chilton AP. National survey of UK endoscopists showing variation in diathermy practice for colonic polypectomy. Frontline Gastroenterol 2019; 10: 120-127
102. Tolliver KA, Rex DK. Colonoscopic polypectomy. Gastroenterology clinics of North America 2008; 37: 229-251, ix
103. Ferlitsch M, Moss A, Hassan C et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2017; 49: 270-297
104. Aslan F, Camci M, Alper E et al. Cold snare polypectomy versus hot snare polypectomy in endoscopic treatment of small polyps. The Turkish journal of gastroenterology : the official journal of Turkish Society of Gastroenterology 2014; 25: 279-283
105. Liu S, Ho SB, Krinsky ML. Quality of polyp resection during colonoscopy: are we achieving polyp clearance? Digestive diseases and sciences 2012; 57: 1786-1791
106. Zhang Q, Gao P, Han B et al. Polypectomy for complete endoscopic resection of small colorectal polyps. Gastrointestinal endoscopy 2018; 87: 733-740
107. Jegadeesan R, Aziz M, Desai M et al. Hot snare vs. cold snare polypectomy for endoscopic removal of 4 - 10 mm colorectal polyps during colonoscopy: a systematic review and meta-analysis of randomized controlled studies. Endoscopy international open 2019; 7: E708-e716
108. Shinozaki S, Kobayashi Y, Hayashi Y et al. Efficacy and safety of cold versus hot snare polypectomy for resecting small colorectal polyps: Systematic review and meta-analysis. Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society 2018; 30: 592-599
109. Qu J, Jian H, Li L et al. Effectiveness and safety of cold versus hot snare polypectomy: A meta-analysis. Journal of gastroenterology and hepatology 2019; 34: 49-58
110. Djinbachian R, Iratni R, Durand M et al. Rates of Incomplete Resection of 1- to 20-mm Colorectal Polyps: A Systematic Review and Meta-Analysis. Gastroenterology 2020; 159: 904-914.e912
111. Efthymiou M, Taylor AC, Desmond PV et al. Biopsy forceps is inadequate for the resection of diminutive polyps. Endoscopy 2011; 43: 312-316
112. Murino A, Hassan C, Repici A. The diminutive colon polyp: biopsy, snare, leave alone? Current opinion in gastroenterology 2016; 32: 38-43
113. Dyer WS, Quigley EM, Noel SM et al. Major colonic hemorrhage following electrocoagulating (hot) biopsy of diminutive colonic polyps: relationship to colonic location and low-dose aspirin therapy. Gastrointestinal endoscopy 1991; 37: 361-364

114. Gilbert DA, DiMarino AJ, Jensen DM et al. Status evaluation: hot biopsy forceps. American Society for Gastrointestinal Endoscopy. Technology Assessment Committee. Gastrointestinal endoscopy 1992; 38: 753-756
115. Weston AP, Campbell DR. Diminutive colonic polyps: histopathology, spatial distribution, concomitant significant lesions, and treatment complications. The American journal of gastroenterology 1995; 90: 24-28
116. Metz AJ, Moss A, McLeod D et al. A blinded comparison of the safety and efficacy of hot biopsy forceps electrocauterization and conventional snare polypectomy for diminutive colonic polypectomy in a porcine model. Gastrointestinal endoscopy 2013; 77: 484-490
117. Norton ID, Wang L, Levine SA et al. Efficacy of colonic submucosal saline solution injection for the reduction of iatrogenic thermal injury. Gastrointestinal endoscopy 2002; 56: 95-99
118. Dobrowolski S, Dobosz M, Babicki A et al. Prophylactic submucosal saline-adrenaline injection in colonoscopic polypectomy: prospective randomized study. Surg Endosc 2004; 18: 990-993
119. Kouklakis G, Mpoumponaris A, Gatopoulou A et al. Endoscopic resection of large pedunculated colonic polyps and risk of postpolypectomy bleeding with adrenaline injection versus endoloop and hemoclip: a prospective, randomized study. Surg Endosc 2009; 23: 2732-2737
120. Di Giorgio P, De Luca L, Calcagno G et al. Detachable snare versus epinephrine injection in the prevention of postpolypectomy bleeding: a randomized and controlled study. Endoscopy 2004; 36: 860-863
121. Paspatis GA, Paraskeva K, Theodoropoulou A et al. A prospective, randomized comparison of adrenaline injection in combination with detachable snare versus adrenaline injection alone in the prevention of postpolypectomy bleeding in large colonic polyps. The American journal of gastroenterology 2006; 101: 2805; quiz 2913
122. Tagawa T, Yamada M, Minagawa T et al. Endoscopic characteristics influencing postpolypectomy bleeding in consecutive 1147 pedunculated colonic polyps: a multicenter retrospective study. Gastrointestinal endoscopy 2021, DOI: 10.1016/j.gie.2021.03.996:
123. Turan AS, Pohl H, Matsumoto M et al. The role of clips in preventing delayed bleeding after colorectal polyp resection: an individual patient data meta-analysis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2021, DOI: 10.1016/j.cgh.2021.05.012:
124. Fetz A, Farnell D, Irani S et al. Spray coagulation with snare-tip versus argon plasma coagulation: An ex vivo study evaluating tissue effects. Endoscopy international open 2021; 9: E790-e795
125. Hassan C, Quintero E, Dumonceau JM et al. Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2013; 45: 842-851
126. Lieberman DA, Rex DK, Winawer SJ et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2012; 143: 844-857
127. Mulder SA, Ouwendijk RJ, van Leerdam ME et al. A nationwide survey evaluating adherence to guidelines for follow-up after polypectomy or treatment for colorectal cancer. Journal of clinical gastroenterology 2008; 42: 487-492
128. Krist AH, Jones RM, Woolf SH et al. Timing of repeat colonoscopy: disparity between guidelines and endoscopists' recommendation. American journal of preventive medicine 2007; 33: 471-478
129. Panteris V, Haringsma J, Kuipers EJ. Colonoscopy perforation rate, mechanisms and outcome: from diagnostic to therapeutic colonoscopy. Endoscopy 2009; 41: 941-951
130. Levin TR, Zhao W, Conell C et al. Complications of colonoscopy in an integrated health care delivery system. Annals of internal medicine 2006; 145: 880-886

