

Appropriateness of colonoscopy in Europe (EPAGE II) Surveillance after polypectomy and after resection of colorectal cancer

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Bibliography

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Background and study aims: To summarize the published literature on assessment of appropriateness of colonoscopy for surveillance after polypectomy and after curative-intent resection of colorectal cancer (CRC), and report appropriateness criteria developed by an expert panel, the 2008 European Panel on the Appropriateness of Gastrointestinal Endoscopy, EPAGE II.

Methods: A systematic search of guidelines, systematic reviews and primary studies regarding the evaluation and management of surveillance colonoscopy after polypectomy and after resection of CRC was performed. The RAND/UCLA Appropriateness Method was applied to develop appropriateness criteria for colonoscopy for these conditions.

Results: Most CRCs arise from adenomatous polyps. The characteristics of removed polyps, especially the distinction between low-risk adenomas (1 or 2, small [< 1 cm], tubular, no high-grade dysplasia) vs. high-risk adenomas (large [≥ 1 cm], multiple [> 3], high-grade dysplasia or villous features), have an impact on advanced

adenoma recurrence. Most guidelines recommend a 3-year follow-up colonoscopy for high-risk adenomas and a 5-year colonoscopy for low-risk adenomas. Despite the lack of evidence to support or refute any survival benefit for follow-up colonoscopy after curative-intent CRC resection, surveillance colonoscopy is recommended by most guidelines. The timing of the first surveillance colonoscopy differs. The expert panel considered that 56% of the clinical indications for colonoscopy for surveillance after polypectomy were appropriate. For surveillance after CRC resection, it considered colonoscopy appropriate 1 year after resection.

Conclusions: Colonoscopy is recommended as a first-choice procedure for surveillance after polypectomy by all published guidelines and by the EPAGE II criteria. Despite the limitations of the published studies, colonoscopy is also recommended by most of the guidelines and by EPAGE II criteria for surveillance after curative-intent CRC resection.

Introduction

Cancer of the colon and rectum (colorectal cancer [CRC]) is one of the most common cancers diagnosed in Western countries and the second most common cause of cancer deaths [1,2]. It is generally accepted that most CRCs develop through a continuous process from normal mucosa to benign adenoma and then to carcinoma [3–5]. While nearly all CRCs arise from adenomas, only a small minority of adenomas progress to cancer. Adenomas with advanced features, i.e. > 1 cm in diameter, with high-grade dysplasia, with $> 25\%$ villous histology, or with invasive cancer, have the highest potential for malignancy. The removal of adenomas, by endoscopic polypectomy or surgical resection, is thus recommended to prevent CRC. After polypectomy, individuals are placed

under colonoscopic surveillance to reduce the risk of development of and death from CRC, by detection and removal of new adenomas at surveillance colonoscopy. However, the overall prevalence of adenomas in the population is high ($\sim 30\%$ at age 50 and $\sim 50\%$ at age 70) and a large number of patients with adenomas are now being identified as a result of the increased use of CRC screening, particularly the dramatic increase in screening colonoscopy, thus placing a huge burden on medical resources applied to surveillance. There is a need for increased efficiency of surveillance colonoscopy practice, to decrease the cost, risk, and overuse of resources for inappropriate examinations.

After diagnosis of CRC, between 66% and 85% of cancers can be surgically resected with curative intent [6–8]. After CRC resection, patients are

also entered into surveillance programs, as approximately one-third of patients experience a recurrence within 5 years of initial surgery [9]. Surveillance strategies are thus employed to detect new polyps, local recurrences (defined as a tumor arising at the original tumor site), distant recurrences, also called metastases, and metachronous cancers (defined as a CRC arising in a bowel site other than that of the index cancer), at a stage when a second curative procedure can be performed. The most effective follow-up procedure is, however, still unclear. While colonoscopy is considered to be the best tool for detecting CRC, its effectiveness in improving survival in patients with previous CRC has not yet been clearly demonstrated in randomized controlled trials (RCTs). Its appropriateness for surveillance purposes after curative-intent resection of CRC is therefore debated.

In April 2008, a multidisciplinary European expert panel convened in Montreux, Switzerland, to discuss and develop criteria for the appropriate use of colonoscopy. This article presents the literature review on surveillance after polypectomy and after CRC resection that was provided to the panelists before the panel meeting, to support their ratings of appropriateness of use of colonoscopy in such circumstances, together with the panel results. It is an update of a previous literature review and consideration of appropriateness criteria published in 1999 [10, 11].

