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Scandinavian surveillance follow-up programmes in patients with malignant colorectal polyps

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ABSTRACT

INTRODUCTION: Following endoscopic removal of malignant colorectal polyps, patients may undergo completion radical resection or surveillance. The optimal surveillance strategy remains unknown. This study included colorectal departments in Scandinavian countries with a focus on follow-up periods and examination modalities for patients with endoscopically removed malignant polyps with a resection margin > 1 mm.

METHODS: This study was conducted as an internet-based survey. A questionnaire was sent to all Scandinavian surgical departments performing > 20 colorectal procedures annually. Questions differed between follow-up on rectal and colonic malignant polyps with presence or absence of histological risk factors. The follow-up period was defined as short (one year), intermediate (three years) or long (five years).

RESULTS: The majority of the departments used a long (five years) (38-59%) or intermediate (three years) (26-38%) follow-up programme. In patients with rectal malignant polyps and presence of histological risk factors, a significant difference was observed in the use of endoscopy according to length of follow-up. No difference in the use of the different modalities was seen according to length of follow-up in patients with colonic malignant polyps.

CONCLUSIONS: The follow-up on patients with endoscopically removed malignant polyps and a surveillance strategy varies both in terms of length and performed modalities. Future studies should compare long-term patient outcomes in departments employing different follow-up strategies.

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Colorectal cancer is the third most common cancer both worldwide and in Scandinavia [1, 2]. It is estimated that malignant polyps account for 15% of all screening-detected colorectal cancers [3]. Malignant polyps often have a benign macroscopic appearance, but when the histological examination reveals invasive adenocarcinoma, the dilemma is whether to proceed to completion radical resection or to adhere to a surveillance strategy. A surveillance strategy following polypectomy is applied in 59-64% of patients, but evidence for optimal follow-up is limited [3-6]. Although there is no evidence for an optimal regime, follow-up of patients with colorectal cancer and radical resection is often standardised nationally and is well-defined. However, evidence for the optimal

surveillance strategy following polypectomy only is poor, and post-operative follow-up of patients with polypectomy for malignant polyps and surveillance may therefore differ between hospitals and regions within the same country.

A nationwide register-based study from Denmark indicates a comparable overall and cancer-free survival between completion resection and surveillance strategy but recurrence rates are higher in patients following a surveillance strategy [6]. Moreover, a more advanced stage of recurrent cancer is observed as the interval between follow-up colonoscopies increases [4].

Thus, evidence for the optimal surveillance programme after colorectal cancer polypectomy leaves much to be desired. The primary aim of the present study was to describe the variety of Scandinavian follow-up programmes for patients with endoscopically removed malignant polyps following a surveillance strategy.

METHODS

This was a cross-sectional study on surveillance follow-up programmes for patients with malignant colorectal polyps in Scandinavian countries (Denmark (DK), Norway (NO) and Sweden (SE)). The study was conducted as an internet-based questionnaire survey. A list of all colorectal surgical departments and chief surgeons was provided by the respective Scandinavian authors. Inclusion criteria were colorectal surgical departments performing > 20 colorectal operative procedures annually.

Patients with endoscopically removed malignant colorectal polyps with a resection margin > 1 mm enrolled in a surveillance strategy were the target population. Patients with an endoscopically removed malignant polyp with a resection margin ≤ 1 mm were not addressed in the questionnaire.

An e-mail containing a link to the questionnaire was sent to all heads of department of eligible surgical departments in DK, SE and NO. The head of each department was asked to fill out the questionnaire or forward the questionnaire to the head of the colorectal section or another responsible party with knowledge of the questions asked. Reminders were sent out every two weeks until an answer had been received or three reminders had been sent out. In case a department failed to respond after three reminders, it was contacted and reminded by phone. Return of the questionnaire was considered consent to participate in the study. The response deadline was October 2018. Departments with a follow-up period that was not defined before the study (two or four years) were excluded from analysis. The platform questionnaire was constructed using advanced logistics, presenting the respondent with only relevant questions depending on previous answers.

The main focus was to identify three pre-study-defined follow-up periods: short (one year), intermediate (three years) and long (five years). The secondary focus was to identify the number and type of follow-up imaging and paramedical modalities during and in between the follow-up programmes.

The questions included the total length of the follow-up programme in years (primary outcome) and the follow-up modality used during follow-up (secondary outcome) (carcinoembryonic antigen, endoscopy, CT, MRI and endoscopic ultrasound (EUS)) and the number of modalities performed per follow-up year.