131. Rabeneck L, Paszat LF, Hilsden RJ et al. Bleeding and perforation after outpatient colonoscopy and their risk factors in usual clinical practice. Gastroenterology 2008; 135: 1899-1906, 1906.e1891
132. Ko CW, Dominitz JA. Complications of colonoscopy: magnitude and management. Gastrointestinal endoscopy clinics of North America 2010; 20: 659-671
133. Zhang Q, Gao P, Han B et al. Polypectomy for complete endoscopic resection of small colorectal polyps. Gastrointestinal endoscopy 2018; 87: 733-740
134. Lee CK, Shim JJ, Jang JY. Cold snare polypectomy vs. Cold forceps polypectomy using double-biopsy technique for removal of diminutive colorectal polyps: a prospective randomized study. The American journal of gastroenterology 2013; 108: 1593-1600
135. Kreftregisteret. https://www.kreftregisteret.no/screening/Tarmscreeningpiloten/Koloskopi/. In; 2018
136. Atkin W, Wooldrage K, Parkin DM et al. Long term effects of once-only flexible sigmoidoscopy screening after 17 years of follow-up: the UK Flexible Sigmoidoscopy Screening randomised controlled trial. Lancet (London, England) 2017; 389: 1299-1311
137. Deenadayalu VP, Rex DK. Colon polyp retrieval after cold snaring. Gastrointestinal endoscopy 2005; 62: 253-256
138. Tappero G, Gaia E, De Giuli P et al. Cold snare excision of small colorectal polyps. Gastrointestinal endoscopy 1992; 38: 310-313
139. de Benito Sanz M, Hernández L, Garcia Martinez MI et al. Efficacy and safety of cold versus hot snare polypectomy for small (5-9 mm) colorectal polyps: a multicenter randomized controlled trial. Endoscopy 2020, DOI: 10.1055/a-1327-8357:
140. Pedersen IB, Bretthauer M, Kalager M et al. Incomplete endoscopic resection of colorectal polyps: a prospective quality assurance study. Endoscopy 2021; 53: 383-391
141. Li DF, Van Overbeke L, Ohata K et al. Efficacy and safety of cold snare polypectomy for sessile serrated polyps ≥ 10 mm: A systematic review and meta-analysis. Digestive and liver disease : official journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver 2022; 54: 1486-1493
142. Ket SN, Mangira D, Ng A et al. Complications of cold versus hot snare polypectomy of 10-20 mm polyps: A retrospective cohort study. JGH Open 2020; 4: 172-177
143. Vleugels JLA, Hazewinkel Y, Fockens P et al. Natural history of diminutive and small colorectal polyps: a systematic literature review. Gastrointestinal endoscopy 2017; 85: 1169-1176.e1161
144. Komeda Y, Kashida H, Sakurai T et al. Removal of diminutive colorectal polyps: A prospective randomized clinical trial between cold snare polypectomy and hot forceps biopsy. World journal of gastroenterology 2017; 23: 328-335
145. Peluso F, Goldner F. Follow-up of hot biopsy forceps treatment of diminutive colonic polyps. Gastrointestinal endoscopy 1991; 37: 604-606
146. Horiuchi A, Nakayama Y, Kajiyama M et al. Removal of small colorectal polyps in anticoagulated patients: a prospective randomized comparison of cold snare and conventional polypectomy. Gastrointestinal endoscopy 2014; 79: 417-423
147. Pohl H, Grimm IS, Moyer MT et al. Effects of Blended (Yellow) vs Forced Coagulation (Blue) Currents on Adverse Events, Complete Resection, or Polyp Recurrence After Polypectomy in a Large Randomized Trial. Gastroenterology 2020; 159: 119-128.e112
148. Health NDo. Handlingsprogram tykk- og endetarmskreft, Helsedirektoratet, Norge. 2022, DOI:
149. Johnson TP, Wislar JS. Response rates and nonresponse errors in surveys. Jama 2012; 307: 1805-1806
150. Knabe M, Pohl J, Gerges C et al. Standardized long-term follow-up after endoscopic resection of large, nonpedunculated colorectal lesions: a prospective two-center study. The American journal of gastroenterology 2014; 109: 183-189

151. Moss A, Williams SJ, Hourigan LF et al. Long-term adenoma recurrence following wide-field endoscopic mucosal resection (WF-EMR) for advanced colonic mucosal neoplasia is infrequent: results and risk factors in 1000 cases from the Australian Colonic EMR (ACE) study. Gut 2015; 64: 57-65
152. Mangira D, Cameron K, Simons K et al. Cold snare piecemeal EMR of large sessile colonic polyps ≥20 mm (with video). Gastrointestinal endoscopy 2020; 91: 1343-1352
153. Dang DT, Suresh S, Vance RB et al. Outcomes of cold snare piecemeal EMR for nonampullary small-bowel adenomas larger than 1 cm: a retrospective study. Gastrointestinal endoscopy 2022; 95: 1176-1182
154. Thoguluva Chandrasekar V, Spadaccini M, Aziz M et al. Cold snare endoscopic resection of nonpedunculated colorectal polyps larger than 10 mm: a systematic review and pooled-analysis. Gastrointestinal endoscopy 2019; 89: 929-936.e923
155. Bettington M, Walker N, Clouston A et al. The serrated pathway to colorectal carcinoma: current concepts and challenges. Histopathology 2013; 62: 367-386
156. Langner C. Serrated and non-serrated precursor lesions of colorectal cancer. Digestive diseases (Basel, Switzerland) 2015; 33: 28-37
157. Lee SP, Sung IK, Kim JH et al. Risk factors for incomplete polyp resection during colonoscopic polypectomy. Gut Liver 2015; 9: 66-72
158. Heldwein W, Dollhopf M, Rosch T et al. The Munich Polypectomy Study (MUPS): prospective analysis of complications and risk factors in 4000 colonic snare polypectomies. Endoscopy 2005; 37: 1116-1122
159. Brenner H, Chang-Claude J, Rickert A et al. Risk of colorectal cancer after detection and removal of adenomas at colonoscopy: population-based case-control study. J Clin Oncol 2012; 30: 2969-2976
160. Brenner H, Hoffmeister M, Arndt V et al. Protection from right- and left-sided colorectal neoplasms after colonoscopy: population-based study. J Natl Cancer Inst 2010; 102: 89-95
161. Adler J, Robertson DJ. Interval Colorectal Cancer After Colonoscopy: Exploring Explanations and Solutions. The American journal of gastroenterology 2015; 110: 1657-1664; quiz 1665
162. Pohl H, Robertson DJ. Colorectal cancers detected after colonoscopy frequently result from missed lesions. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2010; 8: 858-864
163. Patel RV, Barsuk JH, Cohen ER et al. Simulation-based training improves polypectomy skills among practicing endoscopists. Endoscopy international open 2021; 9: E1633-e1639
164. Duloy AM, Kaltenbach TR, Wood M et al. Colon polypectomy report card improves polypectomy competency: results of a prospective quality improvement study (with video). Gastrointestinal endoscopy 2019; 89: 1212-1221
165. Pohl H, Anderson JC, Aguilera-Fish A et al. Recurrence of Colorectal Neoplastic Polyps After Incomplete Resection. Annals of internal medicine 2021; 174: 1377-1384
166. van Doorn SC, Bastiaansen BA, Thomas-Gibson S et al. Polypectomy skills of gastroenterology fellows: can we improve them? Endoscopy international open 2016; 4: E182-189
167. Gupta S, Bassett P, Man R et al. Validation of a novel method for assessing competency in polypectomy. Gastrointestinal endoscopy 2012; 75: 568-575
168. Gupta S, Anderson J, Bhandari P et al. Development and validation of a novel method for assessing competency in polypectomy: direct observation of polypectomy skills. Gastrointestinal endoscopy 2011; 73: 1232-1239.e1232

