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Cancers among Patients Diagnosed as Having Diverticular Disease of the Colon

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ABSTRACT

Objective: To assess the incidence of underlying malignancy in patients with a diagnosis of diverticular disease of the colon.
Design: Retrospective cohort study.
Setting: University hospital, Sweden.
Subjects: 7159 patients discharged from hospital with a first diagnosis of diverticulosis or diverticulitis in central Sweden 1965–1983.
Intervention: The cohort was followed up for two years for the occurrence of cancer.
Main outcome measure: Cancer incidence.
Results: A total of 372 cancer cases were identified (standard incidence ratio = 2.4; 95% confidence interval 2.2 to 2.7). Sites at excess risk during the first year were: colon and rectum, pancreas, prostate, stomach, lymphatic and haemopoietic tissue, liver and bile ducts, ovary and lung, with the highest excess risk in the left colon (standard incidence ratio = 17.8; 95% CI 12.7 to 24.1).
Conclusion: Malignant diseases, especially colorectal cancer, are relatively common among patients with a clinical diagnosis of diverticulosis or diverticulitis of the colon. This may indicate a need for a change in current clinical practice.

Key words: diverticulosis or diverticulitis of the sigmoid colon, cancer.

RÉSUMÉ

But: Déterminer chez les patients pour lesquels a été posé un diagnostic de maladie diverticulaire du côlon, l'incidence d'une affection maligne sous jacente.
Type d'étude: Rétrospective d'une cohorte.
Provenance: Hôpital universitaire, Suède.
Patients: Sept mille cent cinquante neuf patients ayant quitté l'hôpital avec un premier diagnostic de diverticulose ou de diverticulite dans le centre de la Suède entre 1965 et 1983.
Méthodes: Les patients de la cohorte ont été suivis pendant deux ans pour rechercher un cancer.
Principaux critères de jugement: La survenue d'un cancer.
Résultats: Trois cent soixante douze cancers au total ont été identifiés (pourcentage d'incidence standard = 2,4; intervalle de confiance de 95% (IC95%); 2,2 á 2,7). Les sites préférentiels de développement d'un cancer pendant la première année étaient: le côlon et le rectum, le pancréas, la prostate, l'estomac, les tissus lymphatique et hématopoïétique, le foie et les voies biliaires, l'ovaire, et les poumons; le risque le plus élevé concernant le côlon guache (pourcentage d'incidence standard = 17,8; IC 95%; 12,7 á 24,1).
Conclusion: Les affections malignes, et notamment les cancers colorectaux sont relativement fréquents parmi les patients chez lesquels a été posé cliniquement le diagnostic de diverticulose ou de diverticulite du côlon. Cela pourrait inviter á modifier les habitudes cliniques dans ce domaine.

INTRODUCTION

Diverticulitis of the sigmoid colon is a clinical diagnosis and in common clinical practice the diagnosis is considered to be confirmed if diverticulosis is present on a barium enema after the symptoms have settled. The prevalence of diverticulosis of the colon in the western world has been reported to be 10%–20% in patients aged 40–59 years old and from 30% to over 50% in patients 70 years old or more [9, 10, 14]. As the clinical symptoms of diverticulitis resemble those of many cancers the presence of underlying malignant disease, particularly in the gastrointestinal tract, is not unusual in patients with a clinical diagnosis of diverticulitis.

The aim of this study in the Uppsala health care region 1965–1983 was to assess the magnitude of the problem of underlying malignant disease in a population-based cohort of patients with the diagnosis of diverticulosis or diverticulitis of the colon who were followed up for the first two years after discharge from hospital.

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SUBJECTS AND METHODS

The cohort

The Uppsala health care region, which covers six counties, is located in central Sweden and had, during the study period, a population of 1.2–1.3 million people. As there is almost no private inpatient treatment in Sweden, hospital provided medical services are population based and referable to the county in which the patient lives. From 1965 until 1983, the Swedish National Board of Health and Welfare received annual reports from all inpatient medical institutions in Sweden and recorded data on individual hospital admissions and discharges in the inpatient register for all inhabitants within the Uppsala health care region.

As well as a national registration number (a unique personal identifier assigned to all Swedish citizens) each record contains data on place of residence, hospital department, surgical procedures, and up to eight discharge diagnoses. These diagnoses were coded according to the seventh revision of the International Classification of Diseases until the end of 1968 and according to the eighth revision thereafter. A recent publication estimated that the overall extent of under-reporting to the inpatient register was less than 2%. Severe under-reporting occurred in certain counties during a limited period but represented only a few percentage points of the estimated total number of hospital admissions [13].

