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Subsite- and stage-specific colorectal cancer trends in Estonia prior to implementation of screening

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ABSTRACT

Background: The occurrence of colorectal cancer (CRC) in Estonia has been characterised by increasing incidence, low survival and no screening. The study aimed to examine long-term incidence and survival trends of CRC in Estonia with specific focus on subsite and stage.

Methods: We analysed CRC incidence and relative survival using Estonian Cancer Registry data on all cases of colorectal cancer (ICD-10 C18–21) diagnosed in 1995–2014. TNM classification was used to categorise stage.

Results: Age-standardized incidence of colon cancer increased both in men and women at a rate of approximately 1% per year. Significant increase was seen for right-sided tumours, but not for left-sided tumours. Rectal cancer incidence increased significantly only in men and anal cancer incidence only in women. Age-standardized five-year relative survival for colon cancer increased from 50% in 1995–1999 to 59% in 2010–2014; for rectal cancer, from 38% to 56%. Colon cancer survival improved significantly for left-sided tumours (from 51% to 62%) and stage IV disease (from 6% to 15%). For rectal cancer, significant survival gain was seen for stage II (from 58% to 75%), stage III (from 34% to 70%) and stage IV (from 1% to 12%).

Conclusion: In the pre-screening era in Estonia, increase in colon cancer incidence was limited to right-sided tumours. Large stage-specific survival gain, particularly for rectal cancer, was probably due to better staging and advances in multimodality treatment. Nonetheless, more than one quarter of new CRC cases are diagnosed at stage IV, emphasising the need for an efficient screening program.

1. Introduction

Colorectal cancer (CRC) is the fourth leading cause of cancer-related deaths in the world and the second leading in Europe [1]. With its widely varying incidence and mortality rates, CRC is considered a clear marker of the cancer transition in countries undergoing societal and economic changes [2]. A large proportion of CRC incidence and mortality could be avoided by the removal of precancerous lesions during screening colonoscopy [3]. Yet, changing risk patterns and screening may affect subsite-specific trends in a different manner. Recent studies have shown a shift towards right-sided colon cancer [4,5].

CRC is the third leading cancer in Estonia, with approximately 900 new cases diagnosed every year (population 1.3 million in 2011). The incidence of CRC has been increasing since the beginning of cancer registration in Estonia in 1968. CRC mortality has slowly declined only among women over the past decades [6]. Estonia was one of the few countries in Europe where neither organised nor opportunistic CRC screening had been initiated by 2015 [7]. A pilot program started only in 2016. The prognosis of CRC is largely dependent on stage at diagnosis and screening would help to achieve a shift towards earlier detection [8]. In late 1990s, survival from CRC in Estonia was amongst the lowest in Europe, particularly for rectal cancer [9]. Around that time, large treatment disparities were observed between Western and Eastern Europe, with low rate of curative resection and inadequate lymph node assessment in the latter countries, including Estonia [10]. Although the survival gap had narrowed considerably by the time EUROCARE-5 was conducted, the survival deficit of Eastern European countries persisted [11].

The aim of the study was to examine CRC incidence and survival trends in Estonia over a 20-year period prior to the implementation of population-based CRC screening. We specifically focused on cancer subsite and TNM stage, using data from the population-based

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Table 1
Incident cases of colon and rectal cancer in Estonia, 1995–2014.

	Total		1995–1999		2000–2004		2005–2009		2010–2014		
	No	%	No	%	No	%	No	%	No	%	p-value[a]
Total	14852	100	3069	100	3501	100	3855	100	4427	100	
Microscopic verification	13543	91	2734	89	3189	91	3512	91	4108	93	p < 0.001
Death certificate only	176	1	30	1	51	1	55	1	40	1	p = 0.64
Autopsy	177	1	31	1	36	1	61	2	49	1	p = 0.79
Sex											
Men	6773	46	1388	45	1584	45	1782	46	2019	46	p = 0.81
Women	8079	54	1681	55	1917	55	2073	54	2408	54	
Age at diagnosis (years)											
< 45	381	3	100	3	92	3	86	2	103	2	p < 0.001
45–54	1034	7	242	8	253	7	273	7	266	6	
55–64	2902	20	736	24	687	20	705	18	774	17	
65–74	5185	35	1154	38	1345	38	1340	35	1346	30	
75–84	4293	29	655	21	907	26	1195	31	1536	35	
≥85	1057	7	182	6	217	6	256	7	402	9	
Site											
Colon (C18)	8950	60	1860	61	2072	59	2337	61	2681	61	p = 0.4
Right-sided colon (C18.0–18.4)	4289	48[b]	802	43[b]	1003	48[b]	1118	48[b]	1366	51[b]	
Left-sided colon (C18.5–18.7)	4280	49[b]	963	52[b]	991	48[b]	1104	47[b]	1222	46[b]	
Other colon (C18.8–18.9)	381	4[b]	95	5[b]	78	4[b]	115	5[b]	93	3[b]	
Rectum (C19–20)	5611	38	1153	37	1368	39	1444	37	1646	37	
Anus and anal canal (C21)	291	2	56	2	61	2	74	2	93	2	