I

Polypectomy techniques among gastroenterologists in Norway – a nationwide survey

OPEN ACCESS

Authors
Ina B. Pedersen[1,2], Magnus Løberg[2,3], Geir Hoff[2,3,4,5], Mette Kalager[2,3], Michael Bretthauer[2,3,6], Øyvind Holme[1,2]

Institutions
1 Department of Medicine, Sørlandet Hospital Kristiansand, Kristiansand, Norway
2 Institute of Health and Society, Clinical Effectiveness Research Group, University of Oslo, Oslo, Norway
3 Department of Transplantation Medicine and K. G. Jebsen Colorectal Cancer Research Center, Oslo University Hospital, Oslo, Norway
4 Department of research, Telemark Hospital, Skien, Norway
5 Cancer Registry of Norway, Oslo, Norway
6 Frontier Science, Boston, Massachusetts, United States

submitted 14.12.2017
accepted after revision 19.3.2018

Bibliography
DOI https://doi.org/10.1055/a-0607-0727 |
Endoscopy International Open 2018; 06: E812–E820

ISSN 2364-3722

Corresponding author
Ina B. Pedersen, Sørlandet Hospital, Post box 416, N-4604, Kristiansand, Norway
Fax: +47 370 83551
inaborgenheimpedersen@gmail.com

ABSTRACT

Background and study aims Incomplete polyp removal has been estimated to cause 27 % of all colorectal cancers detected soon after colonoscopy. There is limited information regarding polypectomy techniques among endoscopists. The article is a nationwide survey of polypectomy techniques among Norwegian endoscopists.

Materials and methods We invited all board-certified gastroenterologists in Norway to complete a web-based questionnaire about their polypectomy technique. Inadequate polypectomy techniques were defined as using biopsy forceps for polyps larger than 3 mm in diameter, using hot biopsy forceps for polypectomy, and using the same electrocautery output irrespective of polyp size and morphology.

Results Twenty-six of 30 Norwegian gastroenterology departments participated in the study. A total of 119 endoscopists received the survey, and 70 (59 %) responded. Mean duration of endoscopy practice was 11.5 years, and 95 % had performed more than 1,000 colonoscopies during their career. Twenty-eight endoscopists (40 %) used one or more inadequate polypectomy techniques: 10 (14.3 %) used biopsy forceps for removal of polyps larger than 3 mm in diameter, five (7.1 %) used hot biopsy for polypectomy, and 17 (24 %) used the same electrocautery output for all polypectomies. Five (7 %) endoscopists reported that they did not remove polyps smaller than 4 mm.

Conclusion A substantial number of Norwegian endoscopists use inadequate polypectomy techniques. Improved training and certification of endoscopists is warranted.

Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide [1], and Norway has one of the highest incidence rates of CRC in the world [2]. CRC incidence and mortality can be reduced by removal of colorectal polyps [3, 4].

A prerequisite for reducing CRC incidence through polypectomy is complete removal of the polyps. The proportion of incompletely resected polyps vary with size and histology of the polyp as well as with the technique used for resection [5]. Moreover, frequency of incomplete polyp resection varies widely among endoscopists [5, 6]. Approximately 20 % of cancers detected after colonoscopy are caused by incomplete polypectomy [7].

Polypectomy is associated with risk of complications, of which bleeding and perforations are the most severe. Bleeding due to polypectomy occurs in 0.1 % to 0.6 % and perforations in 0.02 % to 0.1 % of colonoscopies [8]. Safe and complete polypectomy is therefore an important consideration for endoscopists and requires complex decision-making, including whether to remove the polyp, what polypectomy technique to apply (e. g. snare, forceps, use of electrocautery, level of elec-

tric current) and if preventive measures should be undertaken to reduce the risk of complications (e. g. clipping of the stalk before removal of pedunculated polys).

Endoscopists use a variety of polypectomy techniques [9, 10]. Many of them use inadequate techniques, which may translate into increased risk of complications or incomplete removal of polyps. Surveillance is recommended after polypectomy, but many endoscopists do not adhere to post-polypectomy guidelines [11 – 14].

We aimed to investigate whether Norwegian endoscopists used inadequate polypectomy techniques, and if they followed the national guidelines for polyp surveillance.

Materials and methods

All board-certified gastroenterologists (consultants) in Norway who perform colonoscopic polypectomies were eligible for the study. No trainees or fellows were approached. To identify eligible endoscopists, we approached 30 Norwegian hospitals with gastroenterology departments to obtain email addresses. The identified endoscopists received an electronic questionnaire by email, using commercially available online survey-software (SurveyMonkey©). If the gastroenterologists did not reply initially, two reminders were sent. The survey was conducted between April 2015 and May 2016.

The first draft of the questionnaire was made using the questionnaires from the two earlier surveys [9, 10] as a basis. We extended the questionnaire to allow for further evaluation of polypectomy techniques. After the first draft, we invited about 360 endoscopists (both surgeons and gastroenterologists), endoscopy assistants and fellows, to comment on the questionnaire and suggest additional items. Some questions were removed and some were added according to these suggestions. Finally, we asked seven experienced gastroenterologists to test the survey, and the final version was created based on their feedback. In the final questionnaire, we included the questions that were most relevant to assess completeness of polypectomy, complications and adherence to post-polypectomy surveillance guidelines.