All patients with records in the inpatient register containing a diagnostic code for diverticulosis (ICD 7 code 572.12 and ICD 8 code 562.10) or diverticulitis (ICD 7 code 572.11 and ICD 8 code 562.11) of the colon and without a diagnosis of cancer were considered for inclusion in the study at the date of first discharge with that diagnosis. The national registration number allowed us to select the first recorded discharge with this diagnosis for each person. A total of 7630 were given a discharge diagnosis of diverticulosis or diverticulitis at least once during the period 1965–1983 and were potentially eligible. We excluded 128 because they were entered on the inpatient register with an incomplete or inconsistent national registration number and were not available for follow up. Through the National Census Bureau and the emigration register we were able to confirm that the remaining members of the cohort who were alive were living in Sweden on 31 December, 1985. A total of 343 cases were not found in any of these registers, probably because they were entered in the inpatient register with an incorrect national registration number and they were excluded. The number of patients available for follow up was therefore 7159, 2478 of whom where men and 4681 women. At the time of first discharge 1410 patients were under 60 years of age, 1665 were 60 to 69, and 4084 were 70 or over.

Follow up

Record-linkage (based on the national registration number) to the nationwide register of causes of death led to information on the date of death among those who had died before the end of 1985. The National Swedish Cancer Registry, founded in 1958 [11], was used to record all cancers diagnosed in the cohort from the start of follow up until two years after the discharge.The incidence of unreported cases of malignant disease to the Swedish Cancer Registry has been assessed at about 3% [11]. The time of observation was calculated from the date of the first discharge with diverticulosis or diverticulitis of the colon until the finding of cancer or the time of death or the end of the two years' observation period.

The expected number of all cancers was calculated by multiplying the number of person years for each gender by age-specific cancer incidence rates for each five year age group and calendar year of observation. These expected rates were derived from the study population, i.e. the Uppsala health care region.

If the colon cancer was diagnosed by examinations planned in connection with the first discharge with a diagnosis of diverticular disease, the cancer was classified as "not missed". If no further follow-up was planned and the cancer was diagnosed during a later contact with the health care the cancer was classified as "missed". We also recorded the Dukes' classification for every colon cancer to compare the Dukes' classification in the two groups of cancers "missed" and "not missed".

Statistical methods

The standardised incidence ratio (SIR) was defined as the ratio of observed numbers of cancers to those expected. The 95% confidence interval (CI) of the standardised incidence ratio was then calculated on the assumption that the observed number follows a Poisson distribution. The significance of the difference in Dukes' classification in missed and not missed colon cancers was compared with the Mann Witney U test for ordered categories [12].

RESULTS

There were 372 cases of cancer (5.2%) diagnosed during the first two years after the first discharge with the diagnosis of diverticulosis or diverticulitis of the colon (SIR = 2.4; 95% CI 2.2 to 2.7). During the first

Table I. *Standardised incidence ratio (SIR) for all cancers by sex and age during the first and second years after discharge and the 95% CI*

	First and second year			First year			Second year		
	Observed no.	SIR	95% CI	Observed no.	SIR	95% CI	Observed no.	SIR	95% CI
All patients	372	2.4	2.2 to 2.7	283	3.6	3.2 to 4.0	89	1.2	0.9 to 1.5
Men	157	2.5	2.1 to 2.9	121	3.7	3.1 to 4.4	36	1.2	0.8 to 1.6
Women	215	2.4	2.1 to 2.7	162	3.5	3.0 to 4.1	53	1.2	0.9 to 1.5
Age (years)									
<60 years	19	1.8	1.1 to 2.8	15	3.0	1.7 to 4.9	4	0.7	0.2 to 1.8
60–69 years	72	2.6	2.0 to 3.3	56	4.2	3.2 to 5.4	16	1.1	0.6 to 1.8
>70 years	281	2.4	2.2 to 2.7	212	3.5	3.1 to 4.0	69	1.2	1.0 to 1.6

Table II. *Standardised incidence ratio (SIR) and 95% CI by site during the first year after the first discharge of 7159 patients with diverticular disease*

	Observed no.	SIR	95% CI
Colon	57	8.6	6.5 to 11.1
Pancreas	33	9.0	6.2 to 12.6
Prostate	30	3.3	2.2 to 4.7
Stomach	27	4.2	2.7 to 6.0
Lymphatic and haemopoietic tissue	20	3.8	2.3 to 5.9
Rectum	16	4.4	2.5 to 7.2
Liver and bile ducts	14	3.7	2.1 to 6.3
Ovary	13	4.1	3.2 to 10.3
Lung	10	2.2	1.0 to 4.0