Methods

The literature review process included a systematic search of websites issuing guidelines and of Medline (1997–February 2008) to select published guidelines, systematic reviews, and primary studies assessing the use of colonoscopy for surveillance after endoscopic resection of colonic polyps and for surveillance after curative-intent resection of CRC. With the exception of certain relevant articles, the literature published before 1997 is presented in the previous literature review [10, 11].

The targeted patients are individuals placed under colonoscopic surveillance after polypectomy or curative-intent resection of CRC, to reduce the risk of development of and death from CRC, by removal of new lesions at surveillance colonoscopy

The application of the RAND/UCLA Appropriateness Method is described in detail in a companion article in this issue [12]. Briefly, this process is a formal explicit expert panel method that allows classification of each indication into one of the following categories of appropriateness: “inappropriate,” “uncertain,” “appropriate,” “appropriate and necessary” (i.e. mandating colonoscopy). To simplify the graphical presentation of the appropriateness results, these four categories were consolidated into two clusters: “Appropriate” (comprising two categories: appropriate, appropriate and necessary), and “Not appropriate” (comprising two categories: inappropriate, uncertain). In addition to simplification and enhanced clarity of presentation, the rationale was that in many instances of a non-appropriate scenario, whether it be uncertain or inappropriate, it was especially important that the decision for not proposing the colonoscopy should be discussed and shared with the patient; this simplified representation would help here. All clinical indications and their ratings are available on the EPAGE website (www.epage.ch).

Results: Literature review

Surveillance after polypectomy

The objective of postpolypectomy surveillance is to reduce the risk of development of and death from a CRC, by detecting and removing metachronous adenomas and cancers. Colonoscopy is the first-choice procedure for postpolypectomy surveillance as it has been shown to be more sensitive than barium enema in detecting recurrence and permits resection of polyps [13].

Incidence of adenomas, advanced adenomas and CRC after polypectomy, according to adenoma characteristics at index colonoscopy

Diagnostic yield of surveillance colonoscopy after polypectomy, as reported in studies published since 1997, is shown in **Table e1**. Results from the National Polyp Study (NPS) and the Funen Adenoma Study were also included, as these studies are major references for guidelines. Recurrence rates vary greatly between studies due to differences in patient characteristics at baseline, duration of follow-up, patient compliance, inclusion criteria, and quality of initial colonoscopy and polypectomy.

In most cases, the recurrence rate varies according to the baseline adenoma characteristics. Indeed, various different adenoma characteristics at index colonoscopy have been associated with subsequent advanced adenomas at surveillance colonoscopy in various RCTs and cohort studies published since 1997, summarized in **Table e2**. Two characteristics at index colonoscopy were reported in most studies as significantly increasing the risk of advanced adenomas at surveillance colonoscopy: 3 or more adenomas [14–20] and polyp size > 1 cm [17–19, 21, 22]. Two studies reported significantly higher rates of recurrence with proximal polyp location at index colonoscopy [15, 22]. Histology findings (a tubulovillous/villous component or high-grade dysplasia) were not a significant predictor of advanced adenomas in the studies reported here, except in the study on predictors of advanced rectal adenomas [23]. One study also found higher rates of advanced adenomas among patients with high-grade dysplasia at baseline (17.4%) compared with patients with small tubular adenomas (6.1%) [17]. In another study [21], adenomas with tubulovillous and villous components at baseline were significantly associated with villous adenomas at follow-up (odds ratio [OR] 3.7, 95% CI 1.3–10.2 and OR 32.0, 95% CI 5.3–191.7, respectively). Increasing age [21, 22, 24, 25] and male gender [15, 19, 21, 22] also increased the risk of subsequent adenomas. A previous history of polyps before baseline polypectomy was also associated with an increased risk of subsequent adenomas [15, 22, 24]. One study reported that patients with a family history of CRC had a higher recurrence rate for advanced adenomas at surveillance [19]. Finally, one RCT reported a higher recurrence rate if the initial colonoscopy was incomplete [16].

