Original Article

TNM and Modified Dukes staging along with the demographic characteristics of patients with colorectal carcinoma

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Abstract: Aim: Colon adenocarcinoma, is the most common cancer in gastrointestinal system (GiS). The whole world is an important cause of morbidity and mortality. TNM and modified Dukes classification which has great importance in the diagnosis and treatment of Colorectal cancer (CRC). TNM and Modified Dukes classification results of histopathological examination and the demographic characteristics of patients and their relation were investigated. Materials and methods: Lower gastrointestinal operation results of 85 patients were examined accepted to clinical Pathology between January 1997-November 2013. Colon cancer had been diagnosed at 85 patients with pathology materials and staging was done according to the TNM and Modified Duke classification. The demographic characteristics of patients, differentiation grade, lymph node involvement, serosa involvement were evaluated retrospectively. Results: In this study 37 patients (43.52%) were men and 48 (56.47%) were women. Ages of patients were between 19 and 87 with a mean age of 57.31 ± 15.31. Lymph node, differentiation, serosa involvement, Modified Dukes and TNM classification was assessed according to sex and age. TNM classification by sex was not statistically significant (p > 0.05). There was no statistically significant relationship between age and differentiation (p = 0.085). Value of differentiation increased towards from 1 to 3 inversely proportional to age. So young patients defined as well-differentiated at the conclusion. Negative relationship was evaluated between age and TNM Class variables. As a result, the relationship between age and TNM was not significant (p > 0.05). However, with increasing age the degree of staging was also found to increase. TNM classification was associated with the differentiation and it was significant (p = 0.043). Conclusion: Colon cancer, when contracted at an early stage, it is suitable for surgery and curative treatment can be done with minimal morbidity and mortality. However, some of the patients have advanced disease at diagnosis and their 5-year survival rate is only 8%. Every year there is prolongation of overall survival of colon cancer. It is so common cancer type so that determination of prognostic factors, disease staging and treatment strategy which affects survival is significant.

Keywords: Gastrointesinal system (GiS), colorectal cancer (CRC), TNM, Modified Dukes staging

Introduction

Colorectal carcinoma (CRC), the most common malignant disease in industrialized societies; 875,000 new cases being reported every year and approximately 500,000 are die to the CRC [1-12]. In the United States metastatic colon cancer is the second most common cause of death from cancer. In 2006, 148,610 patients diagnosed with CRC, while 55,170 people have died due to this disease. The third most frequent type of cancer in developed countries and seen in approximately 9% of all cancers [13-15]. Throughout life, the risk of developing CRC is approximately 6%, and this rate is higher in men than women [16]. The average age is 62 [14]. Risk of developing is increasing after 40 years for men and women [4].
CRC is observed in a wide geographic area. It is most common seen in industrialized countries such as in Western Europe, North America, New Zealand, Australia. Also, in countries the incidence is changing according to regions. For example, in the United States, while the maximum rate is at the industrial northeast, the smallest in the rural southeast. When people migrated to high-risk areas such as United States, Australia from low-risk areas such as Japan, Poland there is a rapid increase in rates of colon cancer. CRC, are multiplied plus by development and westernisation [14, 17].

CRC usually develops from dysplastic adenomatous polyps [18]. Those seated right column, constitute a large portion of CRC and seen more frequently in low-risk societies than high-risk populations. Environmental and genetic influences are active at different points on neoplastic development. A few well-defined colon cancer syndrome has shown that genetic predisposition plays an important role in the pathogenesis of colon cancer.

More than 95% of all cases of CRC are adenocarcinomas, in the rest there are neuroendocrine tumors and small cell carcinomas monitored. Signet ring cell carcinoma exhibits a poorer prognosis in patients with colorectal adenocarcinoma and when compared with other types the high incidence of peritoneal metastasis is detected. Likewise, similar findings have been reported for mucinous adenocarcinoma. Mucinous carcinoma and signet ring cell carcinoma are sub-groups of adenocarcinoma. Mucinous carcinoma and signet ring cell carcinoma are sub-groups of adenocarcinoma and the frequency of are respectively 10-15% and from 0.1 to 2.4%. The prognosis of CRC in a large proportion is due to pathologic stage at diagnosis [3-6, 8, 19, 20]. Almost all of the patients treated with surgical resection. Five-year survival rates for stage Dukes A, more than 90% while only 5% for Dukes stage D.

