Colon cancer: An epidemiological study in Northern Greece.

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ABSTRACT: Colorectal or colon cancer is the third most common form of cancer with 655,000 deaths worldwide per year and the second leading cause of cancer-related death in the Western world.

A variety of risk factors have been linked to colon cancer including genetic factors (age, sex and hereditary mutations of repair enzymes genes), environmental exposures, daily life habits (diet, smoking, obesity and sedentary habits) and inflammatory conditions of the digestive tract.

The present research is a retrospective epidemiological study concerning 280 patients with colon cancer who were hospitalized at Theagenion Cancer Hospital of Thessaloniki during 2006, 2007 and 2008. They were classified according to their age, sex, place of residence, occupation and tobacco consumption. The results revealed that 58.57% were males and 41,43% females, 82,49% of the patients were older than 60 years of age, 38,93% were urban and 60% rural district inhabitants. Pensioners represented 47,50%, farmers 18,93%, housekeepers 13,57%, employers or free lancers 10,71%. For the rest 9,29% no information has been recorded. Regarding the consumption of tobacco, 16,79% of them were smokers, 34,64% non smokers, whereas there was no information about the smoking habits of the remaining (48,57%).

The results of this research with respect to age and sex of the patients are in agreement with bibliographical data, but conclusions can not be drawn about the connection between occupation and colon cancer onset. The fact that among the patients the non smokers were more than smokers, which is in contrast with the international data, could be attributed to the insufficiency of respective information for 48,57% of the patients. The unexpectedly higher frequency of colorectal cancer appearance among rural district inhabitants rather than among urban district inhabitants should be researched as soon as possible.

The deficiency of information about fundamental risk factors of colon cancer, as genetic and environmental factors and lifestyle among Greek population requires the continuation and the extension of this epidemiological study, because prevention is the best cure and epidemiological studies have offered substantial contribution to prevention.

Key Words: Colon cancer, Epidemiological study.

INTRODUCTION

Colorectal cancer is a multifactorial disease. The most important factor that contributed to the recent decrease of colorectal cancer cases is early detection through widely applied screening programs in developed countries[1].

Colon cancer remained the third most common cause of cancer related mortality during 2008 in the United States. The American Cancer Society estimated that in 2008 about 149.000 individuals were diagnosed with colorectal cancer and approximately 50.000 died from this disease in the United States. Furthermore according to the World Health Organization 940,000 individuals were diagnosed with this type of cancer worldwide and 492,000 died in 2003[2].

The lifetime risk of onset colorectal cancer is estimated about 7%, but certain factors elevate an individual's risk of developing this malignant disease such as heredity, age, previous history of cancer related diseases, existence of colon polyps, exposure to viruses, environmental conditions, kind of diet, consumption of tobacco and alcohol[3].

Genetic factors have the greatest correlation to this malignancy[4]. Familial adenomatous polyposis (FAP)

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carries about 100% lifetime risk to be evolved to colorectal cancer.

Increased is the probability of a person who has been previously diagnosed and treated for colorectal cancer to develop the same disease in the future. Women with breast, ovarian or uterus cancer run a higher risk of developing colon cancer.

Adenomatous polyps and other colon polyps enhance the probability of colorectal cancer appearance, but their removal during colonoscopy diminishes the subsequent risk of this malignancy[5]. Inflammatory bowel diseases (ulcerative colitis and Crohn's disease) are also associated with the disease[6].

Age is an essential risk factor for developing colon cancer, as it is for many other solid types of tumour. Most patients develop the disease between the age of 60 and 70.

Environmental factors, such as radiation and asbestos exposure can increase a person's risk to colon cancer onset[7]. Working the night shift may also cause this neoplasia. A new research found that nurses who work during the night shift on a regular basis are exposed to higher risks[8].

According to intense and ongoing studies the kind of diet is being considered a valuable factor of colorectal cancer development[9]. A diet high in red meat and animal fat, low in fresh fruits, vegetables, poultry and fish has been linked to the appearance of the diseases.

As pointed out by epidemiological studies, apart from obesity, daily lifestyle as sedentary habits, smoking and alcohol consumption have also contributed to the development of this malignancy[10]. Physically active individuals run a lower risk of suffering by the disease. Quick walking for three hours every week has decreased the probability of colon cancer appearance[11].