Results from the meta-analysis of Saini et al. [26] on risk factors for recurrence of advanced adenomas showed that patients with ≥ 3 adenomas at index colonoscopy were more likely to have recurrent advanced adenomas than patients with 1 or 2 adenomas ([relative risk] RR 2.52, 95% CI 1.07–5.97), as were patients with adenomas with high-grade dysplasia (RR 1.84, 95% CI 1.06–3.19) compared with patients with low-grade dysplasia.

Compared with patients who were free of polyps, patients with 1 or 2 tubular adenomas of < 1 cm in size at baseline did not have a statistically higher rate of advanced adenomas at follow-up [17]. However, patients with 3 or more small adenomas or with ade-

nomas >1 cm, with a villous component, or high-grade dysplasia, had a significantly higher risk of advanced adenomas. Nonpolypoid adenomas (also called nonpolypoid [i.e. flat and depressed] colorectal neoplasia [NP-CRN]), originally thought to exist primarily in Japan, have now been described throughout the world, and represent between 6% and 37% of adenomas found at colonoscopy in recent studies [27–31]. Left undetected, these flat lesions may evolve into advanced cancer within a few years [32]. Nonpolypoid colorectal adenomas were more likely to contain carcinoma (OR 9.78; 95% CI 3.93–24.4) than polypoid lesions, irrespective of size [31]. In particular, the depressed type of NP-CRN has the highest risk of containing high-grade dysplasia or invasive adenocarcinoma [31]. However, the risk of advanced adenomas at follow-up is unknown for patients with flat and depressed adenomas, as most studies did not distinguish patients with such lesions at baseline. The high prevalence of nonpolypoid adenomas [31], which are more difficult to detect, once again emphasizes the need for high-quality colonoscopy.

Colonoscopic surveillance intervals after polypectomy

While, for ethical reasons, no randomized trial has compared endoscopic surveillance versus no surveillance, a number of RCTs have evaluated the impact of different time intervals between follow-up colonoscopies after polypectomy on the incidence of subsequent advanced adenomas and CRCs.

The National Polyp Study compared follow-up colonoscopy at 1 and 3 years after polypectomy versus at 3 years only. As the incidence of advanced adenomas and cancers was similar in the two groups after 3 years of follow-up, the authors recommended surveillance at a 3-year interval for most patients after polypectomy [20]. The Funen Adenoma Study compared follow-up colonoscopies at 2 and 4 years to 4 years only for patients with pedunculated and small sessile colorectal adenomas [16,33]. The cumulative risk of advanced adenomas did not differ between the two groups after 4 years of follow-up, nor at the end of the long-term follow-up period (up to 20 years). On the other hand, while the CRC prevalence rate was similar between the two groups after 4 years of follow-up, the relative risk for CRC was higher for patients in the 4-year interval group at the end of the long-term follow-up period (RR 6.22, 95% CI 1.06–117.48). In contrast to their initial conclusions stating that the first control colonoscopy may be postponed until 4 years after resection, the authors concluded from the long-term results that the 2-year interval may be safer, although the risk of complications could be higher. In another trial with a shorter follow-up period (6 years) and fewer patients, the same authors compared follow-up colonoscopies every year versus every 2 years for patients with sessile adenomas >5 mm and villous adenomas (high-risk group) [33]. The risk of advanced adenomas and CRC did not significantly differ between the two groups, although more advanced cancers were detected in the 2-year interval group suggesting that the 2-year interval may be too long.

Another RCT compared six surveillance strategies at 1-, 2-, or 5-year intervals using either flexible sigmoidoscopy or colonoscopy, after stratification for high-risk and low-risk of recurrence [34]. After 12 years of follow-up, recurrence rates were low and occurred mostly in high-risk patients (adenoma >2 cm, severe dysplasia, >2 adenomas, or family history of CRC in ≥ 2 first-degree relatives) (RR 1.82, 95% CI 1.2–2.9). The number of cancers observed (4) was also lower than expected (9.1). The authors concluded that follow-up endoscopy can safely be reduced to 5-

year intervals for the majority of patients, using colonoscopy rather than flexible sigmoidoscopy.

