RESEARCH ARTICLE

Survival of Rectal Cancer in Yazd, Iran

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Abstract

Background: Colorectal cancer is common in Iran. However our knowledge about survival of rectal cancer in our province is low. The aim of this study is to evaluate this question. Materials and Methods: Patients with documented pathology of adenocarcinoma of the rectum and rectosigmoid junction referred to our center from September 2004 to September 2012 were enrolled in this study. Metastatic and recurrent patients were excluded. A questionnaire including clinicopathologic parameters, quality and sequence of treatment modalities was filled in for each patient. Patients treated with a combination of surgery, chemotherapy and radiation therapy were divided into standard and non -standard treatment groups, according to the sequence of treatment. Results: One hundred and nineteen patients were evaluated. Mean age was 60.8 year. The median overall survival was 62 months and five year survival was 55%. TNM staging system was not possible due to (Nx) in 21 (17.6%) patients. The others were in stage I, 20 patients (16.8%), II, 35 (29%.5) and III, 43(36.1%). According to our definition only 25 patients (21%) had been treated with standard treatment and 79% had not received it. A five year survival in patients with standard treatment was 85% and in the non-standard group it was 52%.Age, sex, stage and grade of tumor did not show any significant relation to survival. Conclusions: Our study showed a five year survival of rectal cancer in our patients was about 10% lower than the rate which is reported for developed countries. Preoperative concurrent chemoradiation significantly improved local control and even overall survival.

Keywords: Rectal cancer - survival - chemoradiation - Yazd - Iran

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Introduction

Colorectal cancer is one the most common cancers worldwide. Different factors like environmental factors, genetic factors such as aberrant DNA methylation (Wei-Jia Fang et al., 2012) , behavioural and metabolic risk factors (David Stewart Morrison et al., 2013) have been suspected in etiology and outcome of these tumors. Colorectal cancer is the third and fifth common type of cancers seen in Iranian women and men respectively (Azadeh et al., 2008). According to the data from The National Cancer Registry Department of Ministry of Health and Medical Education the overall 5 year survival for colorectal cancer in Iran is 41% (Moradi et al., 2009). Rectal cancer not only potentially affects survival of patients but also deeply decreases the quality of life of patients. Permanent colostomy is a disaster for Iranian Muslim men and women, and impairs their emotional and sexual functions especially in women (Mahjoubi et al., 2012). Although we had some demographic information on colorectal cancer in our province (Salari et al., 2008) our knowledge about treatment quality and survival rate was very limited .We decided to evaluate survival rate of rectal cancer patients and the prognostic factors affecting survival of these patients.

Materials and Methods

Subjects were selected amongst the patients with documented pathology of adenocarcinoma of rectum and recto sigmoid. The subjects referred to ShahidSadoughi Hospital and Shahid Ramazanzadeh Radiation Oncology Center from September 2004 until September 2012. Statistical analyses were performed in October 2013. Metastatic and recurrent patients were excluded.A questionnaire including clinic pathologic parameters, quality and sequence of treatment modalities was filled for each patient. Unfortunately there is no endoscopic ultrasound (EUS) facility in our province; however since 2008 we have two MRI centers capable of performing rectal cancer staging. MRI was not performed for most of the patients before 2008 and for some even after that time. Some of the patients were operated without receiving neoadjuvant therapy and some others solely received two or even more courses of chemotherapy (some of whom referred for surgery and others referred for concurrent chemoradiation) and only a group of patients referred for concurrent neoadjuvant chemotherapy. In the last group we used 5FU (with or without leucovorin) and, in the last two years of the study, Capecitabine. The patients were divided into two separate groups: The standard

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therapy defined if MRI (or EUS) had been performed and patients were treated accordingly; surgery for T1-2 N0 and concurrent chemoradiation for T3-4 and/or N+ followed by surgery. If MRI (EUS) was not performed before any treatment, only the patients placed in standard group that had been operated and pathological staging was T1-T2 N0, or received concurrent chemoradiation followed by surgery and in clinical rectal exam had a fixed mass or CT Scan had been showed extra rectal extension of the tumor. Patients had received neoadjuvant chemotherapy solely or if they had been operated upfront and pathological staging was T3-4 and/or N+ placed in non-standard group. The treatment was completed for the patients who had been receiving concurrent chemoradiation by receiving adjuvant chemotherapy. Surgery had been performed for all of the patients except two cases that refused surgery. The patients received no adjuvant therapy if he/she was already operated and his/her pathologic stage was T1-2, and if the surgical margins were free of tumor and at least 12 lymph nodes were resected and all of which was negative for malignancy. All operated patients whose pathologic staging was T3-T4 and /or N+ or in whom less than 12 lymph nodes were resected, received chemoradiation. Overall survival was calculated from the day of pathology report to death, or last follow up and disease free survival was calculated from the day of ending all treatment to the day of first evidence of clinical, radiological or pathological relapse. For gathering data more than one month after the last visit, telephone contacts were made.