Tobacco consumption is a significant risk factor for colon cancer. Smokers are more likely to die from this malignancy than non-smokers. The results of an American Cancer Society study indicated that women who smoked were more than 40% more likely to die from the disease than women who had never smoked and male smokers had more than 30% increased death probability compared to non smokers[10,12].

Alcohol consumption also may be a cause of earlier onset of the malignant disease, however the data of investigations are not in agreement. The National Cancer Institute does not refer to alcohol as a risk factor, but it accepts that heavy alcohol use may increase the risk of colon cancer[13,14].

Though much about colon cancer genetics remains unknown, the correlation between epidemiology and molecular biology of this malignancy could play an essential role in this field.

This retrospective epidemiologic research is the fist in Northern Greece the lasted years. Because of its interesting results, a new current study is in progress, more extensive than the present one.

MATERIAL AND METHODS

The information for this retrospective epidemiologic study have been gathered using pathology reports that have been registered in the cancer registry forms of 280 patients suffering from colon cancer. They were hospitalized in Theagenion Cancer Hospital during 2006, 2007 and 2008. A special license by the hospital's management has been granted in order for these data to be used. Demographic factors (age and sex), environmental conditions (place of residence and occupation) and lifestyle habits (smoking) were included in the investigation. Data analysis was performed using χ^2 test (chi-square).

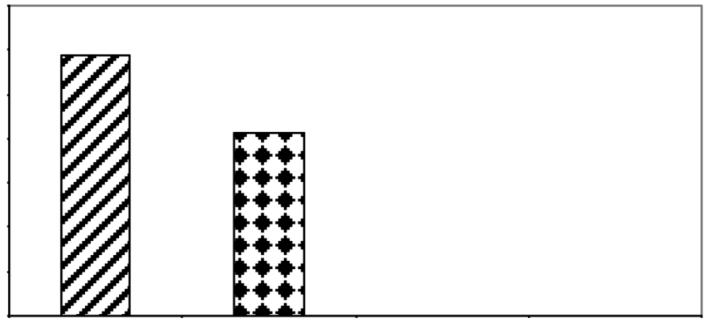
RESULTS

This study is based on the data deriving from cancer registry forms of 280 colon cancer patients. They were classified according to their sex, age, place of residence, occupation and tobacco consumption. The results are presented in Table 1, Table 2, Table 3, Table 4 and Table 5 as well as in the corresponding figures.

As it is shown on Table 1; Figure 1, more men than women in Northern Greece developed colon cancer during the years 2006-2008. This difference is statistically significant ($P < 0,01$ by χ^2).

Table 1. Sex of patients with colon cancer.

	Male	Female	Sum
Frequency	164	116	280
Percentage %	58,57	41,43	100



Age is a remarkable risk factor of developing colorectal cancer in Northern Greece as it is illustrated on Table 2; Figure 2. Patients older than 60 years represented 82,49%. Statistical analysis by χ^2 revealed that this incidence is statistically very significant ($P < 0.0001$).

The percentage of patients living in rural areas was higher (statistically significant, $P < 0,001$ by χ^2) than that of patients who living in urban areas (Table 3; Figure 3), an unexpected data that should be researched as soon as possible.

Table 2. Age of patients with colon cancer.

	≤ 50	51 – 60	61 - 70	71 – 80
Frequency	18	26	77	124
Percentage %	6,43	9,29	27,50	44,28