The study was approved by the Norwegian Centre for Research Data, and completing the survey was considered as consent to participate in the study. The study was waived ethical approval from the regional ethics committee of South-East Norway. An English translation of the questionnaire is available in the supplementary appendix (**Supplement 1**).

Primary outcomes of interest were proportion of endoscopists with inadequate polypectomy technique for removal of polyps smaller than 1 cm in diameter, and adherence to national surveillance guidelines. We also explored whether contemporary polypectomy techniques (e. g. cold snare polypectomy) had been implemented in daily practice. There are no national guidelines for polypectomy in Norway. Based on published research and international guidelines, we therefore defined inadequate polypectomy techniques as: use of biopsy forceps for removal of polyps larger than 3 mm, use of hot biopsy forceps (biopsy forceps with electrocautery for polypectomy), and use of the same electrocautery output (coagulation, cut or blend) irrespective of the size and morphology of the polyp to be removed. Further, we defined hot snare polypectomy as snare polypectomy with use of electrocautery and cold snare polypectomy as snare polypectomy without use of electrocautery.

The questionnaire also included questions concerning adherence to guidelines for post-polypectomy surveillance (see supplement). Norwegian post-polypectomy surveillance guidelines are identical to the guidelines issued by the European Society of Gastrointestinal Endoscopy [11].

Statistics

Descriptive statistics are presented as mean with standard deviation (SD) for normally distributed data. To assess which risk factors predict inadequate polypectomy technique and non-adherence to surveillance guidelines, we fitted univariable logistic regression models using endoscopist sex, age, experience (years of practice) and hospital category (university versus non-university) as explanatory variables. Finally, we fitted a multivariable model using backward removal of variables with a Wald test P values ≥ 0.05. All analyses were conducted with Stata software version 14.2 (StataCorp, College Station, Texas, United States), and $P < 0.05$ was considered statistically significant.

Results

Twenty-seven hospitals (90 %) responded to our initial invitation and 26 endoscopy department chairs provided email addresses for their eligible endoscopists. One department chair did not want to participate in the study.

The questionnaire was distributed to 119 board-certified gastroenterologists (consultants), of whom 70 (59 %) responded. There were 58 (83 %) men and 12 (17 %) women among the responders, and the mean age was 51.5 years (▶ **Table 1**). A total of 18 endoscopists (25.7 %) worked at university hospitals, and 52 (74.3 %) worked at non-university hospitals. Most endoscopists were experienced, 93 % had performed more than 1000 colonoscopies, and the mean duration of endoscopy practice was 11.5 years (▶ **Table 1**).

Inadequate polypectomy technique

Most endoscopists (74 %) removed polyps smaller than 4 mm in diameter with biopsy forceps, but 5 (7 %) endoscopists did not remove polyps of this size at all (▶ **Table 2**). Overall, 28 (40 %) endoscopists used one or more inadequate methods for removal of polyps smaller than 1 cm: 17 (24.3 %) endoscopists did not adjust electrocautery output dependent on size and morphology of the polyp, five endoscopists (7.1 %) used hot biopsy forceps for polyp removal, and 10 (14.3 %) used biopsy forceps for removal of polyps > 3 mm (▶ **Table 2**, ▶ **Fig. 1**).

None of the factors we investigated (endoscopist sex, age, years of practice and hospital category) were associated with inadequate polypectomy technique.

▶ **Table 1** Characteristics of endoscopists.

Age (years), mean (SD)	51.5 (8.0)
Years in endoscopy practice, mean (SD)	11.5 (7.6)
Sex, n (%)	
Male	58 (82.9)
Female	12 (17.1)
Number of colonoscopies performed	
<500	2 (2.9)
500 – 1000	3 (4.3)
1000 – 5000	40 (57.1)
5000 – 10000	19 (27.1)
>10000	6 (8.6)
Number of colonoscopies per year	
<100	7 (10.0)
100 – 300	34 (48.6)
>300	29 (41.4)
Hospital category	

SD, standard deviation

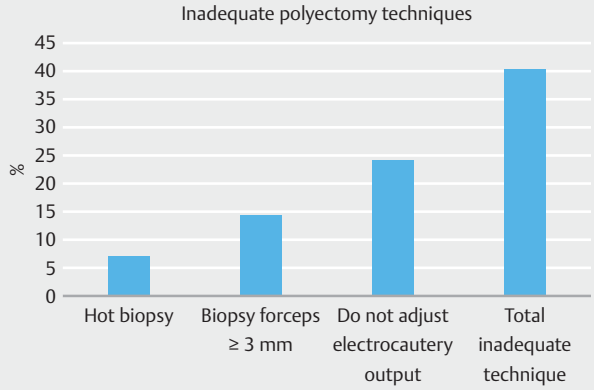
▶ **Table 2** Polypectomy techniques for removal of polyps smaller than 1 cm in diameter, stratified by size.

Polypectomy method	Size		
	1 – 3 mm	4 – 6 mm	7 – 9 mm
Do not remove	5 (7.1)		
Biopsy forceps	52 (74.3)	9 (11.0)	
Hot biopsy	3 (4.3)	2 (2.45)	1 (1.1)
Cold snare	5 (7.1)	17 (20.7)	3 (3.4)
Hot snare	4 (5.7)	37 (45.1)	47 (54.1)
EMR	1 (1.5)	15 (18.3)	34 (39.1)
Other		2 (2.45)	2 (2.3)

EMR, endoscopic mucosal resection

Adherence to post-polypectomy guidelines

Twelve (17 %) endoscopists stated that they did not have written polyp surveillance guidelines at their hospital. In two hospitals, the response was not consistent among endoscopists: some stated they had written guidelines, while some stated they had not. Forty-eight (71 %) endoscopists used the Norwegian guidelines for polyp surveillance. In the multivariable regression model, working at a university hospital was associated with not adhering to the Norwegian guidelines for surveillance after polypectomy, odds ratio 11.8 (95 % confidence interval (CI) 3.0 – 46.2, $P = 0.001$), adjusted for age, sex and experience.



▶ **Fig. 1** Inadequate polypectomy technique. Columns show the percentage of responders who used inadequate techniques: hot biopsy for polypectomy, biopsy forceps for removing polyps >3 mm in diameter and no adjustment of electrocautery output depending on polyp size and morphology. The total is the percentage of endoscopists who used one or more of the inadequate techniques.

Thirty-seven (62 %) endoscopists had been discussing polypectomy technique as part of the department's internal education program within the last 2 years.

