ANALYSIS OF SURVIVAL AND RECURRENCE VS. PATIENT AND DOCTOR DELAY IN TREATMENT OF BREAST CANCER

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Two hundred thirty-seven patients with cancer of the breast treated with radical mastectomy were reviewed. Cofficients of correlation between patient's and doctor's delay vs. survival were not significant at $p < 0.05$. No significant relationship between delay and time of recurrence was found.

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ABOUT 6% OF NEWLY BORN GIRLS, 1 OUT OF 17, are expected to develop breast cancer at some time during their lives. It is anticipated that breast cancer will be diagnosed in about 73,000 women in the United States in 1973, representing by far the most frequent site of cancer in women.

Analysis of the value of early diagnosis and its relation to survival has created mild interest in the past due to confusing data and conclusions. Some publications have stressed the value of early diagnosis,[5,18,23,33] indicating that a shorter preoperative duration of symptoms contributes to better survival. Other investigators have challenged this concept.[7,19,24-26]

In 1951, Park and Lees[28] complained of the paucity of references to the delay-survival relation concerning breast cancer, and of the absence of interest in the matter when the relation was absent or small. The recent literature contains more data concerning this matter, but has failed to establish a direct correlation between delay and survival. In some reports a longer survival rate occurs in those women who have neglected their cancers for long periods of time, indicating that delay may reflect a less aggressive tumor.[3,24] These data, even taking into consideration a process of natural selection, have shaken the rationale behind early treatment.

In order to evaluate the existing relationship among the patient's delay and the doctor's delay in the diagnosis and treatment of breast cancer, the time of recurrence of the disease, and the survival rate, this report reviews data obtained in patients who had a radical mastectomy for breast cancer.

MATERIALS AND METHODS

During the 5-year period from January, 1965 to December, 1970, radical mastectomies were performed on 237 patients at State University Hospital-Kings County Hospital Center, as treatment for carcinoma of the breast. All the patients were female. The patient's delay was defined as the time elapsed between the onset of her symptoms and the first medical visit. The doctor's delay was defined as the elapsed time between the first medical consultation for symptoms of mammary cancer, and its treatment. As a unit of time in this study, the month was chosen, expressing as 0 months any time less than 4 weeks.

The data were entered on computer, and a coefficient of correlation was run between patient's delay or doctor's delay and the total delay vs. survival. Since recurrence of disease may represent an adequate endpoint in breast cancer, this was also evaluated.

The patient's delay was studied by dividing the patients into seven groups: Group 1 <1 month; Group 2, 1 month; Group 3, 2 months; Group 4, 3 months; Group 5, 4-8 months; Group 6, 8-12 months; Group 7, >12 months. Forty (16.8%) patients were found in Group 1, 39 (16.4%) in Group 2, 22 (9.2%) in Group 3, 25 (10.5%) in Group 4, 55 (23.2%) in Group 5, 39 (16.4) in Group 6, and 17 (7.5%) in Group 7. The shortest patient's delay was 0 months, and the longest was 36 months.

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The doctor's delay was studied dividing the patients into three groups: Group 1, <1 month; Group 2, 1 month; Group 3, >1 month. One hundred sixty-one patients were found in Group 1 (67.9%), 56 in Group 2 (23.6%), and 20 in Group 3 (8.4%). The shortest period of time elapsed on doctor's delay was 0 months, and the longest was 5 months.

There were 120 black patients, which accounted for 51% of the group under study, and 102 white patients, corresponding to 43% of the total. Fifteen (6%) Puerto Rican patients have been included in the overall results of this investigation, but were not classified as a separate ethnic group due to the lack of statistical value of such a small sampling. Therefore, when only the white and black populations were under study, this was clearly indicated in the graphs.

For further analysis the patients were broken into groups with pathologically positive nodes and groups with pathologically negative nodes. Radical mastectomy was the standard form of treatment of operative breast cancer at this institution during the time-period studied, representing approximately 98% of the patients coming to operation. In every case evaluated the primary presenting complaint was a mass in the breast.

RESULTS

Two hundred thirty-seven patients were available for study, they were followed up for a maximum period of 91 months and a minimum of 21 months. No patients were lost.

