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Who Needs Follow-Up after Endoscopic Resection of Colorectal Adenomas?

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Keywords
Surveillance colonoscopy · Colorectal cancer · Adenoma · Hereditary colorectal cancer

Summary
Background: Surveillance colonoscopy after endoscopic resection of colorectal adenomas is a crucial step in the concept of colorectal cancer screening. After identifying the patients at risk with screening and resection of adenomas, there has to be a tailored surveillance. Surveillance colonoscopy should detect recurrent and metachronal adenomas at a stage where they can be removed endoscopically. In the following, the criteria for a risk-adapted surveillance interval are presented. **Methods:** A literature review based on American, European, and German guidelines for surveillance after polypectomy and the German guideline for the diagnosis and treatment of ulcerative colitis, as well as a selective literature search into hereditary colorectal cancer were performed. **Results:** State of the art surveillance after endoscopic resection of colorectal adenomas is based on a focused anamnesis and the index colonoscopy. On the basis of existing guidelines, a risk-adapted surveillance strategy can be implemented. **Conclusions:** Adherence to surveillance guidelines is a basic part of colorectal cancer screening and should be the starting point for further research.

Schlüsselwörter
Nachsorgekoloskopie · Kolorektales Karzinom · Adenom · Hereditäres kolorektales Karzinom

Zusammenfassung
Hintergrund: Die Nachsorgekoloskopie nach erfolgter endoskopischer Resektion von Adenomen ist ein wichtiger Baustein der Kolonkarzinomvorsorge. Durch die Vorsorgekoloskopie und die endoskopische Resektion werden Menschen identifiziert, die ein höheres Risiko für die Entstehung eines kolorektalen Karzinoms haben. Eine Nachsorgekoloskopie sollte Adenomrezidive und metachrone Adenome in einem Stadium detektieren, in dem die Adenome noch endoskopisch therapiert werden können. Im vorliegenden Artikel werden die notwendigen Kriterien für die risikostratifizierte Nachsorge vorgestellt und Empfehlungen anhand gültiger Leitlinien dargelegt. **Methoden:** Es wurden eine Literaturrecherche auf Grundlage der amerikanischen, europäischen und deutschen Leitlinien für Nachsorge nach Polypektomie und der deutschen Leitlinie für ulzerative Kolitis sowie eine selektive Literaturrecherche zum hereditären kolorektalen Karzinom durchgeführt. **Ergebnisse:** Die Empfehlungen zur fachgerechten Nachsorge basieren auf einer fokussierten Anamnese und den Befunden in der Index-Koloskopie. Anhand weniger Kriterien lässt sich gemäß den Leitlinien eine risikoadaptierte Nachsorgestrategie implementieren. **Schlussfolgerungen:** Die Umsetzung der Leitlinien zur Nachsorge nach Polypektomie ist ein essenzieller Teil der Vorsorge für das kolorektale Karzinom und sollte Ausgangspunkt für weitere wissenschaftliche Arbeit sein.

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Colonoscopic surveillance plays an important role in the concept of colorectal screening endoscopy. Individuals with adenomas in the index endoscopy have a higher risk of developing metachronal adenomas and carcinomas than individuals without adenomas. Colonoscopy surveillance should detect adenomas at a stage where they can be removed endoscopically. Overuse of colonoscopy surveillance leads to a higher burden for individuals, a higher risk of complications, and potentially a higher proportion of individuals lost to follow-up. Several national guidelines and also a European guideline for surveillance intervals exist [1–4]. The evidence for the intervals is based mainly on empirical data with the endpoint advanced adenoma after a certain post-interventional time interval. This is used as a surrogate marker for the prevention of colorectal cancer. The adherence to established guidelines is poor, even in high-quality centers [5, 6]. The following recommendations are based on the German S3 guideline 'Kolorektales Karzinom' [4].