Finally, in Lieberman and colleagues' cohort study on CRC screening by colonoscopy, patients with small adenomas (<1 cm) at baseline were randomly assigned to surveillance at 2 and 5 years versus 5 years only [17]. Although the rate of advanced adenomas did not differ between the groups at 5.5 years of follow-up, results should be interpreted with caution due to the short follow-up period and potential selection bias due to the study design. In a recent case-controlled study [35], individuals with a history of polypectomy had a significantly lower risk of CRC up to 5 years after polypectomy, even after removal of high-risk polyps, compared with individuals without previous endoscopy. However, a nonsignificant increase in risk of CRC was found between 6 and 10 years after polypectomy, which did not support further extension of surveillance intervals. Results from a multivariate analysis of a cohort study of patients after polypectomy showed that patients with no family history of CRC and only small (<1 cm) tubular adenomas (low-risk group) had a very low risk of advanced adenomas compared to all other patients (high-risk group) [19]. The authors recommend a 10-year interval for surveillance for the low-risk group and a 3-year interval for the high-risk group, based on the estimation that 10% will develop advanced adenomas after 10 years in the low-risk group and after 3 years in the high-risk group. In a recent analysis of the Polyp Prevention Trial [36], the 4-year risk for advanced adenomas was higher for individuals with an advanced and/or proximal adenoma at baseline (9%), compared with 5% for nonadvanced adenomas or distal adenomas. This difference is statistically significant but may not be clinically important. Patients with 3 or more nonadvanced adenomas had the same 6% overall risk for advanced adenoma as the entire cohort.

Impact of initial polypectomy and colonoscopic surveillance on CRC risk and mortality

It is difficult to distinguish the impact of initial polypectomy on CRC risk and mortality from the impact of colonoscopic surveillance, as the study populations in most postpolypectomy studies were subjected to both polypectomy and colonoscopic surveillance. In **Table e3**, the studies presented evaluate the impact of polypectomy and colonoscopic surveillance on CRC incidence and on mortality from CRC [5,21,24,34,37–42].

A number of observational studies, particularly the National Polyp Study, have shown that the removal of adenomatous polyps and subsequent surveillance significantly decrease the incidence of CRC compared with that expected in the general population [5,21,37,38]. On the other hand, other observational studies found no significant difference between the observed and expected incidence of CRC [24,40,41] and one population-based study found a higher than expected incidence of CRC in patients with adenomas [39]. Results from this study should, however, be interpreted with caution as no formal colonoscopic surveillance schedule was in place and it was not known whether adenomas were removed. Differences in adenoma characteristics at baseline may explain different risk estimates for CRC, as patients with large adenomas are at higher risk.

The impact of polypectomy and colonoscopic surveillance on CRC mortality was reported in one study only, based on the analysis of several studies with various follow-up intervals [38]. Results showed that in a population of patients with all types of adenomas, mortality from CRC was significantly reduced (RR 0.12, 95% CI 0.03–0.36). While the overall mortality was not significantly

reduced (RR 0.93, 95% CI 0.86–1.01), a significant small reduction was found in women (RR 0.86, 95% CI 0.74–0.99).

Guidelines on the use of colonoscopy for surveillance after polypectomy

Table e4 presents the recommendations from representative guidelines on endoscopic follow-up after polypectomy [19,43–48]. These guidelines are consolidated in **Fig. e1**. These new guidelines differ from previous postpolypectomy guidelines published before 1997 in that baseline adenoma characteristics play a major role in determining appropriate postpolypectomy surveillance intervals. Patients are stratified into lower-risk and higher-risk groups with a specific surveillance interval. In summary, the next colonoscopic surveillance is recommended at 3 years for patients with high-risk adenomas (large ≥ 1 cm), multiple ≥ 3 , high-grade dysplasia, villous features), and at 5 years for patients with low-risk adenomas (1 or 2, small < 1 cm) tubular adenomas with no high-grade dysplasia).

Patients with small (< 1 cm) and fewer than 5 rectosigmoid hyperplastic polyps are considered to have a normal colonoscopy and therefore not at increased risk for CRC. However, for patients with large (≥ 1 cm) or numerous (≥ 5) hyperplastic polyps, follow-up colonoscopy is recommended at 5 years [43]. Patients with hyperplastic polyposis, ≥ 5 hyperplastic polyps proximal to the sigmoid colon, 2 of which are > 1 cm in diameter, or any number of hyperplastic polyps with a first-degree relative with hyperplastic polyposis, or > 30 hyperplastic polyps of any size distributed throughout the colon [49], should probably be offered annual colonoscopy [45]. Literature is scarce in this field.

Extremely vigilant follow-up, with initial colonoscopy intervals of 3–6 months, is warranted for sessile adenomas (> 2 – 3 cm) [44,48] since 28% recur or persist after piecemeal resection, and 17% later degenerate into carcinoma despite apparently complete removal [50].