Other measures

Thirty (43 %) endoscopists had never performed cold snare polypectomy. Of those who used cold snare, 20 (41.7 %) did not use the recommended cold snare technique but used the same technique as in hot snare polypectomy (pull polyp towards center of lumen before cutting). Fifty-three (75.7 %) of the responders used the size of the forceps or the snare as a reference to determine polyp size, whereas 8 (11.4 %) estimated polyp size without any reference. Only two2 (2.9 %) of the responders used chromoendoscopy, and 33 (47.8 %) used narrow band imaging (NBI) to evaluate polyps. When removing pedunculated polyps with stalk diameter >1 cm, 51 % used detachable snares as bleeding prophylaxis and 64 % used clips.

Discussion

This is the first study of polypectomy practice among Norwegian endoscopists. We found large variation in polypectomy techniques. Surprisingly, 7 % of endoscopists reported that they did not remove polyps smaller than 4 mm, and as many as 40 % used one or more inadequate polypectomy techniques. One-third of endoscopists did not adhere to national guidelines for polyp surveillance.

Colorectal cancer may develop from adenomas and serrated polyps, and endoscopic examination of the colon with polypectomy has been shown to reduce CRC incidence in randomized trials [3, 4]. Patients examined by an endoscopist who detects adenomas in a high proportion of patients have reduced risk of developing CRC compared to patients examined by endoscopists with low adenoma detection rate [15, 16]. Currently,

we are unable to determine which polyps have malignant potential, and therefore all should be removed. A recent literature review [17] found that 6 % of adenomas between 1 and 9 mm in diameter progressed to advanced adenoma over a period of 2 to 3 years. Why some endoscopists (7 % in our study) choose not to remove small polyps is not clear. It may be that some endoscopists do not remove these polyps because they are thought to be hyperplastic and of little clinical significance. In our survey, very few responders used chromoendoscopy and a little under half of the responders used NBI. Both of these could improve diagnostic accuracy. However, the ability of endoscopists to accurately separate hyperplastic polyps from adenomas using virtual biopsy technology is poor even with imaging-enhancing technologies like NBI [18, 19].

Polypectomy to reduce CRC incidence and mortality is most effective if all adenomatous tissue is removed. It has been estimated that 27 % of CRCs detected within 3 years after colonoscopy may be due to inadequate polyp removal [7]. In the present questionnaire, 14 % of endoscopists used biopsy forceps when they removed polyps larger than 3 mm in diameter. Biopsy forceps are adequate for removal of the smallest polyps (≤ 3 mm) [6, 20], but not for larger polyps because of the high risk of incomplete removal. In two studies, the proportion of 3- and 5-mm polyps incompletely removed using biopsy forceps was 17 % and 47 %, respectively [21, 22]. We had few responders using this technique, but given the compelling evidence, there should have been none. The endoscopists in our questionnaire were board-certified with long experience and serve as mentors for new endoscopists. Young fellows may therefore be trained suboptimally.

Perforation is a serious complication of polypectomy, but the frequency is less than 0.1 % [8, 23]. Most perforations are due to use of electrocautery. Five (7.1 %) of the responders in our survey used the hot biopsy technique for polyp removal. Hot biopsy for polypectomy has been abandoned by most endoscopists due to increased risk of perforation and the burned serosa syndrome [24 – 26], and has been replaced with polypectomy by snaring. Recently, cold snare polypectomy (without electrocautery) has been introduced as a safe and effective technique for removing polyps smaller than 10 mm in diameter [27]. For removal of 4- to 6-mm polyps, only 17 responders used cold snare for polypectomy.

We found that 41.7 % of endoscopists using cold snare polypectomy used the same technique as they used for hot snaring. When removing a polyp with electrocautery, it is important to pull the polyp into the colon lumen to avoid tissue damage. With the cold snare, however, one should avoid pulling the closed snare into the lumen to avoid it slipping off the polyp [28]. Some of the responders may be reluctant to use this technique because they fear more bleeding when not using electrocautery. However, post-polypectomy bleeding rates are lower with cold snare polypectomy compared to polypectomy using electrocautery [29], and risk of perforation is very small. Importantly, some studies have found that the cold snare technique is associated with a slightly lower rate of complete polyp resection than snaring with electrocautery. This may be another reason why many endoscopists have not endorsed cold snaring [30].

We found that 25 % of our respondents do not adjust the output settings when using electrocautery. There is good evidence to support that the current should be adjusted. Different types of current (coagulation, cut or blended) have different properties and effects, including risk of complications. When removing a pedunculated polyp, one should use coagulation current in the stalk to prevent bleeding. Sessile polyps should be removed using cutting current to prevent deep tissue damage in the colon wall [28]. It is surprising that so many endoscopists in Norway do not adjust the electrocautery output, considering the risk of tissue damage. The reason is unknown, but it highlights the importance of continuous quality assurance and education to ensure patient safety and good clinical practice.

After polypectomy, guidelines recommend surveillance by colonoscopy. In Norway, new post-polypectomy surveillance guidelines were issued in 2015 by the Directorate of Health [31], and they are similar to the guidelines issued by the European Society of Gastrointestinal Endoscopy [11]. In the current study, 29 % of responders did not adhere to the national guidelines. All the responders work at public hospitals or hospitals on contract with the health authorities, and one would expect that these endoscopists would be aware of, and adhere to, national guidelines. Interestingly, when we compared responders working in academic hospitals to those working in non-academic hospitals, we found that endoscopists working in university hospitals were more likely to be non-adherent to national guidelines than community-based endoscopists. The reason for this is unknown, but the result may be biased: In some hospitals, the responders were not consistent in their replies. Some endoscopists stated that they had written guidelines at their hospital, while others denied the existence of written guidelines. This discrepancy again underlines the importance of continuous quality assurance in the endoscopy unit to ensure that all endoscopists are up to date with existing routines and guidelines.

All the items discussed above show that there is need for more polypectomy training among endoscopists in Norway. Only about 60 % of responders reported that there had been lectures about polypectomy technique in their internal education program during the preceding 2 years. The gastroenterology academic field in Norway has already started a training course called “The Endoscopy School,” where gastroenterologists in training and specialists alike are invited to attend a course in hands-on colonoscopy under the supervision of trained instructors.