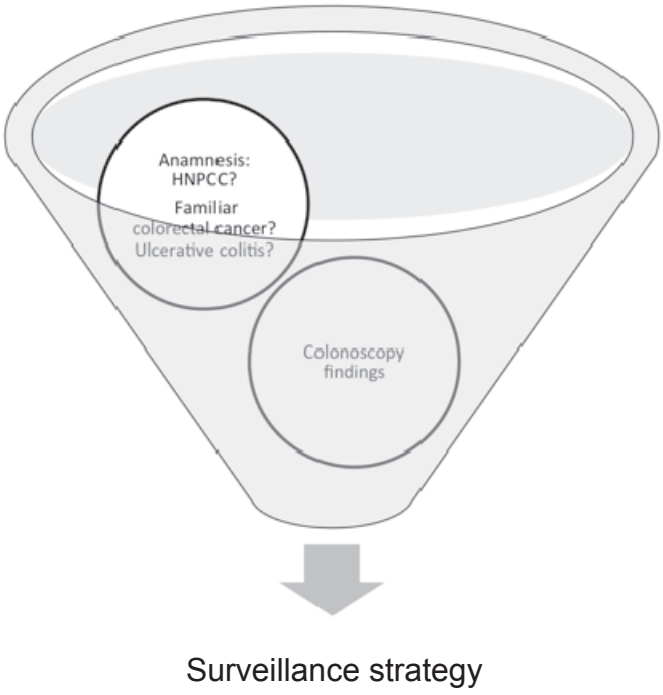

Fig. 1. Risk stratification.

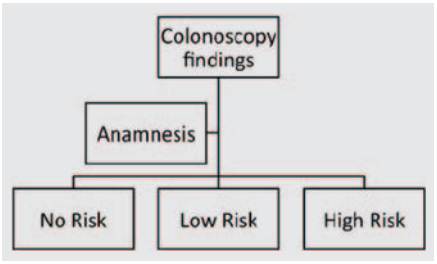

Fig. 2. The three risk groups.

Anamnesis

All recommendations are based on risk stratification. Therefore it is important to assess all known risk factors (fig. 1). Risk stratification is mainly based on the index colonoscopy. The criteria histology, number of adenomas, resection technique, and size allow certain conclusions to be drawn as to whether there is a higher risk of recurrence or development of metachronous adenomas. Besides the index colonoscopy, a focused anamnesis is important to check whether there is evidence of hereditary nonpolyposis colorectal cancer (HNPCC), increased familial risk of colorectal cancer, or ulcerative colitis. Each condition leads to modification of the surveillance strategy. Patients fulfilling the Amsterdam II Criteria or the Revised Bethesda Guidelines are at risk of HNPCC. These patients should receive human genetic counseling and molecular pathologic testing for microsatellite instability (MSI) and mismatch repair protein immunohistochemistry. Patients diagnosed with HNPCC should undergo annual colonoscopy surveillance [7]. Familial risk of colorectal cancer describes a group of people with an inherited form of colorectal carcinoma where the genetic changes are not completely understood [8].

Patients with a first-degree relative, parent, sibling, or child diagnosed at age >50 years with colorectal cancer have a two- to threefold higher risk of colorectal cancer [9]. In the case of a first-degree relative under 45, the risk is three- to sixfold higher [10]. This leads to a shorter interval to colonoscopy in the case of a negative index colonoscopy according to the American guidelines if the first-degree relative is younger than 60 at the time of diagnosis. The German guideline recommends colonoscopy surveillance after 10 years as in the normal-risk population.

Index Colonoscopy

If no adenoma is found in the index colonoscopy, the German guideline for the diagnosis and treatment of ulcerative colitis recommends colonoscopy surveillance every 1–2 years, 8 years after diagnosis of the disease in the case of pancolitis, and 15 years after diagnosis in the case of distal colitis [11].

The criteria histology, number of adenomas, resection technique, and size in the index colonoscopy are used to stratify patients into three risk groups: no risk, low risk, and high risk (fig. 2). Histology as stratification criterion of surveillance is based on the differentiation between tubular adenomas (low risk) and adenomas with villous components of at least 25% or high-grade dysplasia (HGD) (high risk). While the higher risk of advanced adenomas was shown for villous adenomas in a recent pooled analysis of 9,176 patients, HGD was not an independent risk factor in this analysis [12]. One disadvantage of using histology as a risk factor is the high interobserver variability [13, 14]. The surveillance guidelines of the British Society of Gastroenterology do not use adenoma sub-

Table 1. Standard risk groups

Risk group	Adenomas, n	Size < 10 mm	En bloc resection	HIEN or villous histology
No risk	n.a.	yes	yes	no
Low risk	<3	yes	yes	no
High risk	3–9	no	yes	yes

HIEN = High-grade intraepithelial neoplasia; n.a. = not applicable.

