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SURVIVAL EXPECTANCY IN PATIENTS WITH COLORECTAL CANCER UNDERGOING STANDARD TREATMENT METHODS

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ABSTRACT

Colorectal cancer is one of the most prevalent cancers in the world. It's survival expectancy depends on the time of diagnosis, stage and grade of the tumor, and general condition of the patient. Survival expectancy of this type of cancer reveals the quality of diagnostic and therapeutic services in the community. To improve and standardize the treatment modalities in this field, much research has been conducted worldwide. In this study, patients with a confirmed diagnosis of colorectal tumors (CRT) who were under treatment or referred to the Oncology Department of Imam Khomeini Medical, Educational and Research Complex within the years 1987-1991, were selected.

This study showed that the 5 year survival rate of these patients was maximally 21%.

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INTRODUCTION

Colorectal tumors are one of the most prevalent groups of cancers worldwide. The large intestine consists of the colon, rectum and anal canal, and tumoral changes can develop in any of these segments. After lung and prostate tumors, CRT's are the most prevalent tumor in men, and in women they are second only after breast cancer.[5] The mortality rate of colorectal tumors in England is about 20,000 per year and it is the second cause of death due to malignancy. Although this type of cancer is prevalent throughout the world, its prevalence is considerably high in Western countries and very low in Japan. Also, this rate is low in developing countries, especially in rural areas of Africa, and as a general rule the incidence of CRT increases in immigrants to high prevalence areas. The incidence of colon cancer is the same in both sexes.[1] At present, early diagnosis of the disease is the most important factor in successful clinical management of CRT. Unfortunately in most cases, diagnosis occurs in the invasive and metastatic stages. For cases with early stage diagnosis surgical resection of the tumor is the procedure of choice. Sometimes radiation therapy and/or chemotherapy are used in combination to surgery with different purposes including pre- and postoperative management of pain and discomfort and suppression of metastases. In general, the main goal of using any therapeutic method is complete elimination and treatment of the tumor and enhancing survival expectancy as well as improving the sense of wellbeing and quality of life in patients.

One study has shown that in spite of great advances in screening and early diagnostic methods and state-of-the-art therapeutic procedures, the five year survival expectancy is 37% in blacks and 50% in whites.[5] So the purpose of this study on survival expectancy in CRT patients was first, to yield a general picture of the status of this type of cancer in Iran; second, to find the therapeutic methods of choice and optimize and standardize the treatment procedures for each group of patients; and

Table I. Life expectancy without descriptive (demographic) varieties.

Interval start time (mo[nt])	Number entering this interval	Number withdrawn during interval	Number of terminal events	Cumulative proportion surviving at the end	Probability density	Hazard rate	S.E of cumulative proportion surviving	S.E of probability density	S.E of hazard rate
00	216	8	29	0.8632	0.0114	0.0122	0.0236	0.0020	0.0023
12.0	179	15	43	0.6468	0.0180	0.0239	0.0336	0.0024	0.0036
24.0	121	33	17	0.5416	0.0088	0.0148	0.0366	0.0020	0.0036
36.0	71	18	6	0.4892	0.0044	0.0085	0.0388	0.0017	0.0035
48.0	47	11	7	0.4066	0.0069	0.0154	0.0430	0.0021	0.0059
60.0	29	12	11	0.2122	0.0162	0.0524	0.0476	0.0039	0.0150
72.0	6	4	2	0.1061	0.0088	0.0556	0.0582	0.0049	0.0370

third, we want to determine factors other than treatment procedures that have an effect (positive or negative) on life expectancy.

MATERIAL AND METHODS

The study group consisted of patients with a confirmed diagnosis of colorectal tumors (CRT) who were under treatment or had been referred to the Institute of Oncology of Imam Khomeini Hospital within 1987-1991. From this population 235 patients were selected randomly.

All required data were gathered from medical records of patients through mail or phone contacts by using a questionnaire. For some reasons including change of address, misunderstandings about some of the questions or missed information in some medical records, data concerning some patients remained incomplete. Nevertheless due to the nature of our method for analysis of data (Cox and Kaplan methods), we were able to use such incomplete data in our survey. Stage & grade of tumors which had been determined based on Duke's classification scale for colorectal cancer were retrieved from pathological reports in patient's medical files.

Duke's classification is the best and most frequently used classification scale by pathologists. Using this scale the general condition of patients with a 5 year survival expectancy can be estimated as good, moderate or poor. Due to some weaknesses inherent in this classification scale (i.e. about staging & distant metastases), in recent years researchers in the field of oncology have designed and introduced the TNM tumor classification model.[1]

In this study the tool for data gathering consisted of medical records of patients and a researcher designed questionnaire. After data collection, coding was done and descriptive statistics of some variables produced using a statistical index. Then correlation and contingency tables for some varieties were produced. Using SPSS software, life expectancy and Kaplan Meier tables were obtained and Log-Range tests and further statistical analysis was carried out. At the end "Cox regression model" was applied to the obtained data in this study.