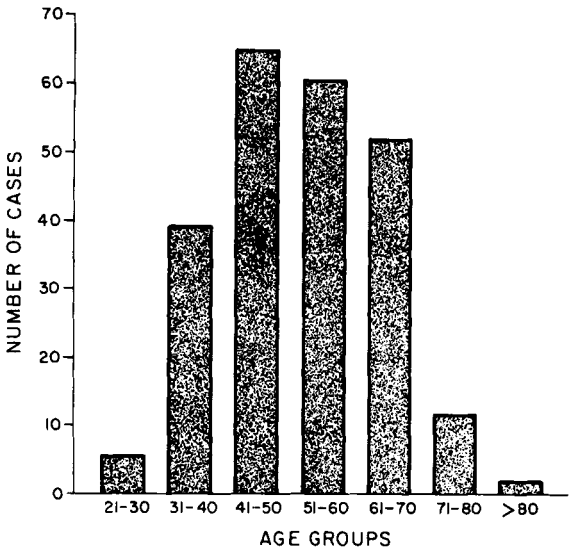

FIG. 1. Patient distribution by age. The preponderance of the disease in women between ages 40-60 is again demonstrated.

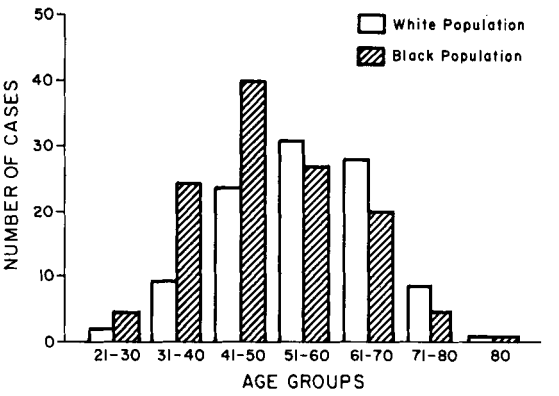

FIG. 2. Patient distribution by age and race. The shift of breast cancer incidence toward a younger population in the black women may be due to sampling error.

Age

The distribution of patients by decade is shown in Fig. 1. The youngest patient was 23 and the oldest 81 years of age, with an average of 52.3 years; 36 (15%) patients were below the age of 40, and 6 (2.5%) below the age of 30. In the group of patients who died as a consequence of the mammary neoplasia, the average age was 41.8 years.

Race

Figure 2 presents the distribution of cases by race and decade. The average age for the white patients was 56.3 years, and for the black patients, 49.3 years; 68 (56.6%) black patients fell between the ages of 21-50. The value for the white group for the same age distribution was 34 (33.3%) patients. The higher incidence of cancer among younger age groups in the black

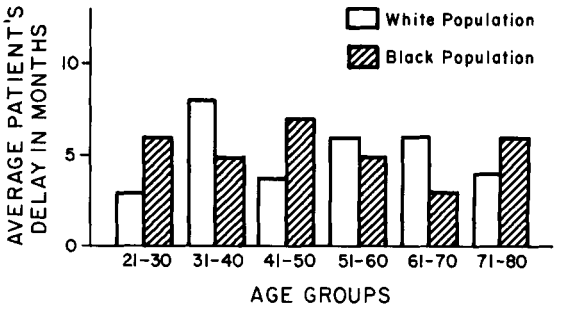

FIG. 3. Average patient's delay in relation to age and race. No significant differences are obvious.

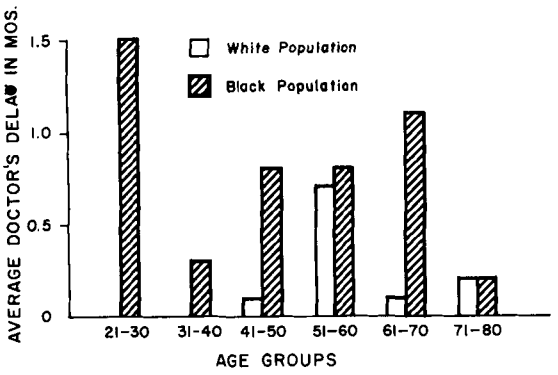

FIG. 4. Average doctor's delay in relation to age and race. There appears to be a longer doctor delay in black women.

population relative to its incidence in the white groups was also reported by us in a previous study concerning gastrointestinal cancer. This may not be significant without an analysis of the age distribution of all our hospitalized patient population.