Many factors affect the prognosis of CRC. The most important prognostic factor is the stage of the tumor [14, 17]. The degree of bowel wall invasion, lymph node metastasis, the distant metastases adversely affects the prognosis of tumor stage [14, 16, 17]. Three different systems are used for the staging of CRC: Dukes system [5, 21], Astler-Coller system [22, 23], TNM system [24, 25].

Modified Dukes staging:

Stage A: Tumor limited to mucosa.
Stage B1: Tumor limited to the submucosa, no lymph node invasion.
Stage B2: Tumors confined to the muscle layer, no lymph node invasion.
Stage C1: The tumor did not exceed the bowel wall, lymph node metastasis.
Stage C2: Tumor exceeded the intestinal wall and lymph node metastasis.

Astler-Coller staging:
T = primary tumor.
TX- Primary tumor of unknown.
T0- No primary tumor.
Tis- Carcinoma in situ.
T1- Tumor invades submucosa.
T2- Tumor invades muscularis propria.
T3- Tumor invasion to subserosa or periocolic/perirectal tissue.
T4- tumor invasion to neighboring organs or structures and/or visceral peritoneum is perforated.

N = Regional lymph nodes.

Stage 0
\[ \text{Tis, N0, M0} \]

Stage I
\[ \text{T1, N0, M0} \]

Stage II
\[ \text{T2, N0, M0} \]
\[ \text{T3, N0, M0} \]

Stage III
\[ \text{T4, N0, M0} \]
\[ \text{Any of T, N1, M0} \]
\[ \text{Any of T, N2, M0} \]

Stage IV
\[ \text{Any of T, Any of N, M1} \]

NX- Regional lymph nodes can not be assessed.
N0- No lymph node metastases.
N1- 1-3 lymph node involvement.
N2- 4 or more lymph node involvement.
M = Distant metastasis.
MX- Distant metastasis can not be assessed.
M0- No distant metastasis.
M1- Distant metastasis.

American Joint Committee on Cancer (AJCC) and the International Association of Cancer...
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(UICC) revealed TNM classification by grouping of the tumor, lymph node and metastasis components, this is a more detailed classification system and easily converted into other classifications. Nowadays, treatment decisions are still based on this classification [14, 18, 24-26].

TNM classification

Histological grade and type: Grade is made according to the degree of tubule formation and cellular array in tumor tissue. 15-20% of patients grade I or well-differentiated, 60-70% of grade II or moderate differentiated, while 15-20% of them grade III or less differentiated [27]. Grade I carcinomas; microscopically similar to the adenoma epithelial, cells are at uniform appearance and there is no or minimal loss of polarity [28]. Grade II carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped. Nuclear polarity is lost in light or medium, they secrete different amounts of mucin. Grade III carcinomas, tubular structures can be simple or complex as may be slightly irregular shaped.

Mucinous carcinomas and signet ring cell carcinomas are considered to be grade III and they have much worse prognosis from classic adenocarcinomas [29]. Histological grade was determined to be related to survival [15, 16, 30].

Lymph node involvement: When the tumor has spread to the lymph nodes, five-year survival rate is falling sharply. As the number of involved lymph node increases prognosis is poor [14, 16]. More than six in lymph node involvement survival over five years seems less than 10% [14, 31] (Table 1).

Table 1. Lymph node involvement by gender

<table>
<thead>
<tr>
<th>Lymph node</th>
<th>No involvement</th>
<th>Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Women</td>
<td>21</td>
<td>43.8%</td>
</tr>
<tr>
<td>Men</td>
<td>22</td>
<td>59.5%</td>
</tr>
</tbody>
</table>

Patient ages: Youth, especially children and very aged elderly has a poor prognosis. This results may be due to rapid progression of the disease in young patients [16, 31]. High-grade tumors are around 53% ratio in young patients; this rate is 20% in the elderly.

In very elderly patients with high mortality due to often immediate implementation approaching.

Patients under 40 years of age has a good prognosis than elderly patients.

Gender: The prognosis is better in women than in men [31, 32].

In this study of factors affecting the prognosis of colon cancer, tumor stage and degree of differentiation according to age and gender distribution was aimed to investigate.

Materials and methods

Admitted to the department of Pathology between January 1997-November 2013 lower gastrointestinal operation results of 85 patients were examined. 85 patients who diagnosed with colon carcinoma TNM and Modified Dukes staging were done. Along with the demographic characteristics of patients, differentiation grade, lymph node involvement, whether serosa involvement were evaluated retrospectively.