	≥ 81		Unknown	Sum
Frequency	30		5	280
Percentage %	10,71	1,79	100	

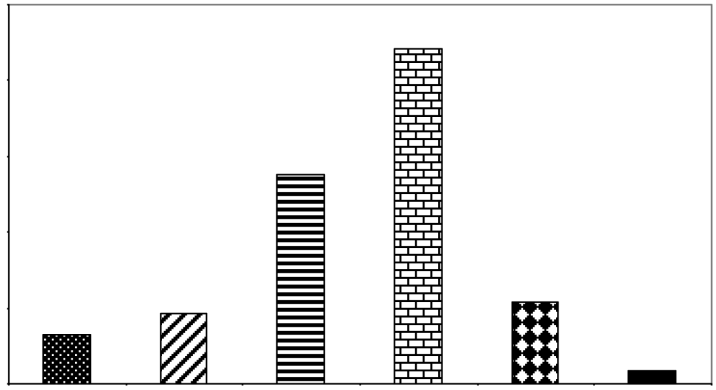
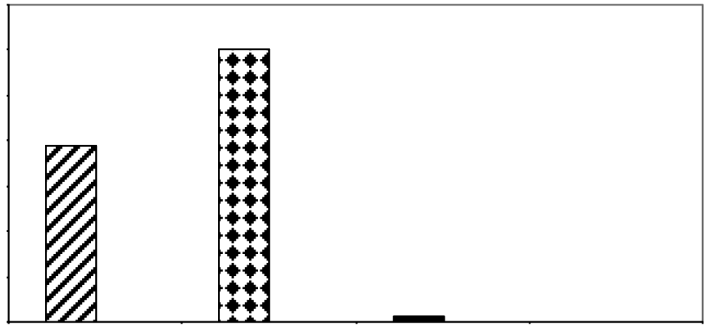


Table 3. Place of residence of patients with colon cancer.

	Urban	Rural	Unknown	Sum
Frequency	109	168	3	280
Percentage %	38,93	60,00	1,07	100



Information about occupation of the patients is incomplete (Table 4; Figure 4). It is evident that many individuals older than 60 years are pensioners, however lifelong professional occupations should be examined, in order to determine whether certain professions can be considered as risk factors provokers.

Table 4. Occupation of patients with colon cancer.

	Pensioners	Agriculture	Unemployed	Administrators
Frequency	133	53	38	21
Percentage %	47,50	18,93	13,57	7,50

			Other	Unknown	Sum
	Frequency		9	26	280
Percentage %	3,21	9,29	100		

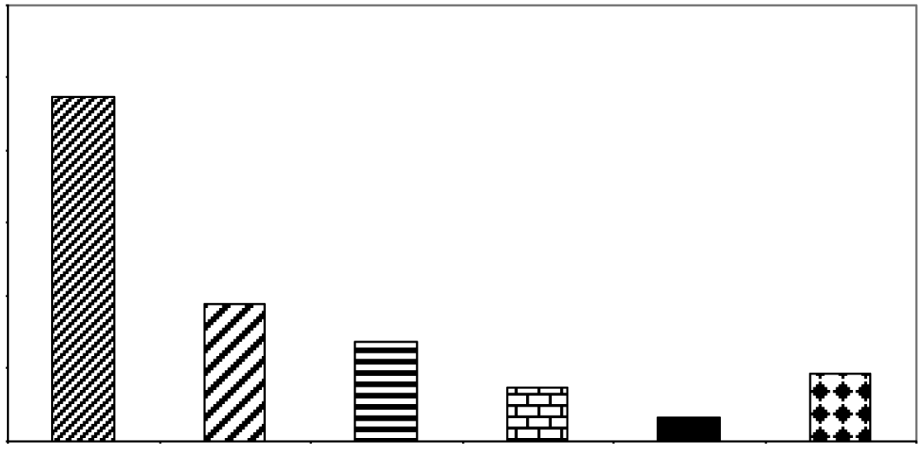
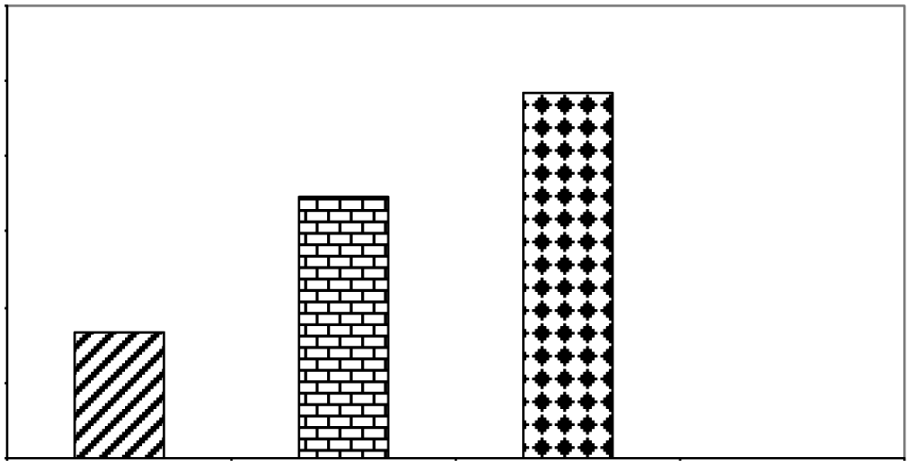


Table 5. Smoking habit of patients with colon cancer.