Delay

The average patient's delay in relation to age and race is shown in Fig. 3. The average patient's delay was 4.8 months, which is in accordance with figures reported in previous surveys. There were two patients in the >80 age group who were not included in the graph. One patient was white and had a patient's delay of 9 months, the other patient was black and had a patient's delay of 7 months. The average doctor's delay in relation to age and race is presented in Fig. 4. The results show a greater doctor's delay in treatment for the black population, especially in the younger age groups, which could be explained by the patients not keeping the appointments after the first medical visit, distrust of the doctor and seeking other opinions, or with inordinate time for workup after their first visit. The patients' delay, on the other hand, does not demonstrate an appreciable direct correlation between race or age in either the white or black groups. This is more clearly shown in Figs. 5 and 6, demonstrating the lack of correlation between short or long delay and age. A more extensive breakdown of these data is shown in Table 1. It can be seen that these age distributions are roughly similar in form.

Delay vs. Survival and Recurrence

Table 2 shows the coefficients of correlation between survival and patient delay, doctor delay, and total delay in the group under study. None of these values is significant at $p < 0.05$. The data from which these coefficients of correlation are derived are plotted in Figs. 7 and 8. All patients were included in the composition of the scatter diagrams.

The relation between patient's delay and average time until recurrence is presented in Table 3. Of interest is the lack of a significant difference in the average time to recurrence. Doctor's delay in relation to average time to recurrence is shown in Table 4. Examination of these values shows no significant differences in recurrence time according to doctor's delay.

A separate analysis of patients followed for at least 5 years was made to determine if there were differences in patient or doctor delay between the group free of disease at 5 years and the

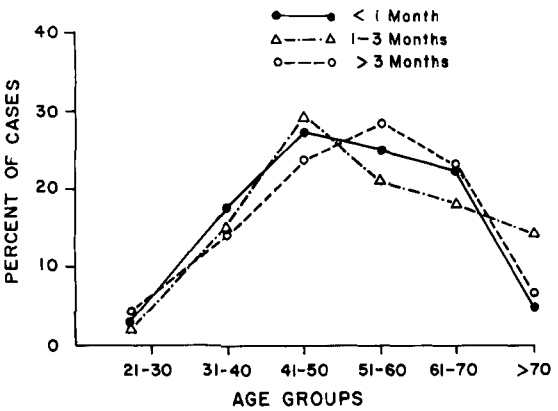

FIG. 5. Patient's delay by age. Note the similar age distributions regardless of length of delay.

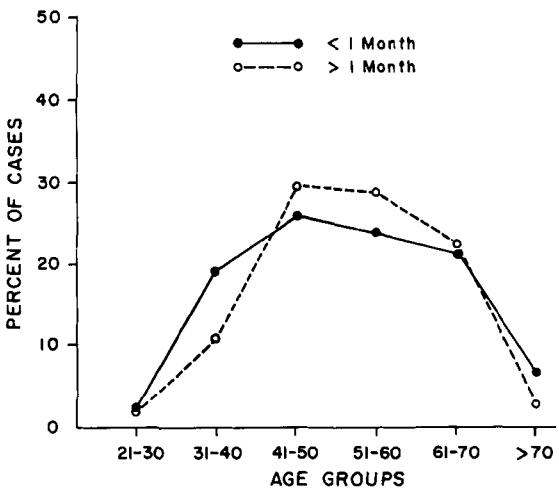

FIG. 6. Doctor's delay by age. The age distributions are similar in both delay groups.

TABLE 1. Age Distribution within Each Patient's Delay Group

Patient's Delay (months)	Age in years 21–30	31–40	41–50	51–60	61–70	> 70
< 1	1 (2.5%)	7 (17.5%)	11 (27.5%)	10 (25.0%)	9 (22.5%)	2 (5.0%)
1	9 0	9 (23.0%)	10 (25.6%)	9 (23.0%)	2 (23.0%)	(5.4%)
2	1 (4.5%)	3 (13.6%)	7 (31.8%)	7 (31.8%)	2 (9.0%)	2 (9.0%)
3	1 (4.0%)	3 (12.0%)	11 (44.0%)	4 (16.0%)	5 (20.0%)	1 (4.0%)
4–8	2 (3.6%)	8 (14.5%)	11 (20.0%)	17 (30.9%)	14 (25.4%)	3 (5.4%)
9–12	1 (2.5%)	6 (15.3%)	10 (25.6%)	11 (28.2%)	9 (23.0%)	2 (5.4%)
> 12	0	3 (17.6%)	5 (29.4%)	3 (17.6%)	4 (23.5%)	2 (11.5%)