RESULTS AND DISCUSSION

Survival expectancy regardless of demographic varieties were calculated (Table I, Fig. 1) and as shown maximum survival expectancy up to one year is 86% and minimum survival expectancy for up to 5 years is 21%. The rest of the survival expectancy calculations were carried out with consideration to other varieties.

Sex variety (X1)

The first level of this variety and also the reference level (laborer) consists of males. Its regression co-efficiency was determined to be B1= 0.2573. It means that it has a negative effect over "risk function" (has a positive effect on "survival function"). In other words, females have less risks compared to males (0.7730) and the relative risk of men over women equals 1.29, i.e. mortality rates in men are 1.29 times more than that of women (Table II).

These results are in contrast to the findings of Zahi (1995) in Norway in which the survival expectancy of patients with colorectal tumor using proportional survival expectancy method and also proportional regression model within a 20

Table II. Survival function considering the sex based life expectancy.

Month	0-12	13-24	25-36	37-48	49-60	61-72
Male	0.8553	0.6225	0.5259	0.4795	0.3942	0.2123
Female	0.8730	0.6777	0.5611	0.5010	0.4219	0.2110

year period showed that a significant number of men survived 20 years after the diagnosis of the disease, but this value for women was determined to be only 10 years.[10]

Age variety (X2)

Our findings are almost completely similar to other studies, it means that mortality will be increased with age. For example, risk of death in a 35 year old patient is 1.0607 times more than a 25 year old patient (Table III).

Slatter and Kerber (1990) reported that factors such as higher age at time of diagnosis, female sex and tumoral involvement of the ascending segment of colon would decrease the survival expectancy.[9]

These determined values are less than those obtained in European countries within the past two decades. As has been shown, survival expectancy up to 1 year was 86% and for cases up to 5-6 years 21%. In our study, data analysis was based on 5 year survival expectancy, therefore for the city of Tehran, Iran it would be 21% for up to 5 years.

Glass et al. (England, 1965-1975) reported that survival expectancy for patients who underwent surgical treatment was 64-82% up to 5 years.[7]

Sant et al. (1978-1989) announced that their patients with colorectal tumors within the ages of 60-69 years old, in ten European countries, had a cumulative relative survival of 40% for up to 5 years.[8] While our study showed that survival probability for up to 5 years was zero for over 60 year olds, it was 32% for up to 4 years. This difference is a very significant warning. We believe that to some extent, this situation is due to factors such as delayed diagnoses, lack of well designed treatment protocols, and quality of medical and surgical care provided in our study center.

The European study reported that greater survival expectancy in these countries is due to the quality and availability of medical services and early diagnosis of tumoral growth.[8]

Residential variety (X4)

This variety has a coefficient equal to 0.3721 with survival expectancy and patients who live in rural regions have a relative risk 1.45 times more than those who live in urban areas. It means that the risk of death due to colorectal tumor in villagers is more than city residents. These findings are comparable to those reported by Blom et al. (1973-1990) in Sweden. They believed that survival probability does not differ between patients who live near university hospitals or distant from the hospital, but there was a difference between patients who lived near hospitals and those who lived in the other states.[4]

Our study showed that villagers were at more risk than city residents. This increase could be due to factors such as knowledge deficit concerning signs & symptoms of CRT among villagers, delayed diagnosis, unavailability of specialized medical services and quality of post-operative care.

Occupation variety (X5)

This variety has 3 levels in the model. The third level, i.e. employee, has a negative effect on risk and positive effect on survival expectancy. The relative risk in employee cases compared to reference level was equal to 0.378. In other words, employed cases had less risk than reference cases and thus had more survival expectancy. This was also true for cases with private business jobs as its co-efficiency was negative. The rate of reference "relative risk" to this level (X5) is 1.84. It means that reference cases (laborers) were 1.84 times more at risk of death due to CRT than those people with private business jobs. Another level of X5 variety was being a student which had a positive effect on risk compared to reference with a co-efficiency of "2.748", thus students with CRT are 2.748 times more at risk of affliction or death due to CRT than the reference level. Those levels that were not entered into the model had no significant statistical difference with the reference level.

Since most of the employed and private business individuals lived in urban areas due to reasons including availability of well-equipped medical centers and laboratories near their residence places, as a result their survival expectancy compared to villagers and farmers who mostly live in underprivileged rural regions is high. The number of students in our study was limited, and since the incidence of CRT with more invasive and metastatic features is higher in younger ages, students are often diagnosed in invasive & metastatic stages.