The major strength of this survey is that we invited all board-certified gastroenterologists at 26 of 30 gastroenterological departments in Norway to participate. Therefore, we have a variety of endoscopists from all over the country, and from different types of hospitals, both university hospitals and non-university hospitals, and hospitals from both rural and urban areas. We also had almost the same sex distribution among our responders as in the register of all board-certified gastroenterol-

ogists (18 % women and 82 % men) [32]. This hopefully makes the response representative for endoscopic practice in Norway.

However, there are also limitations. Approximately 60 % of those invited to participate responded to the questionnaire, and they may not be representative of all Norwegian endoscopists. Without complete response rate, there will always be a risk of selection bias. However, Johnson et al [33] found that the late responders are more like the non-responders than the early responders. When we compared the replies of the 13 late responders (defined as those who replied after the last reminder) with the 57 initial responders, there were no large differences between the two groups, but our number of respondents is small. The similarity between late-responders and initial responders might still indicate that our results may be generalizable to the whole population of Norwegian endoscopists.

Conclusion

In summary, we observed great variability in the choice of polypectomy techniques in Norway. Many endoscopists use methods that are not recommended for polyp removal, and new techniques, like cold snare polypectomy are not widely adopted. We also found that many Norwegian endoscopists do not adhere to national guidelines for surveillance after polypectomy. There is clearly a potential for improvement in the education of endoscopists, which is confirmed by the variability in practice and the high number using inadequate polypectomy techniques.

Competing interests

None

References

[1] Favoriti P, Carbone G, Greco M et al. Worldwide burden of colorectal cancer: a review. Updates Surgery 2016; 68: 7 – 11

[2] Svensson E, Grotmol T, Hoff G et al. Trends in colorectal cancer incidence in Norway by gender and anatomic site: an age-period-cohort analysis. Europ J Cancer Prev 2002; 11: 489 – 495

[3] Holme O, Loberg M, Kalager M et al. Effect of flexible sigmoidoscopy screening on colorectal cancer incidence and mortality: a randomized clinical trial. JAMA 2014; 312: 606 – 615

[4] Zauber AG, Winawer SJ, O'Brien MJ et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med 2012; 366: 687 – 696

[5] Pohl H, Srivastava A, Bensen SP et al. Incomplete polyp resection during colonoscopy-results of the complete adenoma resection (CARE) study. Gastroenterology 2013; 144: 74 – 80.e71

[6] Efthymiou M, Taylor AC, Desmond PV et al. Biopsy forceps is inadequate for the resection of diminutive polyps. Endoscopy 2011; 43: 312 – 316

[7] Robertson DJ, Lieberman DA, Winawer SJ et al. Colorectal cancers soon after colonoscopy: a pooled multicohort analysis. Gut 2014; 63: 949 – 956

[8] Ko CW, Dominitz JA. Complications of colonoscopy: magnitude and management. Gastrointest Endosc Clin North Am 2010; 20: 659 – 671

[9] Carter D, Beer-Gabel M, Zbar A et al. A survey of colonoscopic polypectomy practice amongst Israeli gastroenterologists. Ann Gastroenterol 2013; 26: 135 – 140

[10] Singh N, Harrison M, Rex DK. A survey of colonoscopic polypectomy practices among clinical gastroenterologists. Gastrointest Endosc 2004; 60: 414 – 418

[11] Hassan C, Quintero E, Dumonceau JM et al. Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2013; 45: 842 – 851

[12] Lieberman DA, Rex DK, Winawer SJ et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2012; 143: 844 – 857

[13] Mulder SA, Ouwendijk RJ, van Leerdam ME et al. A nationwide survey evaluating adherence to guidelines for follow-up after polypectomy or treatment for colorectal cancer. J Clin Gastroenterol 2008; 42: 487 – 492

[14] Krist AH, Jones RM, Woolf SH et al. Timing of repeat colonoscopy: disparity between guidelines and endoscopists' recommendation. Am J Prev Med 2007; 33: 471 – 478

[15] Corley DA, Jensen CD, Marks AR et al. Adenoma detection rate and risk of colorectal cancer and death. N Engl J Med 2014; 370: 1298 – 1306

[16] Kaminski MF, Regula J, Kraszewska E et al. Quality indicators for colonoscopy and the risk of interval cancer. N Engl J Med 2010; 362: 1795 – 1803

[17] Vleugels JLA, Hazewinkel Y, Fockens P et al. Natural history of diminutive and small colorectal polyps: a systematic literature review. Gastrointest Endosc 2017; 85: 1169 – 1176.e1161

[18] Kuiper T, Marsman WA, Jansen JM et al. Accuracy for optical diagnosis of small colorectal polyps in nonacademic settings. Clin Gastroenterol Hepatol 2012; 10: 1016 – 1020 ; quiz e1079

[19] Patel SG, Schoenfeld P, Kim HM et al. Real-time characterization of diminutive colorectal polyp histology using narrow-band imaging: implications for the resect and discard strategy. Gastroenterology 2016; 150: 406 – 418

[20] Murino A, Hassan C, Repici A. The diminutive colon polyp: biopsy, snare, leave alone? Curr Opin Gastroenterol 2016; 32: 38 – 43

[21] Komeda Y, Kashida H, Sakurai T et al. Removal of diminutive colorectal polyps: A prospective randomized clinical trial between cold snare polypectomy and hot forceps biopsy. World J Gastroenterol 2017; 23: 328 – 335

[22] Peluso F, Goldner F. Follow-up of hot biopsy forceps treatment of diminutive colonic polyps. Gastrointest Endosc 1991; 37: 604 – 606

[23] Ko CW, Riffle S, Michaels L et al. Serious complications within 30 days of screening and surveillance colonoscopy are uncommon. Clin Gastroenterol Hepatol 2010; 8: 166 – 173

[24] Dyer WS, Quigley EM, Noel SM et al. Major colonic hemorrhage following electrocoagulating (hot) biopsy of diminutive colonic polyps: relationship to colonic location and low-dose aspirin therapy. Gastrointest Endosc 1991; 37: 361 – 364

[25] Gilbert DA, DiMarino AJ, Jensen DM et al. Status evaluation: hot biopsy forceps. American Society for Gastrointestinal Endoscopy. Technology Assessment Committee. Gastrointest Endosc 1992; 38: 753 – 756

[26] Weston AP, Campbell DR. Diminutive colonic polyps: histopathology, spatial distribution, concomitant significant lesions, and treatment complications. Am J Gastroenterol 1995; 90: 24 – 28

[27] Ichise Y, Horiuchi A, Nakayama Y et al. Prospective randomized comparison of cold snare polypectomy and conventional polypectomy for small colorectal polyps. Digestion 2011; 84: 78 – 81