patients with recurrence. One hundred sixteen patients operated upon in 1965, 1966, or 1967 were used. Thirty-six were free of disease at 5 years and had an average patient delay of 5.8 ± 1.4 (S.E.) months and a doctor's delay of 0.56 ± .15 months. These were compared to 70 patients who had recurrent disease (failure of treatment), whose comparable figures were 6.6 ± .84 months and 0.49 ± .13 months. There were no significant differences demonstrated (Table 5).

An analysis of delay vs. survival was carried out for 89 negative node and 148 positive node patients. The results of the coefficients of correlation (Table 6) demonstrate no significant relationship.

As would be expected, the survival of the negative node patients was longer. In spite of this there were no significant differences between these groups in average delay: 4.2 months ± 4.3 (S.D.) (negative nodes) vs. 5.0 months ± 6.9 (S.D.) (positive nodes).

DISCUSSION

The effect of earlier diagnosis on survival rates in cancer is still one of the most controversial topics in the literature. It is our belief that survival after the symptoms have appeared is not related to the duration of the symptomatic period but to established pathologic criteria such as: rate of growth,[28,29] tumor size,[1] lymph node involvement,[5,8,19] the number and location of lymph nodes involved,[11,15,16] blood vessel invasion,[21] and the presence of systemic metastases. Other factors which may also play a role in survival are: absence of lymphocytic infiltration, degree of sinus histiocytosis in the axillary lymph nodes,[4,9] location of the tumor, the characteristics of the advancing margins of the tumor,[19] early age,[24,27] artificial premature menopause,[7] the presence of simultaneous bilateral tumors,[10] and host immune factors.

These defined and accepted parameters convey a definite prognostic value most prominent after the malignant process has been diagnosed. Nevertheless, the apparent lack of correlation between delay and treatment should not imply that early treatment is valueless.

Spratt and Ackerman[30] postulated in 1961 that duration of symptoms reported by the patients is not synonymous with the duration of the malignant process, but represents only a small fraction of its history. A small tumor is not equal to an early tumor; possibly, this lack of correlation between delay and survival is influenced by the presence of the tumor during an unknown period of time before it is clinically evident or symptomatic.[6] It is evident that a clinical cancer has undergone some 30–35 doubling times prior to its diagnosis and that its remaining history prior to killing the patient may only have an additional 6 doublings. One of the un-

TABLE 2. Coefficients of Correlation in Relation to Survival vs. Patient Delay, Doctor Delay, and Total Delay

Group	Coeff. corr.
Survival vs. patient delay	−.053
Survival vs. doctor delay	.108
Survival vs. total delay	−.026