	Yes	No	Unknown	Sum
Frequency	47	97	136	280
Percentage %	16,79	34,64	48,57	100



Another unexpected distribution is presented on Table 5; Figure 5. Contrary to bibliographical data, in this retrospective epidemiological research, the number of smoking patients is smaller than that of non smoking patients in which however about a 50% of the registry forms of the patients did not contain information concerning smoking habit.

DISCUSSION

Colorectal cancer is a disease originating from epithelial cells of the gastrointestinal tract. Though its progression can take many years and early detection of the malignancy greatly improves the chances of cure, it is a major health burden worldwide. Colon cancer is the third most common cause of cancer-related mortality in developing countries[15].

In most cases colon cancer could have been prevented, if its risk factors had been taken seriously into consideration. Studies of its incidence in various countries strongly suggest that except from heredity, a number of factors (sedentary life, overeating, consumption of alcohol, smoking, etc) could also increase the risk of the disease's onset[7,9,10,12,13,16,17,18].

New and descriptive data on colorectal cancer should be made available to the Greek population, where prevention of risk factors is neglected. As bibliographical data regarding a similar epidemiological study in Northern Greece for at least the last decade have not been found, this research is the beginning of an attempt to inform and sensitize both civilian and corresponding authorities about the risk factors of colon cancer concerning the specific area.

Sex and age are the demographic characteristics which have been included in the reports of the above patients. Among them 60,19% were males and 39,81% females, a difference statistically significant ($P < 0,01$ by χ^2) as it is shown in Table 1; Figure 1. According to Safaee Azadeh et al (2008), in a similar retrospective study in Iran, 61,2% were men and 38,8% women[19], though Tomislav Dragovich has sustained that the incidence of colorectal cancer is about equal for males and females[1].

Table 2; Figure 2 present the age as risk factor for colon cancer. This research has revealed that only 6,43% of the patients were younger than 50 years of age, while 82,49% were older than 60, an increase statistically very significant ($P < 0.0001$). Tomislav Dragovich supported that the incidence of the disease peaks at about the age of 651, whereas the data of Safaee Azadeh et al[19] suggested a younger age distribu-

tion in his Country compared to Western Countries. In India 42,9% of the patients were below 50 years of age. According to a study of Penn State University16 the incidence of developing colon cancer peaks at about the age of 65 years. Before the age of 50 the malignancy is uncommon unless there is hereditary risk. It should be taken into consideration that the timeline of progress from early pre-malignant lesion to malignant cancer ranges from 10-20 years[1].

With regards to environmental conditions which could be considered as risk factors of colorectal cancer developing, registry forms of the patients contained only information about their place of residence and their occupation.

It is surprising the fact that 109 patients (39%) lived in towns and 168 (61%) were rural district inhabitants, a much higher percentage, statistically significant, ($P < 0,001$ by χ^2, Table 3; Figure 3). Pierre Band documented a statistically significant increased mortality from colon and breast cancers in the population of Sydney suggesting the possibility of environmental risk factors as contributory causes[20]. Large cities appear to carry greater colon cancer risk because of a higher volume of cars, trucks, construction equipment and gas stations.The causes of the higher proportion of colon cancer patients living in the countryside than those living in the cities that the present study found, should be further looked into in the immediate future.

Data recorded in this investigation, as they are illustrated in Table 4; Figure 4, have not given any information regarding a correlation between occupation and colon cancer onset. Pensioners represented 43,52% of the above patients. A 82,49% of them whoever had passed their 60 years of age, which easily leads to the conclusion that most of them had already retired. Furthermore, the registry form should include a section referring to professional activities of each patient before retirement, in order for researchers to able to separate later on professions with higher risk factors for developing colon cancer.