[28] Tolliver KA, Rex DK. Colonoscopic polypectomy. Gastroenterol Clin North Am 2008; 37: 229 – 251, ix

[29] Horiuchi A, Nakayama Y, Kajiyama M et al. Removal of small colorectal polyps in anticoagulated patients: a prospective randomized comparison of cold snare and conventional polypectomy. Gastrointest Endosc 2014; 79: 417 – 423

[30] Liu S, Ho SB, Krinsky ML. Quality of polyp resection during colonoscopy: are we achieving polyp clearance? Digest Dis Sci 2012; 57: 1786 – 1791

[31] Kreft i tykktarm og endetarm – handlingsprogram. 2015: The Norwegian Directory of Health

[32] Association TNM. Oversikt over godkjente spesialister i gastroenterologi/Board certified gastroenterologists. The Norwegian Medical Association 2017

[33] Johnson TP, Wislar JS. Response rates and nonresponse errors in surveys. Jama 2012; 307: 1805 – 1806

Supplement 1

Questionnaire (answers to the questions are given in percentages in brackets)

1. In what year were you born? Mean age 51,5 years.
2. What is your sex?
   a) Male (83 %)
   b) Female (17 %)
3. In what year, did you become a board-certified gastroenterologist? Mean experience 11,5 years.
4. How many colonoscopies do you perform each year, approximately?
   a) < 100 (10 %)
   b) 100 – 300 (49 %)
   c) > 300 (41 %)
5. How many colonoscopies have you performed during your career?
   a) < 500 (3 %)
   b) 500 – 1000 (4 %)
   c) 1000 – 5000 (57 %)
   d) 5000 – 10000 (27 %)
   e) > 10000 (9 %)
6. What method do you use for determining polyp size?
   a) By eye, without any reference (11 %)
   b) Biopsy forceps/size of snare etc. (76 %)
   c) Measure size after polypectomy and retrieval of polyp (7 %)
   d) Other method. Please elaborate. (6 %)
7. What polypectomy method do you use when removing sessile polyps sized 1 – 3 mm distal to the right flexure?
   a) Biopsy forceps (75 %)
   b) Hot biopsy (4 %)
   c) Cold snare (snare polypectomy without use of electrocautery) (7 %)
   d) Hot snare (snare polypectomy with use of electrocautery) (4 %)
   e) EMR (snare polypectomy after submucosal fluid injection) (2 %)
   f) I do not remove polyps of this size (4 %)
   g) Other method. Please elaborate. (4 %)
8. What polypectomy method do you use when removing sessile polyps sized 4 – 6 mm distal to the right flexure?
   a) Biopsy forceps (13 %)
   b) Hot biopsy (3 %)
   c) Cold snare (snare polypectomy without use of electrocautery) (24 %)
   d) Hot snare (snare polypectomy with use of electrocautery) (53 %)
   e) EMR (snare polypectomy after submucosal fluid injection) (6 %)
   f) Other method. Please elaborate. (1 %)
9. What polypectomy method do you use when removing sessile polyps sized 7 – 9 mm distal to the right flexure?
   a) Biopsy forceps (0 %)
   b) Hot biopsy (1 %)
   c) Cold snare (snare polypectomy without use of electrocautery) (5 %)
   d) Hot snare (snare polypectomy with use of electrocautery) (67 %)
   e) EMR (snare polypectomy after submucosal fluid injection) (27 %)
   f) Other method. Please elaborate. (0 %)
10. What polypectomy method do you use when removing sessile polyps sized 1 – 3 mm proximal to the right flexure?
   a) Biopsy forceps (74 %)
   b) Hot biopsy (4 %)
   c) Cold snare (snare polypectomy without use of electrocautery) (7 %)
   d) Hot snare (snare polypectomy with use of electrocautery) (6 %)
   e) EMR (snare polypectomy after submucosal fluid injection) (2 %)
   f) I do not remove polyps of this size (7 %)
   g) Other method. Please elaborate. (0 %)
11. What polypectomy method do you use when removing sessile polyps sized 4 – 6 mm proximal to the right flexure?
   a) Biopsy forceps (11 %)
   b) Hot biopsy (3 %)
   c) Cold snare (snare polypectomy without use of electrocautery) (16 %)
   d) Hot snare (snare polypectomy with use of electrocautery) (46 %)
   e) EMR (snare polypectomy after submucosal fluid injection) (21 %)
   f) Other method. Please elaborate. (3 %)
12. What polypectomy method do you use when removing sessile polyps sized 7 – 9 mm proximal to the right flexure?
   a) Biopsy forceps (0 %)
   b) Hot biopsy (0 %)
   c) Cold snare (snare polypectomy without use of electrocautery) (1 %)
   d) Hot snare (snare polypectomy with use of electrocautery) (47 %)
   e) EMR (snare polypectomy after submucosal fluid injection) (49 %)
   f) Other method. Please elaborate. (3 %)
13. Do you alter the size of the snare dependent on the size of the polyp?
   a) Yes (82 %)
   b) No (11 %)
   c) There is only one snare size at my hospital (7 %)
   d) I do not know (0 %)
14. Do you practise both cold (without use of electrocautery) and hot (with electrocautery) polypectomies?
   a) Yes, I practice both methods (57 %)
   b) No, I only practice hot snare polypectomy (43 %)
   c) I do not know (0 %)

