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Original Article

Epidemiology and survival of colon cancer among Egyptians: a retrospective study

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ABSTRACT

Introduction: Colorectal cancer is the 4th commonest cancer in the world. Studies had shown different tumor behavior depending on the site, pathology and stage. However the characters of Egyptian colon cancer patients are not well addressed.

Method: Computerized registry of a tertiary cancer hospital in Egypt was searched for colon cancer cases. Demographic, pathologic and treatment data were collected and analyzed using SPSS program.

Results: About 360 colon cancer patients attended our center in the last 12 years. Tumor characters showed great diverse from that of developed countries, with especially different prognosis and survival.

Conclusion: Egyptians have unique tumor characters and behavior, and different compliance with treatment regimens. Multicenter prospective studies, as well as evolving Egyptian treatment guidelines are needed to address this.

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Epidemiologia e sobrevida para o câncer de cólon entre egípcios: estudo retrospectivo

RESUMO

Introdução: Câncer colorretal é a quarta neoplasia mais comum a nível mundial. Estudos demonstraram diferentes comportamentos do tumor, dependendo do local, da patologia e do estágio. Contudo, ainda não estão devidamente definidas as características dos pacientes egípcios com câncer de cólon.

Métodos: Foi realizada pesquisa no registro computadorizado de um hospital terciário para pacientes com câncer, à busca de casos de câncer de cólon. Foi feita coleta de dados demográficos, patológicos e terapêuticos. Tais dados foram então submetidos à análise com o programa SPSS.

Palavras-chave:

Câncer de cólon

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Resultados: Nos últimos 12 anos, cerca de 360 pacientes portadores de câncer de cólon foram atendidos em nosso Centro. As características dos tumores demonstraram grandes diferenças em comparação com os achados de países desenvolvidos e, em especial, com relação ao prognóstico e à sobrevida.

Conclusão: Os egípcios exibem características e comportamentos singulares com relação aos tumores, além de diferentes graus de cooperação com os regimes terapêuticos. Para que tais aspectos sejam sanados, há necessidade de mais estudos prospectivos multicêntricos, bem como de um aprimoramento das diretrizes terapêuticas para os egípcios.

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Introduction

Colorectal cancer is the 7th commonest cancer in Egypt, representing 3.47% of male cancers and 3% of female cancers. The estimated number of colon cancer patients (excluding rectal cancer) in 2015 was slightly more than three thousand.¹

Epidemiology of colon cancer differs in each country. There is a paucity of studies discussing the behavior of this common cancer in Egypt, the largest of which is Abou-Zeid et al. in 2002.² Two decades have passed since this study, at this time a major change occurred in our understanding of cancer patterns in Egypt, with the publication of the first national population based cancer registry in 2014,¹ and also urbanization and change lifestyles should have affected colon cancer pattern.

In order to estimate the scale of our study, we should bear in mind that our hospital is located in Mansoura city (capital of Dakahlia, the fourth largest governorate in Egypt), with a population in the governorate approaching 6 millions.³

Several studies compared right to left sided colon cancers, the conclusion was that right-sided tumors carry a worse prognosis than left-sided ones, and even some authors went more in considering them a two distinct tumors that should be treated in a different manner.^{4,5} However, no studies addressed the difference in the Egyptian population.

Our aim of this study to delineate colon cancer age and sex distribution, stage at diagnosis, pathologic pattern and survival (overall and disease free) plus explaining the important prognostic factors and whether side of the tumor play a role or not.

Patients and methods

This is a retrospective study, where the institutional registry at oncology center Mansoura University (OCMU) is thoroughly revised for colon cancer cases that attended the hospital from its construction in 2004 till April 2016. Forty-six patients were excluded for having tumors at the rectosigmoid junction (defined as any cancer at or near the junction requiring some sort of rectal resection to attain adequate margins), pathology other than carcinoma or inadequate data registered. The minimum time of follow up of the patient's hospital visits is 10 months (till February 2017).

The data of these patients were analyzed and statistical values were obtained using SPSS version 22 (Inc, Chicago, IL).

Continuous variables are presented as mean when symmetrical or median and range when asymmetrical. Categorical variables are presented as proportions. Bivariate analysis was done using chi-square test. Survival analysis was done using Kaplan Meier curve and significance determined by log rank test. Significant factors affecting survival were then processed in multivariate analysis using Cox's regression test. *p*-Value < 0.05 was considered significant.