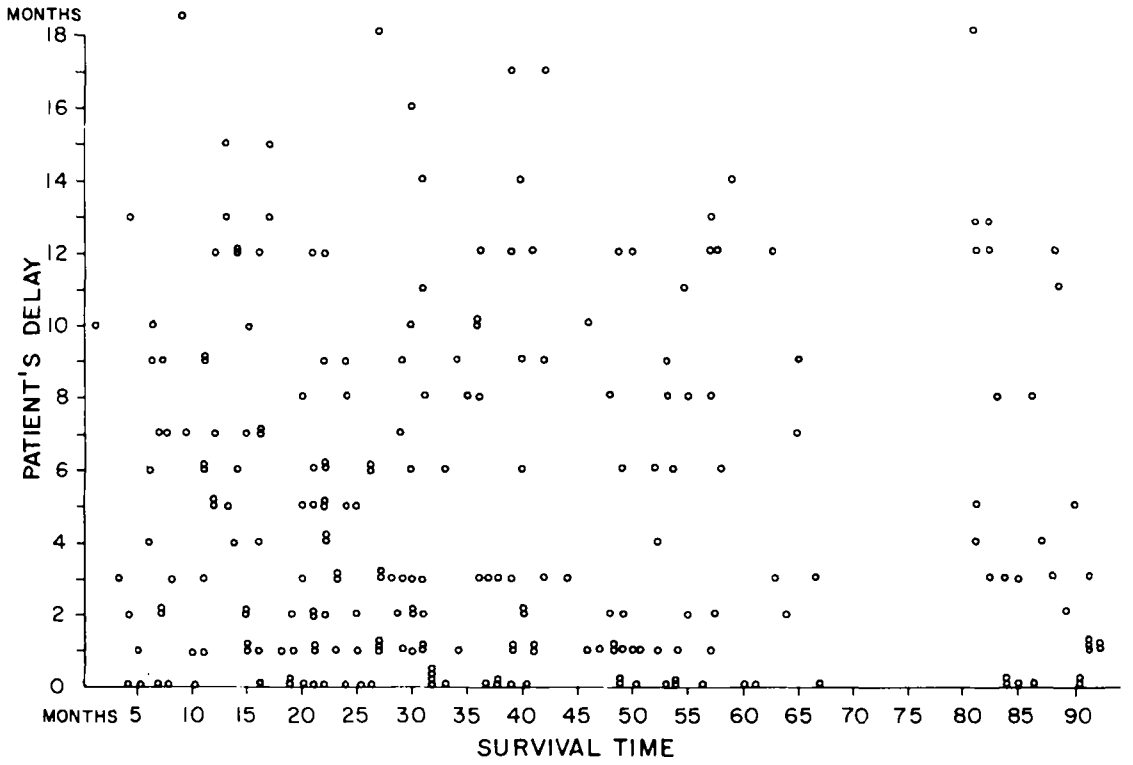

FIG. 7. Scattergram of patient's delay vs. survival. Coefficients of correlation are reported in Table 3.

derlying currents in the data concerning carcinoma of the breast and its prognosis in relation to delay and survival is the fact that the more malignant tumor may produce early symptoms and will induce the patients affected by this rapidly growing tumor to seek medical treatment shortly after their symptoms have become obvious.[5,26] In contrast, patients who have

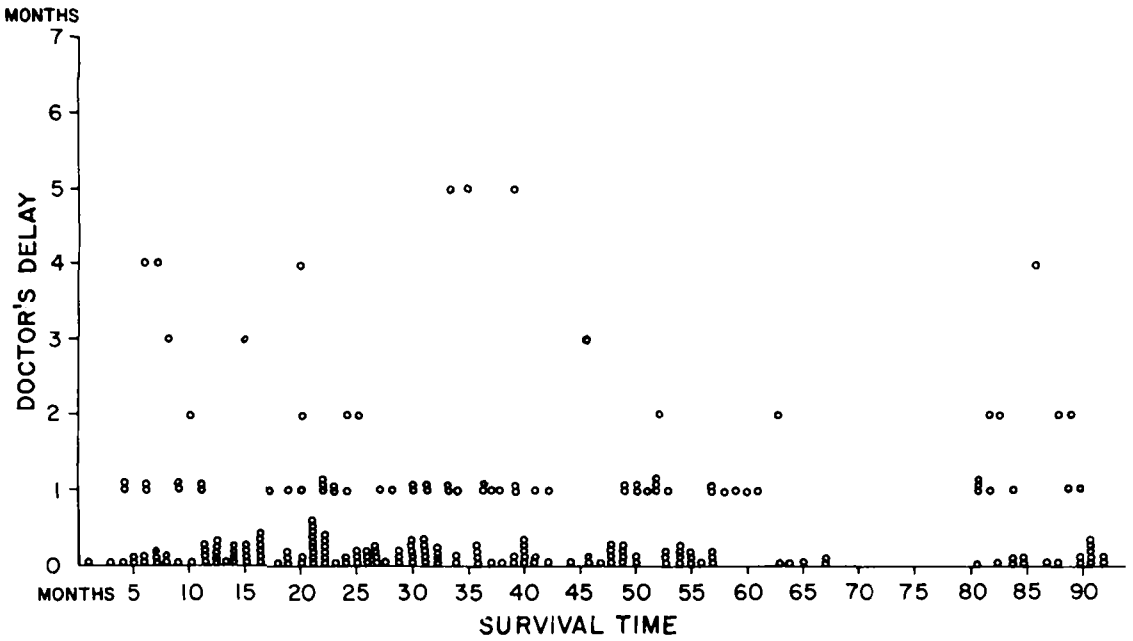

FIG. 8. Scattergram of doctor's delay vs. survival. Coefficients of correlation are reported in Table 3.