15. If “yes” in the last question: Do you choose different types of snares when performing cold (without electrocautery) than when performing hot (with electrocautery) polypectomy?
    a) Yes (41 %)
    b) No (31 %)
    c) We do not have specialized snares for cold polypectomy at my hospital (20 %)
    d) I do not know (8 %)
16. If you use the cold snare polypectomy (without electrocautery) for removal of small polyps, do you use the same technique (grasping the polyp and pulling it into the lumen before closing the snare) for removal as when performing hot snare polypectomy (with electrocautery)?
    a) Yes, I pull the polyp into the lumen before closing the snare (42 %)
    b) No, I do not pull the polyp into the lumen before closing the snare (42 %)
    c) I do not know (16 %)
17. Do you adjust the current type (cut/coagulation/blend or a pre-set program) dependent on polyp size, localisation and morphology?
    a) Yes (76 %)
    b) No (24 %)
    c) I do not know (0 %)
18. Have you, during the last two years, used detachable snares (Endoloop or others) as a prophylactic measure against bleeding when removing stalked polyps?
    a) Yes (51 %)
    b) No, but there are detachable snares available at my hospital (36 %)
    c) No, detachable snares are not available at my hospital (13 %)
    d) I do not know (0 %)
19. Have you, during the last two years, used clips on polyp stalks as a prophylactic measure against bleeding when removing stalked polyps?
    a) Yes (64 %)
    b) No (36 %)
    c) I do not know (0 %)
20. Do you take on any routine measures to prevent bleeding from stalked polyps with stalks larger than 1 cm in diameter? (Multiple answers possible)
    a) No, I do not take on any routine measures (17 %)
    b) Injection of epinephrine (31 %)
    c) Clips (46 %)
    d) Detachable snare (40 %)
    e) Diathermy of stalk after polypectomy (13 %)
    f) I do not remove polyps of this size, I refer the patients to others (4 %)
    g) Other method. Please elaborate. (9 %)
21. When removing stalked polyps with snare: Where on the stalk do you place the snare?
    a) The third part of the stalk nearest the polyp head (7 %)
    b) The midst third part of the stalk (40 %)
    c) The third part nearest the bowel wall (39 %)
    d) I have no rule for where to place the snare (14 %)
    e) I do not know (0 %)
22. What measures do you take on in the case of immediate bleeding after polypectomy of stalked polyps? (Multiple answers possible)
    a) Injection of epinephrine (54 %)
    b) Clips (91 %)
    c) Argon Plasma Coagulation (6 %)
    d) Coagulation the stalk with the snare (57 %)
    e) Endoloop (3 %)
    f) Other method. Please elaborate. (0 %)
23. What measures do you take on in the case of immediate bleeding after polypectomy of sessile polyps? (Multiple answers possible)
    a) Injection of epinephrine (73 %)
    b) Clips (81 %)
    c) Argon Plasma Coagulation (23 %)
    d) Other method. Please elaborate. (7 %)
24. Do you consider systematic injection of fluid in the submucosal space when removing sessile polyps?
    a) Yes (77 %)
    b) No (22 %)
    c) I do not know (1 %)
25. If you do inject fluid into the submucosal space: What are the content(-s) of your preferred fluid? (Multiple answers possible)
    a) Sodium chloride (84 %)
    b) Colloid (14 %)
    c) Epinephrine (43 %)
    d) Dye (44 %)
    e) Other. Please elaborate. (0 %)
26. If you do inject fluid into the submucosal space, is there a specific size of sessile polyps in the colon distal to the right flexure you would choose to do this?
    a) No, no specific size (27 %)
    b) Yes, above 5 mm (18 %)
    c) Yes, above 10 mm (13 %)
    d) Yes, above 15 mm (13 %)
    e) Yes, above 20 mm (5 %)
    f) Yes, above other size. Please elaborate. (1 %)
27. If you do inject fluid into the submucosal space, is there a specific size of sessile polyps in the colon proximal to the right flexure you would choose to do this?
    a) No, no specific size (24 %)
    b) Yes, above 5 mm (34 %)
    c) Yes, above 10 mm (16 %)
    d) Yes, above 15 mm (12 %)
    e) Yes, above 20 mm (1 %)
    f) Yes, above other size. Please elaborate. (1 %)
28. Do you regularly use dye spray/chromoendoscopy to investigate polyps before removal?
    a) Yes (3 %)
    b) No (97 %)
    c) I do not know (0 %)

29. Do you regularly use NBI (Narrow Band Imaging) to investigate polyps before removal?
    a) Yes (48 %)
    b) No (50 %)
    c) No, there is not NBI available at my hospital (2 %)
    d) I do not know (0 %)
30. Do you find dye spray/chromoendoscopy or NBI useful for investigation of polyps?
    a) Yes (67 %)
    b) No (16 %)
    c) I do not use either chromoendoscopy nor NBI (17 %)
31. Do you use classification systems for investigation of polyps before removal? (E.g. Kudos pit pattern, NBI international colorectal endoscopic classification or others.)
    a) Yes (23 %)
    b) No (71 %)
    c) These classification systems are unknown to me (6 %)
32. Do you systematically decide not to remove polyps after investigation with chromoendoscopy or NBI?
    a) Yes (20 %)
    b) No (60 %)
    c) I do not use these methods (20 %)
33. How do you normally treat polyps > 1 cm in size proximal to the right flexure that you suspect to be non-adenomatous (in patients with estimated life expectancy > 10 years)?
    a) Take biopsies (10 %)
    b) Remove by polypectomy (81 %)
    c) Leave untreated/unbiopsied if appearance as hyperplastic polyp (0 %)
    d) No specific routine, depends on the situation (9 %)
    e) I do not know (0 %)
34. Do you regularly use chromoendoscopy/NBI to evaluate complete resection after polypectomy of sessile polyps?
    a) Yes (16 %)
    b) No (84 %)
    c) Other method. Please elaborate. (0 %)
    d) I do not know (0 %)
35. Do you consider routine use of Argon Plasma Coagulation to treat the resection margins after polypectomy of sessile polyps to remove the possible polyp tissue?
    a) Yes (26 %)
    b) No (55 %)
    c) We do not have this equipment at my hospital (17 %)
    d) I do not know (2 %)
36. In your opinion, are there characteristics of the assistant/nurse that have impact on the quality of the polypectomy?
    a) Yes, which nurse assisting does have an impact on the quality of the polypectomy (87 %)
    b) No, which nurse assisting does not have an impact on the quality of the polypectomy (9 %)
    c) I do not know (4 %)
37. If “yes” in the last questions, what characteristics of the assistant/nurse have impact, in your opinion?
    a) How fast the snare is closed (28 %)
    b) How firm the snare is closed? (41 %
    c) Communication between endoscopist and assistant (80 %
    d) Other. Please elaborate. (4 %)
38. In your hospital, have you had lectures on polypectomy over the last two years?
    a) Yes (62 %)
    b) No (31 %
    c) I do not know (7 %)
39. In your hospital, do you have written guidelines for surveillance after polypectomy?
    a) Yes (81 %)
    b) No (17 %)
    c) I do not know (2 %)
40. What guidelines do you use when determining the surveillance after polypectomy in patients with estimated life expectancy > 10 years?
    a) By discretion of the endoscopist (1 %)
    b) Local guidelines (10 %)
    c) Norwegian guidelines (same as ESGE) (71 %)
    d) British guidelines (3 %)
    e) American guidelines (0 %)
    f) Other guidelines. Please elaborate. (15 %)

II

III