Table III. *Observed number of cancers for each quarter of the first year by site*

	Months after discharge			
	1–3	3–6	6–9	9–12
Colon	39	4	7	7
Pancreas	22	4	6	1
Prostate	18	5	3	4
Stomach	18	4	2	3
Lymphatic and haemopoietic tissue	15	2	3	0
Rectum	10	4	2	0
Liver and bile ducts	5	3	3	3
Ovary	8	0	3	2
Lung	4	3	1	2

year 283 cancers were diagnosed (SIR = 3.6; 95% CI 3.2 to 4.0) and 89 during the second year (SIR = 1.2; 95% CI 0.9 to 1.5). Stratification by sex and age did not yield any differences in the estimated risk (Table I). During the first year there was a significant increase in risk of cancer at the following sites in order of magnitude: colon, pancreas, prostate, stomach, lymphatic and haematopoietic tissue, rectum, liver and bile ducts, ovary, and lung (Table II). Most cases were found during the first three months after discharge (Table III). Stratified analysis of the risk of colon cancer during the first year by sex, age, and site showed that there was a substantially increased risk in the left colon which did not differ between men and women but was most pronounced in patients less than 60 years old (Table IV). During the second year after discharge there was still a significantly increased incidence of colon cancer, both in the left and right colon; in all other sites the observed numbers of cancers were close to the expected. Among the 75 colon cancers there were 41 (55%) that were classified as "missed". The examinations which had preceded the diagnosis of colon cancer in the "not missed" cancers and those examinations which had failed to diagnose the cancer are shown in Table V by site. Among the colon cancers the Dukes' classification indicated a more advanced stage in the missed group ($p = 0.04$).

DISCUSSION

During the first year after a discharge diagnosis of diverticulosis or diverticulitis there was an increased risk of cancer in colon, pancreas, prostate, stomach, lymphatic and haemopoietic tissue, rectum, liver and bile ducts, ovary and lung. The risk was most pronounced in the left colon (eighteenfold) both for men and women but most evident in patients less than 60 years old. During the second year an excess risk remained only in colon, both on the left and the right side.

An excess number of cancers in older patients with acute abdominal symptoms has been reported elsewhere. In a prospective study from the Stockholm area 1000 consecutive patients aged 70 years or more

Table IV. *The standardised incidence ratio (SIR) and 95% CI for colon cancer by sex, age, and site during the first and second years after discharge*

	All colon			Right colon			Left colon			Unspecified site		
	Observed no.	SIR	95% CI	Observed no.	SIR	95% CI	Observed no.	SIR	95% CI	Observed no.	SIR	95% CI
All patients	75	5.8	4.5 to 7.2	20	3.0	1.8 to 4.6	48	10.7	7.9 to 14.1	7	3.8	1.5 to 7.9
First year:												
All patients	57	8.6	6.5 to 11.1	10	2.9	1.4 to 5.4	41	17.8	12.7 to 24.1	6	4.9	1.8 to 10.7
Men	18	7.7	4.6 to 12.2	1	0.9	0.0 to 4.8	17	19.5	11.4 to 31.3	0		
Women	39	9.0	6.4 to 12.3	9	4.0	1.8 to 7.6	24	16.7	10.7 to 24.8	6	9.7	3.5 to 21.1
<60 years	7	24.1	9.7 to 49.7	1	8.3	0.1 to 46.4	6	54.6	19.9 to 118.7	0		
60–69 years	14	14.4	7.9 to 24.2	1	2.3	0.0 to 12.9	13	33.3	17.7 to 57.0	0		
>70 years	36	6.7	4.7 to 9.1	8	2.9	1.3 to 5.8	22	12.3	7.7 to 18.6	6	7.7	2.8 to 16.7
Second year:												
All patients	18	2.8	1.7 to 4.5	10	3.1	1.5 to 5.7	7	3.2	1.3 to 6.6	1	1.1	0.02 to 6.2

Table V. *Examinations done for 75 patients with colon cancer by site of the tumour (right colon, transverse colon, descending colon, and sigmoid colon)*

The examinations were done after a discharge diagnosis of diverticulosis or diverticulitis of the sigmoid colon

	Colon cancer found			Colon cancer missed	
Examinations	Unspecified site	Right and transverse	Descending and sigmoid	Right and transverse	Descending and sigmoid
Barium enema only	0	3	13	12	13
Barium enema and rectoscopy	0	1	1	2	4
Barium enema and colonoscopy	0	0	3	0	2
Barium enema and laparotomy	0	0	4	0	4
Laparotomy alone	0	0	3	0	4
Necropsy	0	0	2	0	0
Other	1	1	2	0	0
Total	1	5	28	14	27

