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Screening Colonoscopy Indeed Lowers the Stage of Diagnosed Colorectal Cancer – A Prospective Registration of the Findings by Screening Colonoscopy during the First Year of a National Screening Programme

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Abstract

Purpose: As long-term colon cancer survivors increase, there is a growing need for subgroup-specific analysis of conditional survival. This paper presents five-year conditional relative survival rates of colon cancer, with emphasis placed on subgroup-specific estimates by age, sex, race, ethnicity, marital status, year of diagnosis, and stage at diagnosis.

Methods: Analyses are based on 96,022 males and 101,793 females diagnosed with colon cancer during 2000 through 2008, followed through 2012, using data from the National Cancer Institute Surveillance, Epidemiology, and End Results program.

Results: Mean five-year conditional relative survival increased for years already survived for local staged disease by 2.3% per year ($p<0.05$), 5.0% per year ($p<0.05$) for regional staged disease, and 10.7% ($p<0.05$) per year for distant staged disease. Five-year conditional relative survival rates were significantly lower in those less than 65 years of age ($p<0.05$), more so in unstaged cases; among Blacks ($p<0.05$), more so in distant and unstaged cases; and other race ($p<0.05$), more so in local and regional staged cases. The rates were significantly higher in females ($p<0.05$), more so in regional and distant staged cases; non-Hispanics ($p<0.05$); and married patients ($p<0.05$), more so for local and regional staged cases.

Conclusion: These results provide further useful prognostic information for patients, their families, and physicians tailored to the time already survived since diagnosis. This can be informative in terms of shared decision making and time to "cure."

Keywords: Colon cancer; Conditional survival; Relative survival; Population-based; Prognosis; SEER

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Introduction

Inspired by pioneer studies on screening for colorectal cancer (CRC) [1-3], a large scale feasibility study was carried out from 2005 to 2006 in two Danish counties [4]. Based upon experiences from that study and European guidelines [5], a national screening programme for CRC was launched in Denmark in March 2014. Citizens between 50 and 74 years of age are invited to participate by submitting a faecal sample, which is examined by i-FOBT (immunochemical faecal occult blood test) at a regional centre. Citizens with a positive i-FOBT are subsequently referred for colonoscopy at one of four regional endoscopy units, one of which is the Endoscopy Unit of Herning Regional Hospital. In this study we report the findings of screening colonoscopies during the first year of the new national screening programme.

Materials and Methods

All citizens who had a screening colonoscopy performed at our Endoscopy Unit during the first 12 months of the national screening programme entered the study. Colonoscopy was performed as an outpatient procedure with or without Propofol or Midazolam sedation according to preference of the citizen and/or the endoscopist and after mutual agreement of the course of action. Details of the colonoscopies and findings at the procedures were recorded prospectively as well as the results of the related histopathological examinations. At the end of the study period relevant diagnostic codes were sought in the hospital's electronic databases to identify any patient admitted to the hospital for complications related to the screening colonoscopy.

All detected adenocarcinomas were treated according to national guidelines for treatment of CRC [6], and the stage of cancers (UICC-classification) found by screening was compared (χ^2-test) with the stage of adenocarcinomas found in symptomatic patients referred to our department during the same period of time.

Detected polyps were removed. Adenomatous polyps were histologically divided into low or high grade dysplasia polyps. However, not only the grade of dysplasia, but also the size and number of adenomas removed and the histological type of these indicate the risk of future malignancy and thereby determine scheduled follow up in the individual patient [5] **(Table 1)**.

Before implementing the screening programme in the endocopy units, estimates were made [7] by the screening authorities as to predict various key point outcome measures **(Table 2)** in relation to screening colonoscopy. These estimates were based on results from the feasibility study [4], two recent Dutch studies using i-FOBT [8,9] and recommendations from the National Health Authorities [10]. At the end of the first year of screening colonoscopy the estimated / expected outcome was compared with what was in fact observed.

Results

Screening colonoscopy was performed in 905 citizens with a positive i-FOBT. In five cases (0.6%) a complete colonoscopy could not be performed and a CT-colonography was added in these cases, preferably on the same day. No perforations were seen, but 2 patients (0.2%) were admitted to the hospital with bleeding after polypectomy. Neither of these required surgery, in one patient the bleeding ceased spontaneously and in the other patient endoscopic haemostasis was achieved.

Table 2 shows the estimated and observed key point outcome measures. The rate of positive i-FOBT was 25% higher than estimated causing a larger number of colonoscopies performed than expected. Also, more citizens with positive i-FOBT turned up for colonoscopy than expected. Detected adenocarcinomas were fewer than expected, but the number of patients with polyps was greater than estimated, and more patients were scheduled for later endoscopic follow up than expected.

Cancer

Cancer was found in 71 citizens (7.8%). Of these 70 had adenocarcinoma, one of whom had two synchronous carcinomas. One citizen had a malignant neuroendocrine tumor. 36 citizens (51.4%) had adenocarcinoma Stage I (inclusive of adenocarcinoma in polyps), 12 (17.1%) had adenocarcinoma Stage II, 19 (27.1%) had adenocarcinoma Stage III and 3 (4.3%) had adenocarcinoma Stage IV (distant metastases). This distribution of stages is statistically highly significantly different (χ^2=46.7, p<0.0001) from the distribution of stages in symptomatic patients diagnosed with CRC during the same period of time **(Table 3)**.

Table 1 Classification of adenomas and recommended surveillance following adenoma removal.