Statistical analysis

In this study survival rate was assessed using Kaplan-Meier curves employing Log Rank model and SPSS 15 software. The relation between variables and survival rate was evaluated.

Results

One hundred and nineteen patients were evaluated. Mean age was 60.8 year. The median overall survival was 62 months and one, three and five year survival was 97%, 88% and 55 % respectively (Figure 1). Fifty nine (49.5%) patients were female and 60 (50.5%) were male. Median survival was 61 months (95%CI; 53-69) and 67 months (95%CI; 58-76)in females and males respectively, however this difference was not significant (p value=0.46). The patients were divided into two age groups: under 60 years and above. Fifty three patients were 60 years or less and median overall survival in this group was 66 months (95%CI; 57-73) and 66 patients were in another group the median survival of whom was 59 months (95%CI; 49-69), but the difference was not significant either (p value=0.24). As we mentioned earlier ,the metastatic patients were excluded. Due to(Nx) in 21 (17.6%) patients staging according to TNM staging system was not possible. Twenty patients (16.8 %) were in stage I, 35 patients (29.5%) were in stage IIand 43 patients (36.1%) were in stage III. Median overall survival of patients according to different stages is illustrated in Figure 2. Although the difference was not significant (p value=0.13) patients in

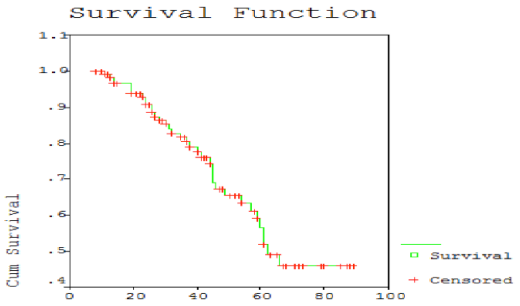

Figure 1. Overall Survival

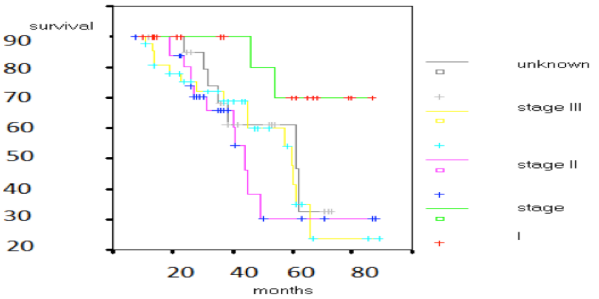

Figure 2. Overall Survival According to Stage of Disease

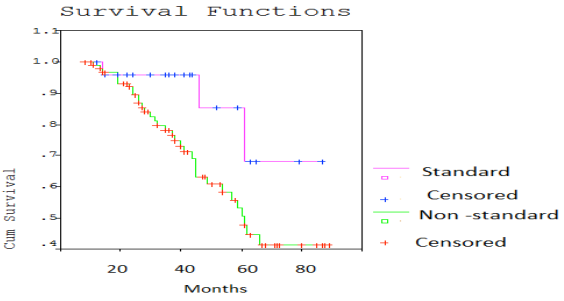

Figure 3. Comparison of Overall Survival in Standard and Non-Standard Treated Groups

stage I had the best and those in stage II had the worst survival rates. Tumor grade as well did not show any significant relationship with overall survival.

According to our definition only 25 patients (21%) had received standard treatment and the other 79% did not receive standard treatment. Since about 70% of patients who had received standard treatment were alive, continuing the line of 50% does not cross this curve (Figure 3) and therefore calculation of median survival for this group was impossible, however mean survival of these patients was 75 months (95%CI; 63-87). Median survival of patients treated with non-standard treatment was 61 months (95%CI; 55-67) and mean survival was also 61 months (95%CI; 55-68). This difference was relatively significant (p value=0.05). A five year survival in patients with standard treatment was 85% and in non-standard group it was 52%.

Median disease free survival was 59 months. Disease free survival also showed no significant relationship with sex (p value= 0.25), age group: (p value=0.25), stage: (p value=0.12), or grade (p value=0.44), however it was significantly better in patients who had received standard treatment (72 months *vs* 47 months; p value=0.03).