The baseline colonoscopy needs to be of high quality for the baseline adenoma characteristics to be suitable for use in planning surveillance intervals, as baseline colonoscopy without a good clearing of the colon places the patient at increased risk of subsequent neoplastic findings. According to the US Multi-Society Task Force, a high-quality colonoscopy reaches the cecum in over 95% of cases, has little fecal residue, and has a minimum withdrawal time from the cecum of 6–10 minutes [51].

Surveillance after curative-intent CRC resection

Colonoscopic surveillance after CRC resection aims at improving survival by the early detection of asymptomatic recurrences of the initial cancer in the bowel (anastomotic or intraluminal recurrence), metachronous CRC, and adenomatous polyps, as early detection increases the chance of successful resection of local recurrence or metachronous cancer [52]. The proportion of patients who undergo a second curative resection has increased in the last 20 years [53]. Curative reoperation is performed more often for metachronous cancers (67%–86%) than for local recurrences (7%–22%) [54]. However, as local recurrence and metachronous CRC are relatively infrequent, it has been considered that colonoscopy alone is of limited usefulness [55,56] and other tests should form part of a surveillance program.

Recurrence, metachronous cancer and adenomatous polyps

As the incidence of recurrences and new tumors after CRC resection is an important factor in determining whether and when colonoscopic surveillance should take place, some evidence per-

taining to these rates, and to risk factors for recurrence and new tumors, is briefly presented. Studies published between 1997 and February 2008 report low rates of intraluminal recurrence and metachronous CRC that are detected by surveillance colonoscopy (1%–9%) [54,57–72] (see **Table e5**). The rate of metachronous CRC is even lower when perioperative colonoscopy is performed to clear the colon of synchronous lesions [57,63,67]. In a recent population-based study using a cancer registry as the source of information [73], the cumulative rate of metachronous CRC was 1.8% (95% CI 1.5–2.2) at 5 years, and 3.4% (95% CI 2.9–4.0) at 10 years, and individuals with previous CRC were at greater risk of developing a new CRC (standardized incidence ratio [SIR] 1.5 [1.3–1.7]). Rates of adenomatous polyps, also reported in **Table e5**, are higher (between 7% and 34%) [59,60,64–70], especially in the presence of synchronous polyps at perioperative colonoscopy [57].

Most recurrences occur within 2 years of initial surgery [52,74–79], while few recurrences (1%–12%) occur after 5 years [52,80–82]. Various risk factors have an impact on rates of recurrence. A more advanced stage of the primary tumor at diagnosis is associated with a higher local recurrence rate [83–86] (**Table e6a–c**). In addition, cancers located at the rectosigmoid junction are more prone to local recurrence than tumors of the right or left colon, and left-sided primary tumors recur more often than right-sided ones; poorly-differentiated tumors, ulcerating tumors, and tumors > 3 cm also showed a higher incidence of recurrence [52,74,75,80,81,83,85]. Finally, recurrence occurs more often in rectal cancer patients than in colon cancer patients [84,85]. Risk factors for metachronous cancers include synchronous cancer and polyps along with index cancer at initial resection, an initial tumor located in the proximal colon, and hereditary nonpolyposis colorectal cancer (HNPCC) [87,88].

Effectiveness of colonoscopy for surveillance after curative intent resection of CRC

The mean yield of surveillance colonoscopy was reported to be 7.6% for colon cancer (range 1%–25%) and 17.2% for adenomatous polyps (range 6%–40%) [89]. In the meta-analysis performed by the US Multi-Society Task Force [90], 157 colonoscopies were needed to detect one metachronous cancer.

No randomized trial was found evaluating whether surveillance colonoscopy alone improves patient outcome. In a case-controlled study [91], surveillance endoscopy (colonoscopy or flexible sigmoidoscopy) was not associated with improved CRC survival (OR 1.01, 95% CI 0.95–1.06). However, the study included only patients > 65 years old, with many competing causes of death, which may have removed any evidence of benefit by surveillance endoscopy. Results from a retrospective cohort study [67] showed that colonoscopic surveillance was associated with improved 5-year survival compared with no surveillance (76.8% vs. 52.2%, $P < .0001$) and that the risk of mortality was decreased by 42% (hazard ratio [HR] 0.58, 95% CI 0.44–.075). Another retrospective cohort study of veterans also found that the risk of mortality decreased by 43% (HR 0.57, 95% CI 0.51–0.64) in patients who had at least one follow-up colonoscopy [92].