Statistics

It was a cross-sectional descriptive study and data intervals were calculated on the 95% confidence. Analysis SPSS 15:00 package program has been used. While data analyzing, descriptive statistics frequency (s), percent (%), mean (x), standard deviation (SD) were evaluated. Pearson correlation and Chi-square test was used.
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The patients enrolled in the study 37 (43.52%) of men and 48 (56.47%) of were women. The age of patients were between 19 and 87 with a mean age of 57.31 ± 15.31. Men between the ages of 19 and 86 with a mean age of 58.72 ± 14.46 and women between 20 and 87 ages and the average age was 56.22 ± 16 (Table 2).

TNM frequency according to the gender was not statistically significant (P = 0.371). Also TNM groups according to gender was not statistically significant (Table 3).

Age and differentiation relationship: To explain this relationship Spearman correlation analysis was performed. Relationship between age and differentiation was not found statistically significant (P = 0.085). Young patients were defined as well-differentiated and the degree of differentiation were increasing according to advanced age.

Age and TNM relationship: Spearman correlation analysis was performed. Negative relationship were evaluated between age and TNM Class variables. TNM relationship between age was found to be insignificant (p > 0.05). However, with increasing age there was increase in the degree of staging. If the number of data were higher our results could be even more significant with chi-square test.

Table 2. Differentiation by gender

<table>
<thead>
<tr>
<th>Differentiation</th>
<th>Mucinosis</th>
<th>Poor</th>
<th>Moderate</th>
<th>Well-differentiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Women</td>
<td>3</td>
<td>6.3%</td>
<td>2</td>
<td>4.2%</td>
</tr>
<tr>
<td>Men</td>
<td>7</td>
<td>18.9%</td>
<td>2</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

Where p = 0.178 for the frequency of differentiation by gender was not significant (p > 0.05). Differentiation according to the gender was not statistically significant.

Table 3. Serosa involvement by gender

<table>
<thead>
<tr>
<th>Serosa</th>
<th>No involvement</th>
<th>Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Women</td>
<td>33</td>
<td>68.8%</td>
</tr>
<tr>
<td>Men</td>
<td>23</td>
<td>62.2%</td>
</tr>
</tbody>
</table>

p < 0.05 was considered as a statistically significant result.

Discussion

Colon cancer is an important cause of morbidity and mortality all over the world and today in terms of gastrointestinal cancer incidence is in the first ranks [33]. CRC, is common in industrialized countries, the risk is increasing at those who migrate to developed countries from underdeveloped countries. Early diagnosis of this cancer can be life saving. Whether depressed lesion or sessile or protruding polyps; adenomatous polyps are the most important preneoplastic lesions of CRC. Identified early and this group of patients with resected there are close to 100% chance of life and is a life saver (5 year survival rate of CRC is 97.6% at carcinoma in situ and CRC settled in the submucosa) [30]. In recent years the development of the method used to promote lesions, screening programs to be implemented widely, the new surgical techniques, with the use of new methods of radiotherapy and systemic treatment; colon cancer captured in early stage and ensures with the higher survival rates [34-37]. Gilberts and Nelms in their sigmoidoscopy screening study over 27,000 patients, the success rate of distal colorectal cancer prevention was found between 60-85%. Only fecal occult blood test screening rate decreased by 20% of CRC [38-44].

CRC which is expressed more common in men than in women. In the majority of studies gender showed no significant difference in terms of prognosis [44-48]. In a study conducted by Han-Shiang et al. [49] on 2,082 patients, male gender was reported to be a poor prognostic factor. Again Asaad et al. [50] in a study of stage II colon cancer patients, male gender was reported to be a poor prognostic factor. In our study 43.52% of cases were males and 56.47% of were women.

Colon cancer incidence is increasing after age 40 and peaks between the ages of 60-75 [49-52]. In our study, our patients aged between 19 to 87 with a mean age of 57.31 ± 15.31. Some authors have reported that young age is a poor prognostic factor [51]. Some of the hereditary
Colon cancer goes more aggressive and is seen more in young patients, as well as, lack of symptoms during the application, signs come up later due to these points young patients usually have the diagnosis advanced stage [53]. Some researchers stated that there is not a significant difference between settlement, in terms of stage and prognosis of colon cancer in the elderly than of colon cancer seen in young people (30.52). In a study conducted by Fietka et al. [54] on 6,016 patients, colon cancer incidence increases with age, but there is no statistically significant difference in the survival rates. In another study conducted with Chung et al. [55] in 2064 patients, the 5-year survival rate was found 54.8% in the group before age 40; 54.1% in the group aged over 40 years and did not show a significant difference at ratios. In a study by Mitry et al. [53] comparison of 4643 patients over 45 years and young age was not found as a poor prognostic factor for colon cancer; but in the younger age group of patients predisposing factors were mentioned more frequently (Table 4).