	Risk factors	Scheduled follow-up colonoscopy
Low risk	<3 adenomas and all adenomas <10 mm and tubular adenoma and low grade dysplasia	None
Intermediate risk	3-4 adenomas or at least 1 adenoma between 10 and 20 mm or villous component or high grade dysplasia	3 years
High risk	5 or more adenomas or one adenoma >20 mm or adenoma removed by piecemeal technique	Within 1 year

Table 2 Estimated and observed key point data during the first year of screening colonoscopy.

	Estimated	Observed
Rate of positive iFOBT	5.3 %	6.8 %
Rate of iFOBT-positive citizens appearing for colonoscopy	87 %	96 %
Rate of detected adenocarcinoma	9 %	7.8 %
Rate of colonoscopy with one or more biopsies/polypectomies	50 %	61 %
Rate of patients in whom endoscopic follow up was indicated	43 %	63 %
Rate of CT-colonography	5 %	0.6 %

Adenomas

In 482 (53.3%) of the citizens adenomatous polyps were detected and removed, in the individual ranging from 1 to 37 polyps. Of these 77 (16%) had one or more adenomas with high grade dysplasia. Risk classification and the scheduled follow up is shown in **Table 4**. Intermediate or high risk polyps were found in 63.1% of those with polyps, and they were consequently scheduled for a later follow up endoscopy. In 13 patients (2.7% of patients with adenoma) the adenoma was either too large or located in such an awkward position that endoscopic removal was considered impossible, and these patients had an operation (11 right hemicolectomy, 1 sigmoid resection, 1 TEM (transanal endoscopic microsurgery).

Discussion

The incidence rate for CRC in Denmark is high and CRC is a significant public health burden. The officially declared purpose of the national screening programme for CRC is to lower the stage of cancers diagnosed and to reduce future incidence of CRC by removing detected adenomas [10]. A possible effect of the latter will show in 5 to 10 years, whereas the former purpose is clearly evident by now as seen in **Table 3**. At colonoscopy we found cancer in 7.8% of citizens with a positive i-FOBT, which is a little less than the expected 9% [4,7], and we observed a significantly larger number of patients with low stage cancer and significantly lower number of patients with high stage cancer than found in patients referred to our department with symptomatic cancer. This observed distribution of stages is compatible with those of previous randomised trials done in research settings [2,3,11,12] and in population-based first round screening programmes [13,14], whereas the observed detection rate of cancer and adenomas in the present study is higher than in these studies. This might be explained by the fact, that Guaiac based FOBT (g-FOBT) was used in the mentioned studies, while i-FOBT is used in the Danish national screening programme. It has been demonstrated that using i-FOBT in population-based screening for CRC has superior detection rates (higher sensitivity) compared to g-FOBT screening [8,9,15]. Our observations are compatible with the findings of other screening studies using the i-FOBT [8,9].

One of the concerns in relation to implementing the national screening programme has been the risk of complications to colonoscopy. In a recent survey of literature on screening colonoscopy the risk of perforation and bleeding was found low and without mortality [16]. Six relevant studies published from 2000 to 2006 were identified and reviewed, and the risk of perforation varied from 0% to 0.24% and the risk of bleeding from 0% to 0.3%. In our first year of screening colonoscopy we had no perforations and 0.2% of patients with bleeding after polypectomy, which is considered acceptable.

The introduction of the national screening programme has added a greater workload to our endoscopy unit than expected as more than 25% more citizens have been referred for colonoscopy than estimated **(Table 2)**. The number of needed screening colonoscopies is determined by the number of i-FOBT positive faecal samples, which in turn is influenced by the chosen cut off value set to categorize the test as positive or negative. If the cut off value is too low, many unnecessary colonoscopies will be performed, and if it is too high a number of adenomas and even cancers will be missed and probably show up later as interval cancers between screening rounds. This dilemma will undoubtedly be addressed by the national screening authorities, as will evaluation of the rapidly evolving evidence regarding other CRC screening tests (flexible sigmoidoscopy, CT-colonography, faecal DNA test), but it is beyond the scope of the present study to discuss these issues.

Unforeseen screening colonoscopies have turned out to be more time consuming on average than other colonoscopies due to a great number of citizens with polyps (53.3%) that have to be removed. This in combination with the finding of intermediate or high risk polyps causing future scheduled endoscopic follow up in almost 50% more citizens than expected will further add to the workload of the endoscopy unit, and these observations have to be taken into account when planning the future capacity of our and other units for screening colonoscopy. On the other side, the high number of detected high and intermediate risk adenomas calls for action. A number of intervention studies have suggested that treatment with 75 mg aspirin can significantly reduce the occurrence of future high risk adenomas in such patients [17] and aspirin has also been shown to reduce the occurrence of later colorectal cancer in high-risk populations [18,19]. Based on these data with aspirin and the present data from the Danish colorectal screening program, we are now planning a medical intervention study with an aim to prevent occurrence of new adenomas or future CRC in high-risk adenoma patients.

Table 3 Total number of patients diagnosed with CRC in the Department of Surgery, Herning Regional Hospital, during the first year of screening colonoscopies. The distribution of stages is significantly different ($p<0.0001$) between cancers diagnosed by screening and in patients with symptoms.

	Stadium I (incl adenocarc. in polyp)	Stadium II	Stadium III	Stadium IV	Un-classified	Total
Non-screening	41 (15.2%)	77 (28.6 %)	74 (27.5 %)	71 (26.4 %)	6 (2.2 %)	269
Screening	36 (51.4 %)	12 (17.1 %)	19 (27.1 %)	3 (4.3 %)	0	70
						339

Table 4 Risk classification of 482 patients with adenomatous polyps.

		Scheduled follow-up colonoscopy
Low risk	178 patients (36.9 %)	none
Intermediate risk	174 patients (36.1 %)	3 years
High risk	130 patients (27 %)	within 1 year

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