The questions differentiated between follow-up depending on presence or absence of histological risk factors (sessile morphology, polyp diameter ≥ 2 cm, lymphatic or vascular invasion, tumour budding, low tumour differentiation, tumour level Haggitt 3 or 4, Kikuchi level SM3, and piecemeal resection) and the location of the malignant polyp (colon or rectum) due to the different type of modalities available for follow-up depending on the location of the polyp. Finally, departments were asked whether they would consider a surveillance strategy in patients with a malignant polyp and a resection margin ≤ 1 mm.

Statistical analysis

The study was explorative and sample size calculation was not possible. Descriptive non-parametric statistics were used to describe frequencies and percentages for categorical variables. Data were collected and analysed using a statistical package.

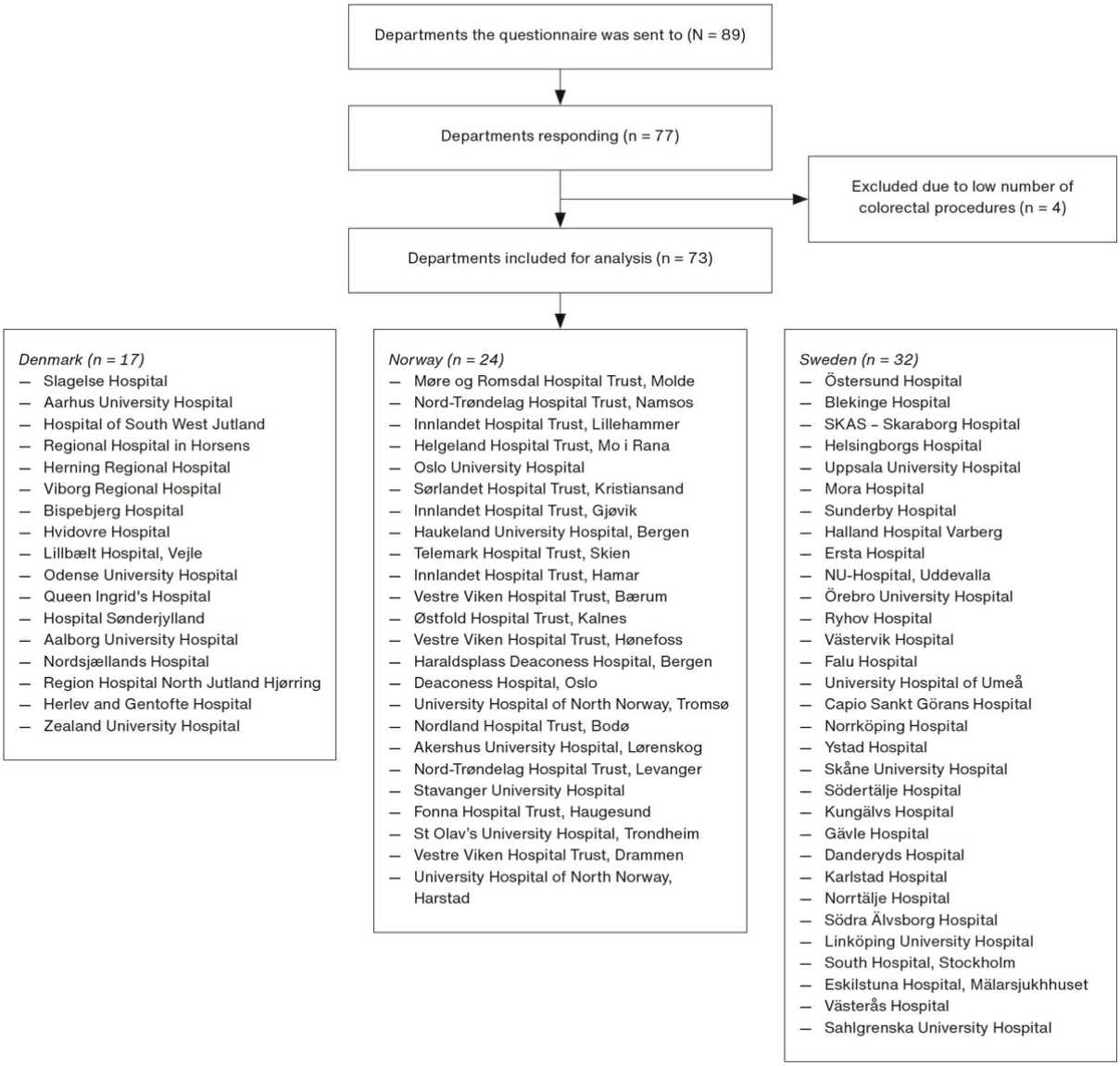
Since the study included no patients or patient-sensitive information, ethical approval by The National Research Ethics Committee was not necessary.