Results

Searching data with the diagnosis of colon cancer revealed 360 cases. Patients with rectosigmoid junction cancer were excluded, due to different epidemiology and management plans. So, 314 cases of colon carcinoma were included in our study, some of these cases were completely managed in the center, while others came to the clinic for chemotherapy or for management of a recurrence (Fig. 1).

Demographics

The mean age at diagnosis of colon cancer was 53.32 years (SD = 14.326), the youngest case was diagnosed at 16 years old and the oldest was 88 years old. Data show a slight female preponderance approximately 1.2:1. Initial colonoscopy was done in about 60% of cases, in which the most common finding was a mass (about 68%), followed by stricture then ulcer. Right colon represent the commonest site (about 48%), then sigmoid colon (about 27%), descending colon (about 19%) and finally transverse colon (about 5%). Only 4 cases with multifocal cancer were found, one of them had synchronous rectal cancer.

Management

CT imaging showed just wall thickening in approximately 65% of cases, in the remaining a mass was visualized. The mean size of the tumors was approximately 9.3 cm, with the maximum size detected 22 cm. Initial chemotherapy (either as a neoadjuvant or a palliative therapy) was given in only 15.5% of cases. Right hemicolectomy was the commonest operation (33%), followed by left hemicolectomy (17.1%), and then sigmoidectomy (13.7%). Eighty percent of the cases underwent exploration. However, only 34 cases underwent laparoscopic approach with 13 converted to open (Fig. 1). Diversion was

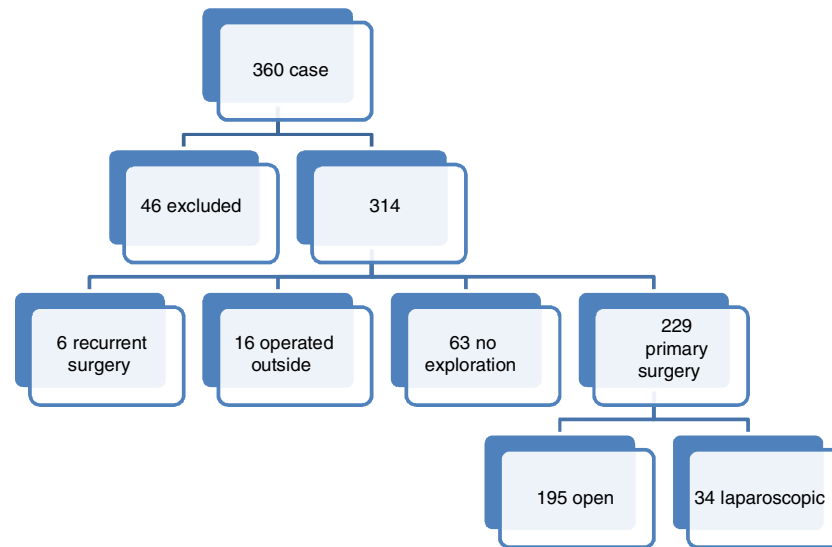


Fig. 1 – Flow chart showing the number of cases admitted, number proceeded for surgery for primary and recurrence, and number operated laparoscopically.

quashed in 78% of cases, while loop ileostomy was exteriorized in 8.3% of patients, followed by loop colostomy in 7.6% of patients. Adjuvant radiotherapy was only used in 4 cases, while 58% of patients received adjuvant chemotherapy.

Pathology

About 53% of cases are of moderate grade. Postoperative pathology showed classic adenocarcinoma in 64.2% of cases, colloid adenocarcinoma in 22%, and signet ring carcinoma in 6.1%. While another 6.1% showed adenocarcinoma with mucinous activity <50%, and only two cases showed neuroendocrine differentiation and one case had anaplastic carcinoma. According to AJCC 8th edition staging,⁶ stage III was the most common, representing 30%, then stage II 29.5%, followed by stage IV 22%, and finally stage I 5.7% of patients (Fig. 2). Number of lymph nodes retrieved ranges from 0 to 69 with median 10, but unfortunately 54% of patients have less than 12 nodes retrieved (inadequate lymphadenectomy). Number of nodes infiltrated range from 0 to 18. Margins were free in about 71% of patients, no data in about 25%, infiltrated distal margin in 9 cases (one retreated by redo) and infiltrated radial margin in only 2 cases.