Five RCTs were published between January 1997 and February 2008 [54,68,77,79,93] comparing standard follow-up programs with intensive programs, including colonoscopy along with other tests, in addition to the two RCTs published before 1997 [94,95] (**Table e7**). A significant improvement in overall survival in the intensive follow-up group was reported in only two RCTs [79,93], while the other trials failed to show any benefit from an

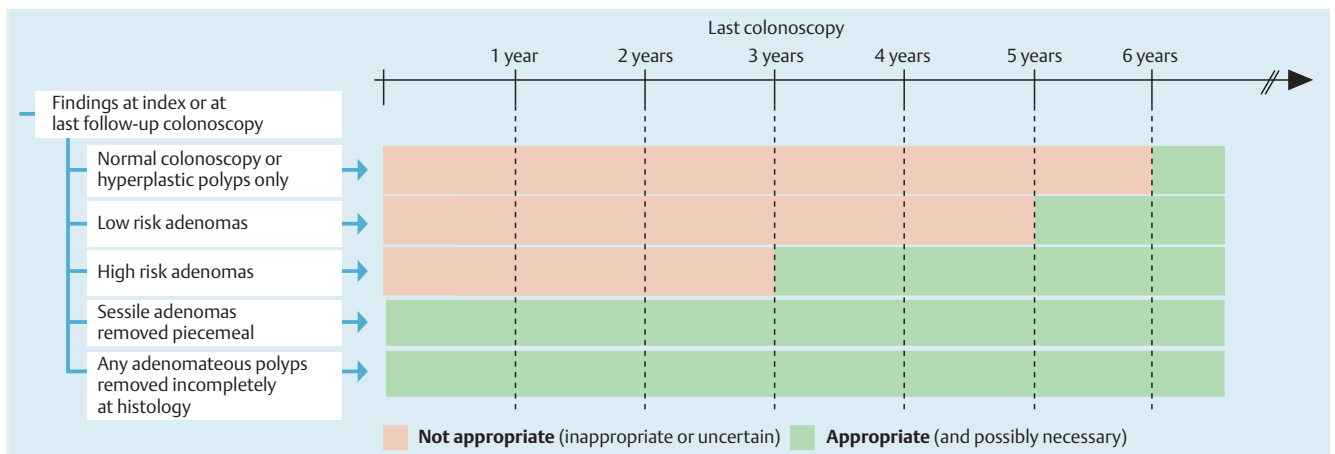


Fig. 2a Appropriateness ratings of clinical indications for performing colonoscopy for surveillance after polypectomy (simplified decision tree). Copyright © 2008 IUMSP/CHUV, Lausanne, Switzerland – EPAGE II.

intensive follow-up regimen on survival rate [54,68,77,94,95]. This absence of benefit may be due to a lack of statistical power, as these trials included between 100 and 600 patients only, and due to the small proportion of patients with a potentially curable recurrence. In one of these RCTs [68], yearly colonoscopy failed to detect any asymptomatic local recurrence, while in another trial [77], yearly colonoscopy detected 44% of resectable tumor recurrences. Six systematic reviews and meta-analyses of follow-up studies were also identified in the literature published since 1997 [76,96–100]. Results from the two meta-analyses published in 2007 [97] suggested that there is an overall survival benefit with intensive follow-up of patients after curative surgery for CRC, and that more curative reoperations for recurrences were performed in the intensive follow-up groups, leading to better survival. The specific role of endoscopic surveillance in improving survival cannot, however, be estimated from these studies. In the subgroup analyses of one of the meta-analyses [100], surveillance programs including colonoscopy and serum carcinoembryonic antigen (CEA) measurement showed a significant impact on overall mortality.