One of the most important prognostic factor is the presence of lymph node metastasis [28, 30]. As tumor spread to the lymph nodes the five-year survival rate shows a significant decline. The large numbers of lymph node, when in the roots of mesenteric veins, pericapsular invasion is a poor prognostic factor. In less than four lymph node involvement 5 years survival is 44%, more than four lymph node involvement 5-year survival for patients decreases to 6% [51]. AJCC/UICC TNM staging system in 2002 has been revised and N staging was classified according to the number of metastatic lymph nodes [56]. However, metastatic lymph nodes affected from the total number of removed lymph nodes and this causes incorrect staging. In the study conducted by Swanson et al. [57] on 35,787 patients with T3N0 stage; the number of lymph nodes removed was associated with poor prognosis. Chang et al. [58] in the analysis of the 17 studies from nine countries, they reported that survival increases with increasing number of lymph nodes removed in stage II and stage III colon cancer patients. Johnson et al. [59] in the study of 20,702 patients with stage IIIb and IIIc colon cancer, in terms of the extracted lymph node number increases due to this mortality decreases (Table 5).

Colorectal cancer staging affects the extent of surgery, postoperative and follow-up treatment. Accurate staging shows the path in thin line, to keep patients from the side effects of the drug and to avoid the risk of tumor recurrence. The other most important prognostic factor in colon carcinoma is tumor stage at diagnosis [28, 30]. According to the stages when we look at five-year survival rates 99% for stage I, 85% for stage II, 67% for stage III and 14% for stage IV.

One of the major factors associated with prognosis is the degree of tumor differentiation [60, 62, 63]. Histological grade of the tumor; is marker showing the degree of differentiation of the tumor.

Our other findings in the study were: Women at a higher rate of lymph node involvement. Large proportion of colorectal cancer in women were medium-well-differentiated and moderately differentiated in men and mucinous character was higher in men. There was no significant differences between differentiation and gender. Nearly 30% serosa involvement was found both in men and women. According to Modified Dukes staging; the most common grade was C2 in women and B2 phases were also found in the second frequency. In men, the exact opposite most common stage was B2 and the second most common stage was C2. According to TNM classification both sexes were at stage 3 (60% of women and 45% of men). Differentiation

### Table 4. Modified Dukes Classification according to gender

<table>
<thead>
<tr>
<th></th>
<th>Modified Dukes</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stage B1</td>
<td>Stage B2</td>
<td>Stage B3</td>
<td>Stage C1</td>
<td>Stage C2</td>
<td>Stage C3</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Women</td>
<td>4</td>
<td>8.3%</td>
<td>16</td>
<td>33.3%</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Men</td>
<td>2</td>
<td>5.4%</td>
<td>16</td>
<td>43.2%</td>
<td>2</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

### Table 5. TNM classification by gender

<table>
<thead>
<tr>
<th></th>
<th>TNM classification</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stage I</td>
<td>Stage II</td>
<td>Stage III</td>
<td>n</td>
</tr>
<tr>
<td>Women</td>
<td>5</td>
<td>10.4%</td>
<td>14</td>
<td>29.2%</td>
</tr>
<tr>
<td>Men</td>
<td>4</td>
<td>10.8%</td>
<td>16</td>
<td>43.2%</td>
</tr>
</tbody>
</table>
degree was increasing with age, despite no significant relationship between differentiation and age. Also TNM stage was increasing with age, despite no significant relationship between TNM staging and age. But TNM staging had relation with differentiation and this was significant. When we look at the literature there are insufficient data in this way. In particular, we believe that more studies are needed in the classification based on demographic characteristics.

Early diagnosis and prevention of CRC is so important. The incidence of CRC doubles every 10 years between 40 and 80 years of age and two-thirds of patients diagnosed when they are above 65 years of age. In western countries, the average life expectancy known to be extended and the proportion of elderly people is increasing gradually. The mean survival time is prolonged in our country as young population is increasing. Industrialization and the popularization of the “western-style”, we expect increasing number of elderly patients with colorectal cancer.

Disclosure of conflict of interest

None.

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