Treatment procedure variety (X6)

Only two levels of this variety were entered into the model. "X6-6" (3 procedures) and "X6-7" (chemotherapy and radiotherapy) residual levels could be aggregated with the reference level because there was no significant difference between them. "X6-6" level, with a co-efficiency of "B6-6= 0.294" had a positive effect over "risk function". Patients who were treated by all 3 procedures (surgery, chemotherapy and radiotherapy) were 1.341 times more at risk of death due to colorectal tumors than reference level. "X6-7" with a co-efficiency of B6-7= 0.442 also had a positive effect on "risk function", and patients in this group were 1.557 times more at risk than reference level (Table IV).

As expected these findings confirm the results of other similar studies. Physicians often prescribe combined treatment (i.e. surgery + radiotherapy+chemotherapy) for patients in invasive and metastatic stages of disease to suppress tumoral growth and metastasis. Most patients whose tumors are diagnosed as inoperable receive che-

Table III. Survival expectancy in different age groups (Kaplan table).

Month	12	24	36	48	60	72
<25	0.7179	0.5385	0.4038	0.3365	0.1683	0.0841
26-35	0.7202	0.6145	0.5641	0.5641	0.4231	0.3137
36-45	0.8353	0.6014	0.6014	0.5412	0.3947	0.1316
46-55	0.8305	0.6170	0.6170	0.5656	0.4713	0.2357
56-65	0.9000	0.6263	0.5243	0.4642	0.3979	0.0995
>65	0.8831	0.5687	0.4295	0.3221	00.000	00000

Table IV. Survival function considering the treatment procedure.

Month / Treatment procedure	12	24	36	48	60	72
Chemotherapy	0.6923	0.0865	000000	00000	000000	000000
Surgery	0.9005	0.8182	0.7773	0.7125	000000	0000
Surgery & radiotherapy	0.9130	0.7826	0.6522	0.6522	0.6522	0.1739
Surgery & chemotherapy	0.8862	0.7124	0.6474	0.5615	0.3861	0.1287
Mixed (sur.+rad.+chem.)	0.8190	0.5698	0.4657	0.4269	0.2846	00000
Chemo & radiotherapy	0.5333	000000	00000	00000	00000	00000

motherapy in conjunction with radiation as palliative therapy for management and control of pain. There is a significant correlation between stage of tumor and choice of therapeutic modality (i.e., chemotherapy plus radiotherapy, surgery plus chemotherapy and surgery plus radiotherapy).

Past studies have shown that stage of tumor is the main predictor of survival expectancy. Our study indeed showed that the highest survival expectancy belongs to "surgery & chemotherapy" and "surgery + radiotherapy" groups. As we know surgery is the most effective therapeutic modality and findings of our study to a great extent support this concern. Because both modalities with a high success rate in our study envisaged surgery as part of the treatment and since in our country health care organizations have constraints in screening and case findings, patients are often diagnosed in the acute invasive & metastatic phase and micrometastatic tumors are overlooked in pathological inquiries, so inadequate suppression of these micrometastases to adjacent tissues could aggravate the condition and even jeopardize the patient's life. Suppression of these micro-metastases by chemotherapy or radiotherapy can postpone this aggravation and increase the survival expectancy of patients. We believe that these findings are very important issues and should be considered by surgeons and oncologists.

Stage variety (X13)

Both levels of this variety were entered into the model. It's second level has a co-efficiency of "B13-2= 0.6602" which means it has a positive effect on "survival risk" and patients who are in B and C stages of "Duke's classification" are 1.935 times more at risk of exposure and death due to colorectal tumor compared to patients in stage A. The third level of this variety (stage D) with a co-efficiency of "B13-3= 2.429" has the largest effect on risk function and the patients of this group are 11.35 times more at risk of affliction and death due to CRT than the reference groups. Relative risks of other levels can be obtained, compared with each other. For instance, the relative risk of "stage D" level to "stages B & C" equals 11.35794: 1.935225= 5.869, meaning that patients of stage D, compared with patients of stages B & C are 5.869 times more at risk of affliction and death due to colorectal tumors (Table V, Fig. 2).

These results are confirmed with findings of other studies. By moving forward in stages of the tumor from A to D, the tumor becomes more invasive and metastatic and as a consequence survival expectancy decreases. All other studies including those of Zahi et al.,[10] Slatter and Kerber in 1990,[9] and Sant et al. in 10 European countries[8] confirm this finding. They all reported that the stage of the tumor at the time of diagnosis or treatment is the most reliable factor in predicting "survival expectancy" of patients with colorectal tumor.