According to the registry forms used for this study (Table 5; Figure 5), 47 patients (16,79%) were smokers, 97 (34,64%) non smokers, whereas there was no information regarding the smoking habits of the rest 136 (48,57%). As it is known long-term cigarette smoking increases a person's risk of developing colorectal cancer for two main reasons. First, inhaled or swallowed tobacco smoke transports carcinogens to the colon. Second, tobacco use appears to increase polyp size. In general, the bigger the polyp, the greater the chance it will become cancerous. Studies indicate that 12% of fatal colorectal cancers may be attributable to smoking. Edoardo Botteri et al (2008) performed a comprehensive literature search and a meta-analysis of observational studies considering both incidence and mortality in order to clarify the association between cigarette smoking and colorectal cancer. Their conclusion was that cigarette smoking is significantly associated with both colorectal cancer incidence and mortality[21]. Since there was no information about 48,57% of our patients with regards to their smoking habits, the results of the present epidemiological study can not be considered controversial to international bibliography.

Though our data doesn't permit us to know whether development of colon cancer among the above mentioned patients had any correlation with heredity, a lot of evidence suggests that colon cancer is a hereditary disease. In other words, genetic factors are strongly related to this malignancy[4]. Patients with one or more close relatives presenting similar malignancies by the age of 55, have an elevated risk of colorectal cancer onset. The cause of FAP (Familial adenomatous polyposis) is hereditary mutation of APC gene. FAP carries about 100% lifetime risk to be evolved to colorectal cancer. On the other hand, individuals with hereditary non-polyposis colon cancer syndrome (Lynch syndrome) still carry an increased risk (40%) of developing the disease[22]. Deficient mismatch repair due to inherited mutation in one mismatch repair genes (hMLH1, hMSH2, hMSH6, hPMS1, hPMS2) characterizes Lynch syndrome[1].

Registry forms of our patients didn't contain any information about their diet. However diet has been thought of as a valuable factor of colorectal cancer development9. Recently a study by the European Prospective Investigation into Cancer and Nutrition showed that a diet rich in processed meat, especially red, but poor in fibers increases the risk of the disease[17]. Nevertheless, results from other investigations have been skeptical towards the connection between low-fiber diet and colorectal cancer onset[23]. Industrial

countries are at a relatively elevated risk compared to less developed countries which traditionally have low- meat and low-fat, but high-fiber diet.

Association between body mass index (BMI) and risk of colorectal adenomas and cancer has been reported[18]. An investigation by Jacobs et al. has indicated that BMI was significantly related to most histologic characteristics of metachronous adenomas among men but not among women.

Concluding, it should be emphasized that the present retrospective epidemiological study is based on the data using pathology reports registered in the cancer registry forms of the above patients. Unfortunately, as it has already been mentioned, the registry forms do not contain information about fundamental risk factors related to genes, heredity, diet and obesity. So this study must be considered as a forerunner research, the objective of which is to assess whether colon cancer in the population of Northern Greece is associated with age and sex (demographic factors), place of residence and occupation (environmental conditions) and last but not least smoking (lifestyle habit).

According to Cummings and Bingham (1998) 24 lifestyle changes could decrease the risk of colon cancer as much as 60-80%. Bearing this in mind as well as due to the unexpected results of this study, the insufficient amount of data used to carry out the present research (occupation, smoking habit, place of resident) and especially the insufficiency of any kind of information regarding fundamental risk factors of colon cancer in Northern Greece prompt us to continue and extent the investigation by carrying out a current study.

Καρκίνος παχέος εντέρου: Επιδημιολογική μελέτη στη Βόρειο Ελλάδα.