Survival

The estimated median overall survival was 2 years, where in stage I was 44 months, while in stage IV was 8 months (Fig. 3A) with p -Value=0.00. The estimated median disease free survival was 1 year, where stage I was 24 months, while stage IV was zero, p -value=0.00 (Fig. 3B). Comparing mucinous carcinomas (colloid and signet ring) to non-mucinous carcinomas showed non-significant overall and disease free survival; although non-mucinous tended to be better. Comparing young age (≤ 40) with old age (>40), overall survival and disease free survival was significantly better in the younger group (p -value 0.001, and 0.02, respectively) (Fig. 4). Comparing

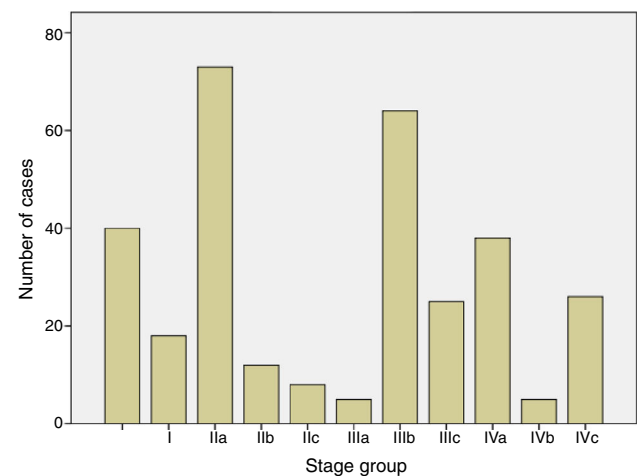


Fig. 2 – A bar chart showing the stage distribution according to AJCC 8th edition.

sex, OAS and DFS were insignificant. Tumor size significantly affected OAS (p -value=0.019), but not DFS. Grade was not significant in either parameters. Margin status was a significant factor in DFS (p -value=0.00), but insignificant factor in OAS, although free margins showed higher estimated lifespan (47.6 versus 31.6 months respectively). Number of lymph nodes retrieved was an independent prognostic factor of OAS and DFS (p -value=0.06, and 0.02 respectively). Number of infiltrated lymph nodes also directly affected OAS and DFS (p -value=0.00 for both). Comparing right and left sided tumors (excluding transverse and multifocal), the mean age at diagnosis of left sided tumors was about 51 years, which was 5 years younger than right sided tumors, although insignificant.

Left sided tumors was more common in females (60%), while right sided tumors were slightly more common in males (52%), with p -value=0.039. The estimated median overall survival for left-sided tumor is 22 months, which is slightly higher

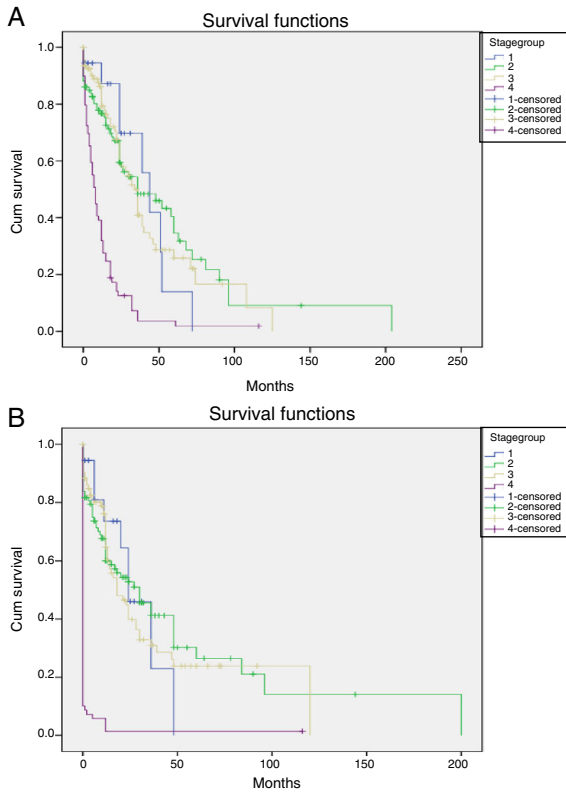


Fig. 3 – Kaplan Meier curve showing (A) overall survival by stage and (B) disease free survival by stage.