TABLE 3. Patient's Delay vs. Time of Recurrence

	Delay (months)						
	<1	1	2	3	4–8	4–12	>12
Average time until recurrence ($\bar{x}$ ± S.E.)	24 ± 4.2	21 ± 3	20 ± 4.1	20 ± 6.2	17 ± 2.1	22 ± 3.3	22 ± 4.5

been affected by a slow growing tumor carrying a low grade of malignancy may routinely delay longer in looking for advice and consequently are treated later in the course of their disease.

MacDonald[25] and Bloom,[5] among others, emphasized in the past the importance of the factors concerning the tumor-host relationship as one of the main determinants in the outcome of this disease. This concern has been supported by the discovery of CEA, and other specific antigens, demonstrated by Gold,[13] Lo Gerfo et al.,[22] and Baldwing,[2] which are a clear indication of an active cancer immunity system possibly able to inhibit or control tumor growth by a still obscure, immunologic mechanism. Patient's delay, on the other hand, is largely influenced by a wide range of psychological factors, which are being studied to some extent and have been the object of several publications in the past. Gold in 1964[12] spoke largely about the emotional factors such as fear and anxiety, negativism, compulsion, and guilt which contributed in his study to delay. Hackett et al.[14] described, paradoxically, that fear or worry were some of the motivating factors in bringing an early response and therefore early treatment. These studies have stressed the lack of success of educational activities concerned with early diagnosis to establish a true communication with the population. New efforts need to be made in order to discover the real factors behind the delay, in seeking to understand the failures in current cancer educational programs.

Kaae[20] noted that about 66% of the patients in his study came under medical care after 1 month of symptoms, which agrees with Sutherland's report of 70%.[31] In our experience, 187 (78.1%) of the patients delayed more than 1 month. Of these, 58.2% delayed 3 months and 15.5% delayed over a year. Data from Hackett et al.[14] showed that 33.7% of their population reported for medical advice within the first month. Our study found that only 21.9% consulted a physician during the first month.

In a previous report,[21] we indicated a younger age incidence among blacks regarding gastrointestinal cancer; this result has been shared by some other authors. Our findings in this study have also shown a higher incidence of malignancy among younger age groups in the black population. It is possible that the age distribution of our hospital population of white and black groups is not the same. However, among females in the United States, breast cancer death rates are higher among blacks through age group 45–49.[32]

Doctor delay was greater in the black population, especially in the younger age group, which can reflect failure of the patients in keeping their appointments after medical advice has been obtained, probably indicating poor educational background, fear and anxiety, or both. It is our feeling that even when the patients have obtained medical help, further delay which then would theoretically correspond to doctor delay is still paradoxically caused by patients' indecision in obtaining a radical surgical procedure.

Many recurrences were observed within the first 3 years after radical treatment. This lack of deterioration of prognosis concerning the time

TABLE 4. Doctor's Delay vs. Time of Recurrence

	Delay (months)		
	<1	1	>1
Average time until recurrence ($\bar{x}$ ± S.E.)	23 ± 1.7	25.6 ± 3.4	28 ± 9.2

TABLE 5. Doctor and Patient Delay in Patients Operated Upon in 1965–1967

	No. pts.	Patient delay (months ± S.E.)	Doctor delay (months ± S.E.)
Free of disease at 5 yrs.	36	5.8 ± 1.4	0.56 ± .15
Recurrence within 5 yrs.	70	6.6 ± .84	0.49 ± .13

TABLE 6. Coefficient of Correlation between Delay and Survival in Positive and Negative Node Patients (Staged Pathologically)

Group	Coeff. Corr.
Positive nodes	0.15
Negative nodes	.009

till recurrence, regardless of delay, and the inability to find any significant difference evaluating this parameter with doctor's delay is further evidence that the duration for which the tumor has been clinically present is not a valuable guideline in the outcome of carcinoma of the breast. These results are compatible with our overall conclusions.

We still recommend early treatment for cancer after diagnosis, in order to reduce the effects of a growing malignancy on results of treatment. This is more evident in gastrointestinal cancer, where protein depletion, anemia, sepsis due to perforation, obstruction, etc. may severely affect the results of operation for removal of the lesion. However the survival appears to be more definitely related to still poorly understood factors relating to host-tumor interaction.

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