Trial registration: not relevant.

RESULTS

The questionnaire was sent to 89 departments in Scandinavia (**Figure 1**). The response rate was 87% (n = 77). Four departments were excluded (< 20 annual colorectal procedures), and 73 departments were included for analysis (DK: 17; SE: 32; NO: 24).

FIGURE 1 Flow chart illustrating the included departments in the three Scandinavian countries.



Four departments failed to provide answers regarding their patients' follow-up time and were therefore excluded from the analysis of the length of follow-up but included in analysis of type of follow-up modalities performed. The number of departments using a short, intermediate and long follow-up time and the number of surveillance modalities performed are presented in **Table 1.** A majority of the departments used a long (38-59%) or intermediate (26-38%) follow-up programme regardless of location or risk factors. 13-23% of the departments used a short follow-up programme. Roughly, the median number of surveillance modalities increased with length of follow-up (Table 1).

TABLE 1 Follow-up time and number of surveillance modalities performed, based on length of follow-up time and location of the malignant polyp.

		Risk factors[a]						No risk factors					
Location	Follow-up time, yrs	depart-ments, n (%)	endoscopy, median (range), n	CT, median (range), n	MRI, median (range), n	EUS, median (range), n	CEA, median (range), n	depart-ments, n (%)	endoscopy, median (range), n	CT, median (range), n	MRI, median (range), n	EUS, median (range), n	CEA, median (range), n
Rectum													
	1	12 (18)	1.5 (1-2)	1 (1-1)	1 (1-2)	1 (1-1)	1 (1-2)	10 (19)	1 (1-2)	1 (1-1)	1 (1-1)	1.5 (1-2)	1 (1-1)
	3	17 (26)	6 (4-14)	3 (2-9)	3 (1-6)	7 (1-10)	6 (2-7)	20 (38)	4 (1-12)	3 (1-5)	3.5 (1-5)	4 (1-5)	4 (2-6)
	5	37 (56)	7 (2-12)	3 (1-8)	5 (1-11)	6 (2-11)	6 (1-12)	23 (43)	6 (2-12)	2 (1-12)	4 (1-7)	7 (4-10)	5 (1-12)
Colon													
	1	8 (13)	1 (1-2)	1 (1-1)	-	-	1 (1-2)	12 (23)	1 (1-2)	1 (1-1)	-	-	1 (1-2)
	3	17 (28)	5 (2-13)	4 (2-11)	-	-	4 (2-7)	20 (38)	4 (1-11)	3 (2-9)	-	-	2.5 (2-5)
	5	35 (59)	5 (1-12)	3 (1-8)	-	-	6 (1-12)	20 (38)	4.5 (1-12)	2 (1-8)	-	-	5 (1-12)

CEA = carcinoembryonic antigen; EUS = endoscopic ultrasound; SM = submucosal invasion.
a) Sessile morphology, polyp diameter ≥ 2 cm, lymphatic or vascular invasion, tumour budding, low tumour differentiation, tumour level Haggitt 3 or 4, Kikuchi level SM3, piecemeal resection.

Among patients with malignant rectal polyps and presence of histological risk factors, a significant difference was seen in the use of endoscopy in the follow-up programme based on the length of follow-up (short: 83%; intermediate: 100%; long: 100%; p = 0.031). A tendency was seen in the difference in use of MRI and EUS based on the length of follow-up (short: 33%; intermediate: 77%; long: 51%; p = 0.065 for MRI, and short: 8%; intermediate: 41%; long; 16%; p = 0.074 for EUS). No difference was seen in use of the different modalities based on length of follow-up in patients with malignant rectal polyps without risk factors and colonic malignant polyps regardless of presence of risk factors.

The follow-up programme deferred depending on the location of the polyp (colon versus rectum) in 59 % of departments (n = 43). Presence of histological risk factors influenced the follow-up programme in 90% of departments (n = 66).

A total of 34% (n = 25) of all Scandinavian departments reported that they would consider a surveillance programme in patients with a malignant polyp with a resection margin ≤ 1 mm.

DISCUSSION

Overall, this study established that Scandinavian colorectal departments employ three different lengths of follow-up periods and use a variety of surveillance modalities. To our knowledge, this is the first study to survey the surgical follow-up programmes and surveillance of patients with endoscopically removed malignant colorectal polyps without completion surgery.