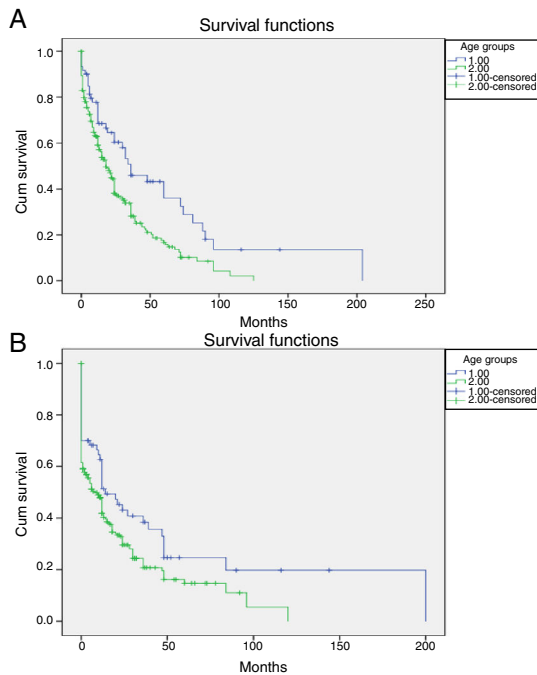


Fig. 4 – Kaplan Meier curve showing (A) overall survival by age group and (B) disease free survival by age group. 1 patients <40, 2 patients ≥40.

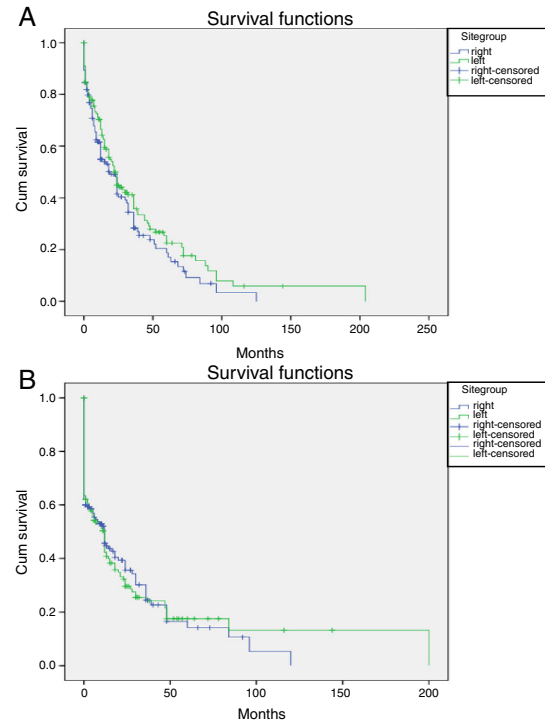


Fig. 5 – Kaplan Meier curve showing (A) overall survival by site and (B) disease free survival by site.

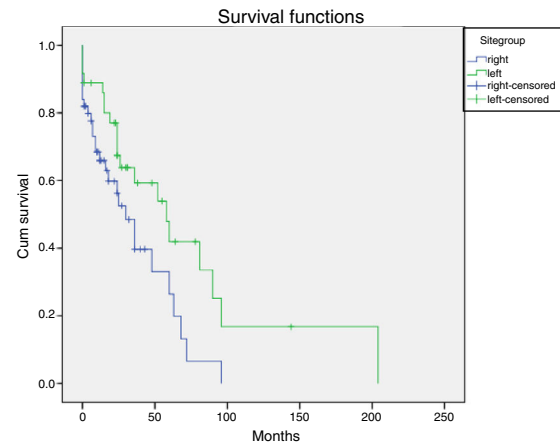


Fig. 6 – Kaplan Meier curve showing overall survival for stage II colon cancer according to the site.

than right-sided tumors 19 months, but insignificant (Fig. 5A). However, the estimated median disease-free survival is one year on both sides. Although the curve seems confusing in the first 3.5 years, it clearly demonstrates better DFS toward the left-sided tumor afterward, but still insignificant (Fig. 5B). Analyzing site for each stage group alone, left side cancers had only statistically significant better OAS in Stage II disease, p -value = 0.024 (Fig. 6).

In multivariate analysis, the OAS was only affected by age (0.004); while the DFS was affected by stage (0.013), number of nodes infiltrated (0.024), and margin status (0.044).