Guidelines on the use of colonoscopy for surveillance after curative-intent resection of CRC

Table e8 presents a summary of the recommendations from representative guidelines on endoscopic follow-up after resection of CRC [43,46,47,90,96,101–105]. Despite the lack of evidence to support or refute any survival benefit of colonoscopic follow-up, surveillance colonoscopy is recommended by all guidelines. According to the American guidelines [90], candidates for surveillance colonoscopy are patients who undergo a curative-intent resection of colon and rectal cancers of all stages. Guidelines on the timing of the first surveillance colonoscopy after the perioperative colonoscopy differ. According to some guidelines [90,104,105], the first surveillance colonoscopy should be performed 1 year after resection (or 1 year following perioperative colonoscopy), based on the high incidence of metachronous lesions within the first 2 years after resection. The timing of subsequent colonoscopies if results from the previous one are normal varies from 3 to 5 years according to the different guidelines. The interval should be reduced if adenomas are found at colonoscopy [90].

Table 9 Definitions of terms used to characterize clinical indications for the use of colonoscopy in surveillance after polypectomy and after resection of colorectal cancer (CRC).

Term	Definition
Low-risk adenomas	All of the following: No more than 2 adenomas Size < 1 cm Tubular histology No high-grade dysplasia No family history in first-degree relative
High-risk adenomas	Any of the following: Villous or tubulovillous histology or serrated adenoma (any size, number or grade of dysplasia) Size ≥ 1 cm Multiple adenomas (≥ 3) Large sessile adenoma High-grade dysplasia

EPAGE II appropriateness criteria

Surveillance after polypectomy

Out of 463 indications, 77 pertained to colonoscopic surveillance after polypectomy. The proportions of indications related to colonoscopic surveillance considered appropriate, uncertain, or inappropriate were 56%, 7%, and 38% respectively. Disagreement between panelists occurred in only 3% of cases. The panel deemed 36 indications (47%) to be necessary (mandating colonoscopic surveillance). **Fig. 2a** shows the overall color-coded panel results as a simplified dichotomy: “Not appropriate” (inappropriate or uncertain), versus “Appropriate” (appropriate and possibly necessary). **Fig. e2b** shows appropriateness criteria in more detail, with the full range of categories: inappropriate, uncertain, appropriate, and necessary (mandating colonoscopic surveillance). Terms used for the definition of these scenarios are listed in **Table 9**.

When the index or follow-up colonoscopy revealed hyperplastic polyps or the follow-up examination was normal, follow-up colonoscopy was considered appropriate at 5.5 years.

For low-risk adenomas at index or at last follow-up colonoscopy, the next follow-up colonoscopy was considered appropriate at 5 years and necessary after 5.5 years. For high-risk adenomas, follow-up colonoscopy was considered appropriate and necessary at 3 years after the index or the last follow-up colonoscopy. For sessile adenomas removed piecemeal, follow-up colonoscopy

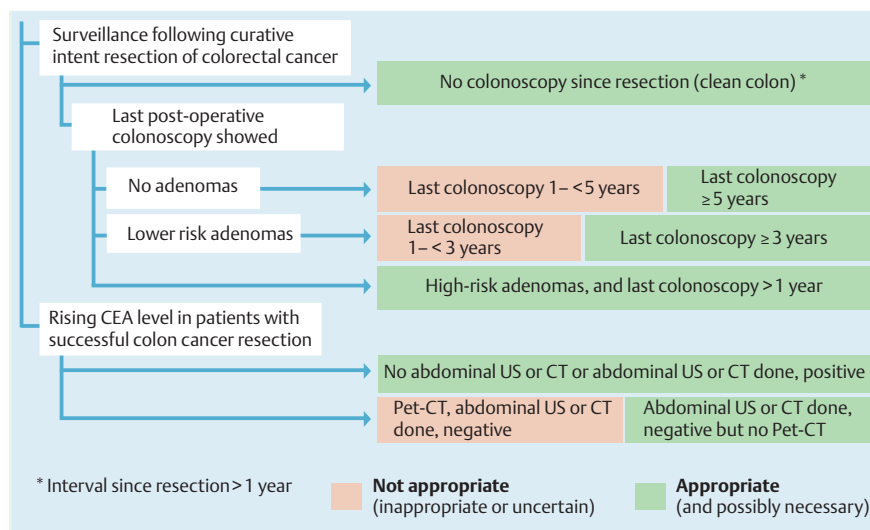


Fig. 3a Appropriateness ratings of clinical indications for performing colonoscopy for surveillance after curative-intent resection of colorectal cancer (CRC) (simplified decision tree). Copyright © 2008 IUMSP/CHUV, Lausanne, Switzerland – EPAGE II.

was considered appropriate and necessary within the first 9 months following the index colonoscopy. For any adenomatous polyp incompletely removed histologically, follow-up colonoscopy was considered appropriate within 9 months of the incomplete resection and necessary after 9 months.