Discussion

Five year survival in this study was 55%. In this study only non-metastatic patients were evaluated, because we had decided to compare sequence of loco regional and systemic treatments and their effect on survival rate (in some of the metastatic patients loco regional therapies were omitted or had become palliative). It was expected that survival rate be more than studies which evaluated all of the patients. According to our knowledge none of the previous papers in our country which evaluated survival rate of colorectal cancer patients, separated non-metastatic and metastatic patients. Some of them reported survival of colorectal patients together and others separately (Esna-Ashari et al., 2007; Safaee et al., 2009; Ghabeljoo et al., 2011; Mehrabani et al., 2012; Heidarnia et al., 2013). Heidarnia et al. (2013) reported a 68.3% five year survival rate in colorectal cancer in the residencies of Tehran, capital of Iran, that we believe is the highest reported value in Iran. Although it emphasizes upon socioeconomic risk factors and stage of the disease it does not mention directly, there are two leading items that the readers can imagine most of the patient were in stages I and II. The authors showed 86% of patients had completed the treatment, and surgery was the only treatment modality in 85% of patients. Everybody knows that patients in stages III and IV need multimodality treatment and therefore this high rate of five year survival was due to diagnosis of patients at early stages. Another reason is that death occurred in 28% of patients in surgery group and 42% of multimodality treatment group. In another study from Tehran, Safaee et al. (2009) showed a 61% five year survival and 104.99 months mean survival in colorectal cancer. They did not report a one or three year survival and median survival. However, the study had been performed between Jan 2002 to Jan 2007 as a failure date. Therefore, it seems that at least a portion of patients were following up for a short time. In this study pathologic stage of the patients was reported. It is not clear how they could report pathological stage in 971 patients since the extent of wall penetration (T stage) reported for 940 patients from 1127 patients, regional lymph node metastasis in 850 patients (N stage) and distant metastasis in 766 patients (M stage). The survival of colon and rectal cancer did not show a significant difference in their study. They also did not mention about treatment modalities. In another large scale study, 2342 cases of colorectal cancer were evaluated in Tehran and a five year survival rate was 47.36% (Esna-Ashari et al., 2009), although survival of colon and rectal cancers were not reported separately. According to cancer fact and figures 2012, five year survival of colorectal cancer patient was 64% in the USA. For 39% of the patients who were diagnosed in the early stage this figure reached to 90%, however in lymph node positive patients it dropped to 69%. In metastatic patients it was only 12 %.(American Cancer Society, 2012). According to EUROCARE3, five year rectal cancer survival in the Nordic countries and Scotland between 1990-94 was variable between these countries: for men it was highest in Norway (62.8%) and lowest in Finland (33.9%) and for women it was highest in Sweden (62.4%) and lowest in Iceland (33.1%) (Folkesson et al., 2009).

In many studies due to similar clinical features colon and rectum cancers are evaluated together (Rosenberg et al., 2010; Lee et al., 2013). However, at least there is an important difference in local management: radiation therapy (usually with concurrent chemotherapy) has a crucial role in treating rectal cancer; however, this role is very pallor in colon cancer. Although survival of colon and rectum cancers is similar, but they are not the same .In our country Akhoond et al. reported 56.8% and 41.9% five year survival in colon and rectum cancers respectively in a study which had been performed in Tehran between Jan 2002 to Jan 2007(Akhoond et al., 2010). According to SEER data Lee at al. showed that there is no difference in survival of colon and rectum cancer in stages I, II A and III A. For stage IIB survival in colon cancer is better, but in stages IIIB, IIIC and IV patients with rectal cancer have a better survival rate (Lee et al., 2013). In our study stage did not show significant relationship to survival, however survival was the best in stage I and the worst in stage II. Most of our patients had no adequate lymph node resection and/or evaluation, and almost all of them had less than 12 resected lymph nodes, and at least some of the patients in stage II were underestimated. Akhoond et al.(Akhoond et al., 2010) showed a significant relation between stage of rectal cancer and survival. They also explained that risk of death was significantly higher in rectal cancer patients who received chemotherapy and / or radiotherapy as first treatment in comparison to surgery. Our study showed that in T3-T4 and lymph node positive patients, neoadjuvant concurrent chemoradiation (not induction chemotherapy and then radiation or chemoradiationtherapy) and then surgery ,relatively increases survival. (p value =0.05) This discrepancy could be explained with these facts: 1- there were metastatic patients (about 11%) in the former study and in this group surgery might have been performed as palliative treatment. 2- they compared surgery with chemotherapy and / or radiotherapy and no concurrent chemoradiation therapy. We also showed that induction chemotherapy itself in non- metastatic rectal cancer compromises overall survival and with more power local control. Although the final update of German rectal study group did not show any survival differences between pre or post operative chemoradiation, however they emphasized on better local control in the preoperative group (Sauer et al., 2012).

Our study revealed that a five year survival of rectal cancer in our province is about 10% lower than United States and some of the Nordic countries even when we considered non-metastatic diseases. On the other, hand staging was inadequately performed for our patients. Preoperative concurrent chemoradiation improves local control and even overall survival in this part of Iran.

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