Discussion

Colon cancer was commonly diagnosed in elder people with a mean age about 53 year-old, which is still more than a decade younger than the corresponding age in the USA (69 in men and 73 in women).⁷ However it is consistent with age distribution in previous published studies from Egypt.^{2,8,9}

In our study, females appeared to be at a slightly higher risk of developing colon cancer with current prevalence 1.2:1, in contrast to previous studies where males predominated.^{2,9} The tumors were nearly equally distributed in the right side (caecum and ascending colon) and the left side (descending colon and sigmoid) 1.04:1.

Upfront surgery for colon cancer cases was the dominant strategy in nearly 85% of our patients. Laparoscopic resection although proved oncologically equivalent to open resection,¹⁰ in our study only 34 cases underwent laparoscopic colectomy with conversion rate about 38%. This may be reasoned by the locally advanced nature in most cases (59.5% stages II and III), the large size of the tumors (mean 9.3 cm), and the still uncompleted learning curve. Fecal diversion was infrequently done (only in 22% of cases).

It is currently accepted that lymphadenectomy is an integral part of oncologic colon resection, with the adequate minimal number of retrieved lymph nodes ≥ 12 nodes.¹¹ However, about half of our patients had less than this number. The comparison of nodes retrieved in open and laparoscopic surgery was not done because of the fact that almost all cases of laparoscopic resection in our series were done after 2011, which was actually concomitant with shift of our practice toward complete mesocolic excision.

In other hand, the pathologic analysis of the resected specimens showed more than half of the cases with grade II adenocarcinoma. Conventional (nonmucinous) type represented about two-third of the cases, while mucinous types (colloid and signet ring) constituted 28% of cases. This is consistent with Foda et al. study showing excess mucinous carcinoma among Egyptians, especially signet ring variant in comparison with the world rates.⁸

Overall (OAS) and disease free (DFS) survival was directly affected by the disease stage at diagnosis significantly, this is consistent with previous Egyptian studies directly correlating stage with the overall survival.¹² However, data for stage I cancers seems confusing, this is explained by the fact that 7 patients of the 18 patients with stage I has inadequate lymphadenectomy, which worsen the OAS and the DFS of that group in the Kaplan Meier curve, as probably these patients should have been upstaged otherwise.

Also OAS and DFS were directly related to the number of lymph nodes retrieved during surgery as previously proved by Le Voyer et al. study,¹¹ and inversely related to the number of nodes infiltrated by the tumor, as shown in Eisa study.¹²

In our study, young patients (≤ 40 years) showed significantly better OAS and DFS. This is also consistent with a previous study in Upper Egypt, although it was not significant statistically. However, this is against other studies showing equal survival.¹³

Large tumors were found to be associated with shorter OAS, but did not affect DFS. In contrary, the patients with

infiltrated margin showed a higher recurrence rate, but without significantly affecting the OAS.

The worse prognosis of mucinous types was highlighted by another study from Mansoura,⁸ but in our study pathologic type (mucinous versus nonmucinous) was not a significant survival predictor.

Another issue showed in multiple studies from around the world is the significant worse prognosis of the right side tumors, mostly in stage III disease.^{4,5,14} Others showed better survival for right sided tumors in stage I disease while, worse survival for stage II/III disease.¹⁵ Limitations of most of these studies is considering rectal cancer with (left sided tumors), although it differs much in management, and also considering transverse colon with (right sided tumors), although it had a mixed embryologic origin. In our patients, the site (right sided versus left sided) did not significantly affect neither survival nor recurrence rate in general. However, stage II left colon cancer patients showed significantly better OAS. Also, left tumors showed significant increase among the females.

In other hand, neither grade nor sex showed to be of a survival value, as in other studies.¹²

Finally, the most import prognostic factors in the multivariate analysis were age for OAS as highlighted by Aquina et al.¹⁶ in contrast to the stage, number of nodes infiltrated, and margin status for the recurrence hazard.

Conclusion

Colon cancer in Egypt has a different epidemiologic profile and survival pattern. Surgical oncologists as well as colorectal surgeons should emphasis on adequate lymphadenectomy, as an integral part of staging and prognosis. Minimally invasive colon cancer surgery in Egypt should be further employed. Relatively advanced tumors at diagnosis should highlight a need for screening program, but being relatively uncommon cancer in Egypt, studies on cost benefit of such program is encouraged.

Conflicts of interest

The authors declare no conflicts of interest.

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