Table VI. *Dukes' classification in "not missed" and "missed" colon cancers*

Dukes' classification	Not missed	Missed
A	0	1
B	15	7
C	8	17
D	7	12
Unknown	4	4
Total	34	41

were admitted to hospital between January 1977 and March 1978 with abdominal symptoms, and 13.8% of them were diagnosed as having cancer during the admission [3]. In a British study in 1979, 347 patients more than 50 years old who had been admitted to an emergency ward with abdominal pain and in whom no initial cause could be found were followed up [2]. Cancer was diagnosed in 10.7% of the patients during the first year. In the present study 4% of the patients were found to have cancer during the first year after discharge with a clinical diagnosis of diverticular disease. These results do not necessarily contradict each other as the present study is confined to patients with a clinical diagnosis at discharge after clinical investigation has been initiated though not necessarily completed. We therefore have potentially two kinds of diagnosis of cancer among our patients: asymptomatic malignant diseases found during surveillance and malignant diseases with clinical symptoms similar to those of diverticulitis when the patients were erroneously assigned that diagnosis. As 55% of the colon cancers registered during the first two years after discharge with a clinical diagnosis of diverticular disease of the sigmoid colon were missed, the latter is the most common explanation. This is further substantiated by the worse Dukes classification among the "missed" cancers compared with those "not missed". As the clinical diagnosis was diverticular disease the examinations after the discharge of the patients were most likely focused on the large bowel

resulting in an even greater proportion of "missed" cancers likely among diagnosis of other cancers.

In common clinical practice in Sweden patients with left sided abdominal pain or suspected diverticulitis will have a double contrast barium enema or some kind of endoscopy of the lower or whole colon and rectum or both. To check the validity of the diagnosis of diverticulosis we reviewed the medical records of all 812 patients given a discharge diagnosis of either diverticulosis or diverticulitis at the Department of Surgery, Uppsala University Hospital 1969–1989. The diagnosis was confirmed by operation in 219 (27%) and barium enema in 506 (62%) and the diagnostic method was clinical examination alone in 38 (5%) of the patients, where the radiograph failed to give the diagnosis in 49 (6%) patients. Of the 593 patients treated medically 355 (60%) had had their diverticulosis diagnosis confirmed by barium enema before the medical treatment was initiated (Stefánsson T, unpublished data).

As diverticulosis is common among elderly people (30%–50% among patients over 70 years old [9, 10, 14]) the combination of abdominal pain and diverticulosis is common. There are two main reasons why these underlying cancers can be missed: the cancers are outside the colon and some cancers of the left colon can be missed by barium enema because they are concealed by the diverticulosis. As almost all patients had both a double contrast barium enema and an endoscopy and the left colon was the site with the highest excess risk for cancer, our results cast serious doubt on the sensitivity of a barium enema to detect tumours or polyps in the left colon among patients with diverticulosis. This finding was verified in a recent study where both the specificity and the sensitivity of double contrast barium enema and sigmoidoscopy were reported as low in diagnosing polyps of the left colon in patients with diverticulosis [17]. Additional diagnostic procedures are therefore necessary to avoid undetected malignancies and premalignant lesions of the left colon in this group of patients. It is, however, doubtful if the prognosis of cancers outside the colon implicated in the present study can be altered by earlier detection, but polypectomy might reduce both the incidence of colorectal cancer and the mortality [4, 7, 16, 18]. One feasible way to improve the diagnosis in patients with diverticulitis is to focus on diagnosing the diverticulitis during the acute phase of the disease, unlike our present clinical practice. Such a method would enable the clinician to identify patients without diverticulitis and consequently lead to earlier detection of the underlying malignancy. Computed tomography or water soluble contrast enema or both have shown promising results in diagnosing diverticulitis in the sigmoid colon [1, 5, 6]. Other options are percutaneous ultrasound [15], endoscopic ultrasound, ^{99m}Tc pertechnate imaging [8]; and finally diagnostic laparoscopy probably has great potential in this group of patients.

In conclusion, malignant diseases (particularly colorectal cancer) are common among patients with a clinical diagnosis of diverticulosis or diverticulitis of the colon. In patients with left sided abdominal pain therefore the diagnosis of diverticulitis should not be made without ascertainment of that diagnosis during the acute phase of the disease with a combination of new and traditional diagnostic methods.

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