Scandinavian 30-day mortality rates following colorectal cancer surgery fall in the 2-5% range [7, 8], and surgical morbidity rates requiring intervention (Clavien-Dindo grade ≥ 3) 11% [7]. Furthermore, there are reports of no residual disease in up to 80% of patients with completion radical resection [3, 4, 6] and similar overall and disease-free survival [3, 6, 9, 10]. A surveillance strategy following local resection of malignant polyps is therefore tempting, especially in the elderly patient. An increase in colorectal cancer screening increased the incidence of reported colorectal malignant polyps [5, 11, 12] and a surveillance strategy following polypectomy is now applied in up to two thirds of these patients [3-6]. However, adherence to a surveillance strategy carries a risk of residual disease, recurrence and an impaired survival outcome. Adequate follow-up is therefore important to detect recurrences early and initiate further treatment.

The lack of solid evidence for the optimal surveillance and follow-up strategy following polypectomy only for malignant polyps is reflected in our study, where we found differences in the type of modalities performed and lack of uniformity in follow-up time. The follow-up strategy may affect time to diagnosis of recurrences, thereby affecting treatment options and subsequently patient survival.

Although there are no studies designed specifically to investigate an optimal surveillance strategy, a few studies on patients with malignant polyps have addressed time to recurrence when in active surveillance [3, 4, 6, 13-15]. In these studies, the median time to recurrence ranged from 22 to 53 months. In the two largest studies, the cancer-related mortality following recurrence was 42-48% [4, 6]. In a Dutch multicentre cohort study on malignant polyps, Backes et al. found that recurrences presented after a median of 30.9 months in patients with locally recurrent cancer [4]. The median duration between the previous colonoscopy and recurrence was significantly longer for patients with T2-T4 recurrences than for patients with recurrent T1 cancers. Furthermore, a longer duration was observed between previous colonoscopy and local recurrence for advanced stage recurrence (American Joint Committee on Cancer (AJCC) stage 3-4) than for early-stage recurrence (AJCC stage 1-2).

In our study, we found that for the majority of patients with both rectal and colonic malignant polyps, the follow-up time was three years or above. However, there were departments in all three countries where the patients were followed-up for one year only, both in the presence and absence of histological risk factors.

We also found a widely differing number of modalities performed during the intermediate and long follow-up programmes. The intensity of the surveillance programme may also have a psychological effect on the patients, which has yet to be explored. On one hand, patients may experience that an excessive surveillance causes inconvenience, pain and fear of risk of complications (bleeding and perforation). On the other hand, longer intervals between surveillance modalities may cause anxiety or feelings of neglect. Fear of cancer recurrence is an important issue among patients [16], although a recent Dutch study indicated that endoscopic treatment provoke no more fear of recurrence than surgical treatment for T1 colorectal cancer [17].

One interesting finding of our study was that 34% of all Scandinavian departments would consider a surveillance programme in patients with a malignant polyp and a resection margin ≤ 1 mm, which runs counter to current European recommendations [18, 19]. The setup of this study did not allow us to investigate this further. A positive resection margin, defined as ≤ 1 mm, is associated with residual cancer at completion radical resection as well as risk of recurrence. However, recent studies suggest that a > 0.1 mm resection margin is adequate [3, 20].

This study was explorative and presented no answers as to the optimal surveillance strategy in patients with malignant polyps without completion resection, nor did it postulate which patients should undergo completion radical resection or surveillance strategy. However, as it is reported that more than half of patients with malignant polyps do not undergo completion radical resection, an exploration of the surveillance programmes seems justifiable.

One limitation of using a questionnaire survey is ensuring that conscientious responses are received. The questions may also be understood and interpreted differently, thus providing us with data that might be unrepresentative of the individual department's follow-up strategies. Another limitation of our study is that it provides no information about why there is a difference in follow-up and why the departments have a specific type of setup for the follow-up programme. We have not asked the departments to describe their decision algorithms.
However, this study had a high response rate, and we therefore believe that our results are representative of follow-up of malignant colorectal polyps across Scandinavian surgical departments. This study has also identified comparable follow-up programmes for endoscopically resected malignant colorectal polyps and may provide a setup for a future Scandinavian prospective follow-up study. Hereby, it will be possible to obtain long-term recurrence and survival results from comparable inter-centre surveillance programmes.

CONCLUSIONS

The follow-up of patients with endoscopically removed malignant polyps and surveillance lacks uniformity in terms of length and performed modalities although most patients receive intermediate or long follow-up. Future studies should identify the optimal follow-up strategy by comparing long-term patient outcome between departments with different follow-up strategies.

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