Table 2. Special constellations

	Surveillance interval, months
Piecemeal resection	3–6
≥10 adenomas	12
Hyperplastic polyposis syndrome	12
pT1 cancer	3–6

typing as a criterion [2]. Serrated lesions are new components of risk stratification. More and more serrated lesions are being diagnosed, and there is an increase in the awareness of this entity [15]. The serrated neoplastic pathway is established, and there are indications that serrated polyps progress fast into colorectal cancer [16, 17]. The number of adenomas detected in the index colonoscopy is a strong risk factor for metachronal adenomas; this has been shown in several pooled analyses [12, 18]. The number is also an indicator of missed lesions. Miss rates are higher if more adenomas are detected [19]. In the case of more than 5 adenomas, the British guideline recommends an interval of 1 year, while the German and the American guidelines recommend a 3-year interval [2]. A large size of >10 and >20 mm, respectively, was a risk factor for metachronal adenomas in two large pooled analyses [12, 18]. Resection technique is a risk factor for recurrence of adenoma. In the case of piecemeal resection, the pathologist cannot assess the completeness of the resection; therefore it is important to check the resected area. There is no good evidence regarding the time when the resected area should be checked [1]. The German and the American guidelines recommend surveillance after 3–6 months. In the opinion of the author, this is too soon. We could show in our cohort with a median 6-year follow-up that there is a small proportion of patients with recurrence beyond the first endoscopy surveillance and, as also described in the literature, late recurrence after the first surveillance [20, 21]. In our opinion, check-ups carried out too early are misleading and result in too many endoscopies per patient.

Risk Groups

The risk groups are defined as follows (table 1):

- No risk: if the index colonoscopy shows only small hyperplastic polyps <10 mm, there should be no colonoscopy surveillance; the next colonoscopy screening should be done 10 years after the index colonoscopy.
- Low risk: maximum of 2 adenomas with low-grade dysplasia or tubular histology, <10 mm in size, and resection in en bloc technique.
- High risk: high risk must be assumed if one of the following criteria applies – HGD or histology with villous components, serrated lesions without dysplasia measuring ≥10 mm, sessile serrated polyps with dysplasia (SSA/P), traditional serrated adenoma (TSA), 3 or more adenomas, size ≥10 mm, and resection in en bloc technique.

In addition, there are special constellations (table 2). In the case of a piecemeal resection, a first colonoscopy surveillance should be done in 3–6 months. In the case of 10 or more adenomas in the index colonoscopy, patients should get human genetic counseling and a genetic diagnostic work-up for APC mutations for attenuated FAP (aFAP) and MUTYH mutations for MUTYH-associated polyposis (MAP). Patients with aFAP or MAP should undergo annual colonoscopy. In the case of nondysplastic polyposis syndromes, there is little evidence of recommendations for surveillance intervals. For hyperplastic polyposis syndrome (HPP), there is increasing evidence that this syndrome leads to a higher risk of developing colorectal cancer. The World Health Organization (WHO) criteria for HPP are 5 or more polyps proximal to the sigmoid with at least 2 polyps of >10 mm, 20 or more polyps distributed throughout the entire colon, or 1 hyperplastic polyp and a first-degree relative with HPP. In the case of HPP, patients should undergo annual colonoscopy surveillances [22]. For endoscopically resected pT1 colorectal carcinomas with the low-risk constellations G1 or G2 and L0, there are two scenarios: in the case of a pathologically proven complete en bloc resection, the next colonoscopies should be done in 6 months and in 2 years; in the case of a piecemeal resection, it should be documented that the base of the carcinoma has been pathologically completely resected, and a local surveillance should be done in 3 months, 6 months, and 2 years.

All these recommendations are based on a high-quality index colonoscopy. There is increasing evidence that good quality is as important as the other risk factors. A recent publication in the *New England Journal of Medicine* showed that the adenoma detection rate is an independent predictor of carcinoma interval after the index colonoscopy [23]. Inadequate bowel preparation as a quality criterion leads to a higher rate of missed lesions [24, 25]. These quality factors need to be considered when implementing risk stratification. Colonoscopy surveillance is important for reducing the incidence and mortality of colorectal cancer. Only if guidelines are adhered to can the maximum benefit of screening for colorectal cancer be obtained.

Disclosure Statement

No conflicts of interest.

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