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ΠΕΡΙΛΗΨΗ: Η παρούσα αναδρομική επιδημιολογική μελέτη έχει στόχο την ενημέρωση σχετικά με τους παράγοντες που ενοχοποιούνται για την πρόκληση καρκίνου του παχέος εντέρου στη Βόρειο Ελλάδα, με απώτερο σκοπό τη βελτίωση της πρόληψης. Πρόσφατες επιδημιολογικές έρευνες αποκάλυψαν ότι ο καρκίνος του παχέος εντέρου παγκοσμίως είναι ο τρίτος κατά σειράν πιο κοινός τύπος καρκίνου, εξαιτίας του οποίου ετησίως σημειώνονται περίπου 655,000 θάνατοι, ενώ στο Δυτικό Κόσμο αποτελεί τη δεύτερη θανατηφόρα μορφή κακοήθειας. Για την επαγωγή του ενοχοποιούνται πολλοί παράγοντες, γενετικοί (ηλικία, φύλο, μεταλλάξεις γονιδίων επιδιορθωτικών ενζύμων) και περιβαλλοντολογικοί (διατροφή, κάπνισμα, παχυσαρκία, έλλειψη σωματικής άσκησης).

Στην παρούσα εργασία δίνονται τα πρώτα αποτελέσματα αναδρομικής επιδημιολογικής έρευνας που αφορά 280 ασθενείς με καρκίνο παχέος εντέρου, οι οποίοι νοσηλεύτηκαν στο Θεαγένειο Αντικαρκινικό Νοσοκομείο Θεσσαλονίκης κατά τα έτη 2006, 2007 και 2008. Ταξινομήθηκαν, σύμφωνα με τους ατομικούς τους φακέλους ως προς το φύλο, την ηλικία, τον τόπο διαμονής, το επάγγελμα και τη συνήθεια του καπνίσματος. Τα αποτελέσματα έδειξαν ότι 58,57% ήταν άνδρες και 41,43% γυναίκες. Ποσοστό 82,49% είχαν ηλικία μεγαλύτερη των 60 ετών. Από τους ασθενείς το 38,93% διέμεναν σε αστικές περιοχές και το 60% σε μη αστικές. Σχετικά με το επάγγελμα 47,50% καταγράφηκαν ως συνταξιούχοι, 18,93% αγρότες, 13,57% οικιακής ενασχόλησης, 10,71% ελεύθεροι επαγγελματίες και υπάλληλοι, ενώ για το υπόλοιπο 9,29% δεν καταγράφηκαν πληροφορίες. Σχετικά με τη συνήθεια του καπνίσματος 16,79% δήλωσαν καπνιστές, 34,64% μη καπνιστές, ενώ δεν υπήρχαν πληροφορίες, για το 48,57%. Τα ευρήματα της μελέτης συμφωνούν με τα βιβλιογραφικά δεδομένα στο ότι η ηλικία αποτελεί σοβαρή αιτία εκδήλωσης καρκίνου στο έντερο. Αποκαλύπτουν επίσης ότι οι άνδρες έχουν μεγαλύτερη πιθανότητα από τις γυναίκες να εμφανίσουν τη νόσο, δεν επιτρέπουν όμως την εξαγωγή συμπερασμάτων για τη συσχέτιση επαγγέλματος-κακοήθειας. Το γεγονός ότι οι μη καπνιστές ασθενείς βρέθηκε να υπερτερούν των καπνιστών, που έρχεται σε αντίθεση με τα βιβλιογραφικά δεδομένα, θα μπορούσε να αποδοθεί στο ότι για ένα σημαντικό ποσοστό (48,57%) δεν υπήρξαν συγκεκριμένες πληροφορίες. Τέλος η αυξημένη συχνότητα εμφάνισης της κακοήθειας σε κατοίκους μη αστικών περιοχών συγκριτικά με κατοίκους πόλεων δημιουργεί πολλά ερωτηματικά και η αιτία της απαιτείται να διερευνηθεί διεξοδικά. Η πλήρης έλλειψη πληροφοριών σχετικά

με ουσιαστικούς παράγοντες κινδύνου εμφάνισης καρκίνου του παχέος εντέρου στον Ελληνικό πληθυσμό υπαγορεύουν την συνέχιση και επέκταση της επιδημιολογικής αυτής μελέτης, καθώς η πρόγνωση αποτελεί την καλύτερη θεραπεία και οι επιδημιολογικές μελέτες συμβάλλουν σημαντικά στην πρόγνωση.

Λέξεις Κλειδιά: Καρκίνος παχέος εντέρου, Επιδημιολογική μελέτη.

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