CONCLUSION

1- "Surgery" was the best treatment procedure, sur-

Table V. Survival expectancy considering the type of tumor.

Month / Kind of tumor	12	24	36	48	60	72
Adenocarcinoma	0.8460	0.6039	0.5427	0.4927	0.3263	0.1579
Squamous cell carcinoma	0.6250	0.5000	0.4286	0.4286	0.4286	0.2143

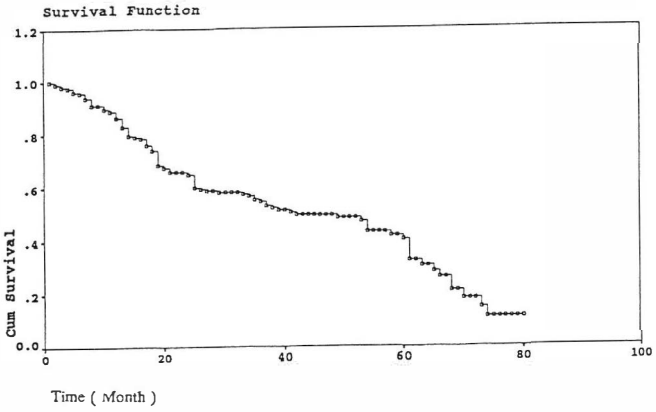

Fig. 1. Survival function and life time table (without descriptive variables).

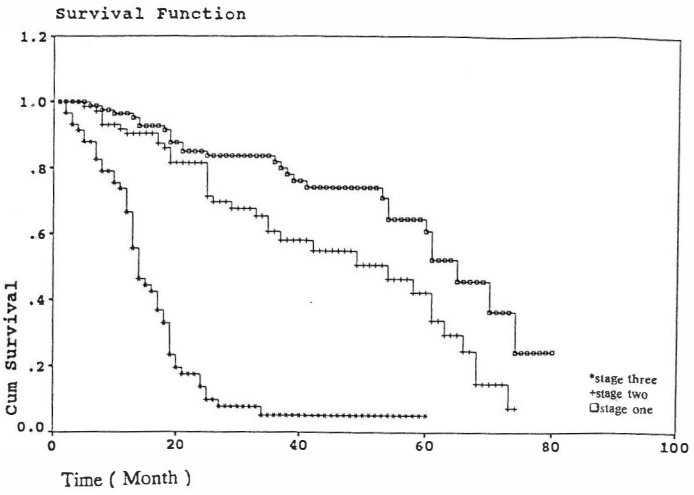

Fig. 2. Survival and risk functions and life time table based on the tumor stage.

vival expectancy up to 1 year was 90%, up to two years 81%, up to three years 77%, up to 4 years 71% and up to 5-6 years was zero.

As expected, with an early diagnosis the highest survival expectancy was achieved. Most of our patients in the acute phase of illness were scheduled to receive chemotherapy & radiotherapy after surgery.

2- Chemotherapy is another treatment procedure, with a survival expectancy of 69% for up to one year, 0.08% for up to 2 years and for more it was zero. As we know chemotherapy by itself is not an effective treatment for CRT and often it is used as palliative therapy for patients in acute stages of CRT.[5]

3- Radiotherapy is also another treatment procedure, which is used as palliative therapy for relieving pain or combined with surgery and/or chemotherapy to treat colorectal tumors. In this study, since we used it infrequently, statistical analysis for these data seemed unnecessary.

4- Surgery & radiotherapy is the most effective procedure in the treatment of CRTs. Survival expectancy up to 6 years was 17%, and this combined therapy yielded the greatest survival expectancy in our study.

5- Surgery & chemotherapy is another combined treatment procedure of choice. Its survival expectancy was determined to be 88% up to 1 year, 71% up to 2 years, 64% up to 3 years, 59% up to 4 years, 38% percent up to 5 years and 12% up to 6 years. It is the most effective treatment procedure after surgery & radiotherapy.

6- The mixed procedure of surgery + chemotherapy + radiotherapy is another effective treatment protocol for cancer patients. In our study survival expectancy was estimated to be 81% up to 1 year, 56% up to 2 years, 46% up to 3 years, 42% up to 4 years, and 28% up to 5 years. Effectiveness of this procedure is in third place after the two above mentioned procedures (i.e. surgery + chemotherapy and surgery + radiotherapy.

7- Chemotherapy & radiotherapy is used as palliative therapy in invasive stages of the disease. In our study survival expectancy was only calculated for up to one year and it was 53%. In our study the most important factors in survival expectancy of CRT patients were determined to be the stage of the tumors, availability of medical services, occupation and type of treatment procedure.

Finally, surgery + radiotherapy was determined to be the treatment of choice for colorectal tumors.

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