[a] Chi-square test comparing proportions over time periods.
[b] Proportion of colon cancers.

nationwide Estonian Cancer Registry (ECR).

2. Material and methods

The ECR provided data on all adult (age ≥15 years) cases of CRC (ICD-10 codes C18–21) diagnosed in 1995–2014, regardless of cancer sequence. Reporting to the ECR is mandatory by law for all physicians and pathologists in Estonia who diagnose or treat reportable tumours. Multiple sources are used for case ascertainment, including trace-back of cases first identified via death certificates as well as linkages with the electronic patient records of two cancer centres. The ECR uses ICD-O-3 for coding and follows international definitions and rules, including those for multiple primaries, issued by the European Network of Cancer Registries and the International Association of Cancer Registries [12], for reporting incidence and survival.

Percentage of microscopically verified cases (%MV), percentage of death certificate only cases (%DCO) and percentage of cases discovered at autopsy were used as data quality indicators. Subsite was categorised into right-sided colon cancer (RCC), including appendix, caecum, ascending colon, hepatic flexure and transverse colon (ICD-10 C18.0–18.4), left-sided colon cancer (LCC), including splenic flexure, descending and sigmoid colon (C18.5–18.7), other or overlapping colon (C18.8–18.9), rectum and rectosigmoid junction (C19–20), anus and anal canal cancer (C21).

Stage was coded into grouped stage according to the Union for International Cancer Control version 7 of the TNM classification. The hospitals report stage information to the ECR according to one or more of the three following classifications: 1) component T, N and M codes; 2) grouped TNM stage; 3) extent of disease (EoD), categorised as local, spread to neighbouring tissues, regional lymph nodes, distant metastasis, unknown. Starting from 2012, TNM variables are routinely recorded at the ECR and quality control procedures are applied. In case of conflicting information, component TNM codes take priority, and grouped stage and/or EoD are corrected accordingly. For 1995–2011, TNM stage was coded as part of this study and similar rules were applied. If EoD was reported as distant metastasis and TNM variables were missing, stage IV was assumed. If grouped TNM stage was reported, but all or some component TNM values were missing, and the reported TNM values were not in conflict with the stage grouping, we assumed the grouped TNM stage to be correct.

Follow-up for vital status from the date of diagnosis until December 31, 2014 was conducted by the ECR at the Estonian Population Registry using unique personal identification numbers. In case of death or emigration, the respective dates were obtained.

Relative survival ratio (RSR) was calculated as the ratio of observed survival and expected survival of the underlying general population. The latter was calculated according to Ederer II method [13], based on national life tables, stratified by age, sex and calendar year. DCO and autopsy cases were excluded from survival analyses. Patients who were diagnosed and died on the same day were included with one day of survival time. Cohort method was used for patients diagnosed in 1995–1999, 2000–2004 and 2005–2009; period method for 2010–2014 [14]. RSRs were calculated using the strs command in STATA 14 (StataCorp, College Station, Texas, USA) [15]. International Cancer Survival Standards were used for age-standardisation [16].

Age-specific and age-standardized (world) CRC incidence rates were modelled and the estimated annual percentage change (APC) with 95% confidence intervals (CI) calculated with Joinpoint Regression Program (version 4.1.1.1) from the Surveillance Research Program of the US National Cancer Institute (http://surveillance.cancer.gov/joinpoint/).

The study protocol was approved by the Tallinn Medical Research Ethics Committee.

3. Results

The total number of CRC cases diagnosed in Estonia in 1995–2014 was 14,852 (Table 1). The average annual number of cases increased from 614 in 1995−1999 to 885 in 2010−2014. The%MV increased significantly from 89% to 93%; %DCO and%autopsy remained stable at around 1%. Median age increased from 69 to 73 years. Overall, 71% of the cases were diagnosed at age ≥65 years. Age distribution shifted significantly towards the elderly as the percentage of patients diagnosed at age ≥75 years increased from 27% to 44%. The proportion of cases diagnosed in right-sided colon increased and those in left-sided