Surveillance following curative-intent CRC resection

Out of 463 indications, 16 pertained to colonoscopic surveillance after curative-intent resection of CRC. The proportions of indications for colonoscopic surveillance considered appropriate, uncertain, or inappropriate were 63%, 25% and 12%, respectively. Disagreement between panelists occurred in 13% of cases. Six indications (37.5%) were deemed necessary (mandating colonoscopic surveillance) by the panel. **Fig. 3a** shows the overall color-coded panel results as a simplified dichotomy: “Not appropriate” (inappropriate or uncertain), versus “Appropriate” (appropriate and possibly necessary). **Fig. e3b** shows appropriateness criteria in more detail, with the full range of categories: inappropriate, uncertain, appropriate, and necessary (mandating colonoscopic surveillance). Terms used for the definition of these scenarios are listed in **Table 9**.

When there had been no colonoscopy since resection but the colon was clean at the time of surgery, follow-up colonoscopy was considered appropriate 1 year after resection and necessary after 3 years. When the last postoperative colonoscopy revealed no adenoma, the next colonoscopy should be scheduled after 5 years. If the last postoperative colonoscopy revealed low-risk adenomas, colonoscopy was appropriate after 3 years and necessary after 5 years. If the last postoperative colonoscopy revealed high-risk adenomas, a follow-up colonoscopy after 1 year was appropriate and necessary. If the CEA level was shown to be rising, a colonoscopy was only appropriate if abdominal ultrasound or computed tomography (CT) scan were negative and there had been no positron emission tomography-computed tomography (PET-CT) scan.

Conclusions

Most, but not all, of the available evidence has shown that polypectomy followed by colonoscopic surveillance is effective in decreasing the incidence of and mortality from CRC. There is also a fair amount of evidence that the characteristics of removed

polyps at the index colonoscopy, especially whether low-risk vs. high-risk adenomas, has an impact on the finding of advanced adenomas at surveillance colonoscopy. In accordance with the literature review and clinical practice guidelines, the expert panel recommended a 3-year interval for the high-risk group and a 5-year interval for the low-risk group.

The available evidence from RCTs and systematic reviews for surveillance after CRC resection indicates a minor improvement of survival rate with intensive follow-up including colonoscopy. However, the specific role of colonoscopy in improving patient outcome cannot be clearly determined based on available studies. Nevertheless, published guidelines recommend colonoscopy in a surveillance program after curative-intent resection of a CRC. Colonoscopy is considered specifically useful for the detection of metachronous cancers, even though rates are low.

In surveillance after CRC resection, the expert panel considered colonoscopy appropriate after 1 year. The recommended interval for subsequent colonoscopies was 5 years when results are normal, but shorter (3 years) in the presence of low-risk adenomas and after 1–3 years in the presence of high-risk adenomas.

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Competing interests: None

Appendix: The EPAGE II Study Group



See page 205.

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Fig. e1 Colonoscopic surveillance in asymptomatic people after adenoma removal. Other considerations include age, comorbidity, and family history.

Fig. e2b Appropriateness ratings of clinical indications for performing colonoscopy for surveillance after polypectomy (full decision tree).

Fig. e3b Appropriateness ratings of clinical indications for performing colonoscopy for surveillance after curative-intent resection of colorectal cancer (CRC) (full decision tree).

Table e1 Diagnostic yield of surveillance colonoscopy after polypectomy.

Table e2 Risk factors at baseline colonoscopy for advanced adenomas at surveillance colonoscopy.

Table e3 Impact of polypectomy and colonoscopic surveillance on colorectal cancer (CRC) incidence and mortality.

Table e4 Guidelines for colonoscopy surveillance after polypectomy.

Table e5 Diagnostic yield of colonoscopy surveillance programs after curative resection of colorectal cancer (CRC).

Table e6 a Local recurrence rates of colorectal cancer (CRC) according to primary tumor stage (5-year overall rate). **b** Cancer classifications. **c** Tumor–node–metastasis (TNM) definitions.

Table e7 Randomized controlled trials (RCTs) of surveillance follow-up programs after colorectal cancer (CRC) surgery.

Table e8 Guidelines on surveillance colonoscopy after curative intent resection of colorectal cancer (CRC).