

Incidence of Gastric Cancer in Atomic Bomb Survivors Residing in the Hiroshima Area^{*}

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ABSTRACT

Review of the prevalence rate of gastric cancer in A-bomb survivors who had undergone X-ray examination of the stomach during the period November 1972 to March 1982 was made based on estimated A-bomb exposure dose using the 7,188 cases on whom dose information was available. The results obtained are as follows.

1) The gastric cancer prevalence rate for the 0 rad group was 0.75% for males and 0.31% for females or 0.45% for both sexes combined, which increased with dose. The rate for the 100 rad and over group was significantly high being 3.15%, 1.22% and 1.89% respectively.

2) The relative risk of the prevalence rates for the 100 rad and over group were significantly higher than those of the 0 rad group being 4.29 for males, 4.02 for females and 4.28 for both sexes combined.

3) The prevalence rate of males who were 20 to 34 years of age at time of exposure demonstrated a higher rate than those 35 and over in the 10 rad and over group, but the difference was largest in the ≥ 100 rad group.

Thus, as pointed out in reports based on analyses of death certificates and autopsy studies it is obvious that the prevalence rate is significantly higher in the 100 rad and over exposure group.

INTRODUCTION

Thirty-eight years have elapsed since the A-bomb, and the current most important late effect of the A-bomb is the development of malignant neoplasms. Particularly, whether or not there will be an increase in gastric cancer which has the highest neoplasm prevalence rate among the Japanese, is an extremely grave issue, and as such it is being studied by many groups^{2,3,5,8,10,11,12}. Up until about 1970, most reports were negative towards the relationship with radiation^{11,12}, but subsequently the gastric cancer mortality rate was reported to have become significantly elevated^{3,5,8,10}. However, with the remarkable progress in medicine during recent years, gastric cancers are being detected earlier, and the advances in treatment have been remarkable. As the 5-year and over

survival rate is very good, it has become more meaningful to review the problem of gastric cancer on the basis of analysis of prevalence rate rather than mortality rate. With the objective of pursuing the relationship between radiation exposure and development of gastric cancer, we carried out a mass gastric survey program on A-bomb survivors over the age of 40 for a period of 7 years from 1964, and reported that the prevalence rate tended to be high in the proximally exposed survivors³. This time we made a study of those who had undergone a gastric examination during the 10-year period from 1972 and on whom estimated exposure doses (T65DR) were available at the Radiation Effects Research Foundation (RERF). The gastric cancer prevalence rate by exposure dose was compared, and the relationship between exposure dose and prevalence rate was reviewed.

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MATERIALS AND METHODS

The subjects were a total of 7,188 cases selected from among 15,354 who had received X-ray examination of the stomach at our clinic during the period November 1972 to March 1982. Of the selected sample, RERF had available estimated exposure doses on 3,369, and in addition there was a group of 3,819 who had been exposed beyond 3,000 m from the hypocenter and were thus estimated to have received an exposure dose of 0 rad. The age and exposure dose composition of the subjects are shown in Table 1. There were 4,243 in the 0 rad group, 1,160 in the 1 to 9 rad group, 1,133 in the 10 to 49 rad group, 281 in the 50 to 99 rad group and 371 in the 100 rad and over group. The ratio of gastric survey cases of this study included among the living survivors in the RERF Life Span Study as of 1979 was 15.0% in the 10 to 49 rad group, 15.1% in the 50 to 99 rad group, 16.7% in the 100 to 199 rad group, 16.7% in the 200 to 299 rad group and 17.8% in the 300 rad and over group, indicating that there was no great difference

by group. In the tabulation of the gastric survey data for those who had received two or more examinations, the most recent examination results were used and the findings at time of cancer detection were used for the analysis. Those who were found to have received gastrectomy were excluded at the time of initial examination. The diagnosis of gastric cancer had been established in 41 out of 43 cases by histological examination for a confirmation rate of 95.3%. Of the 2 cases in whom diagnosis was based on clinical findings alone, 1 was an 81-year-old, male who died 29 months later of gastric cancer. X-ray examination of the stomach is performed at the individual's request, when anemia is noted and when the occult blood test of the stools is positive. When indicated repeat X-ray examination, endoscopic studies and biopsy studies are provided as detailed examinations. The mean age and standard deviation (S. D.) of the subjects by exposure dose are shown in Table 2. There is no difference in age by sex, the males being 58.9 ± 13.9 and females being 58.2 ± 12.0 . Further, of the survivors who undergo general

Table 1. Examinees of Gastric Surveys from November 1972 to March 1982

Age (yrs) Dose (rad)	26-49			50-59			60-69			70-91			Total		
	Male	Fe- male	Total												
0*	429	884	1313	255	770	1025	328	787	1115	317	473	790	1329	2914	4243
1- 9	109	185	294	76	239	315	81	203	284	111	156	267	377	783	1160
10-49	91	158	249	52	192	244	82	252	334	114	192	306	339	794	1133
50-99	14	38	52	13	62	75	21	59	80	29	45	74	77	204	281
100-	33	58	91	30	79	109	30	52	82	34	55	89	127	244	371
Total	676	1323	1999	426	1342	1768	542	1353	1895	605	921	1526	2249	4938	7188

* Including survivors who were exposed at $\geq 3,000$ m from the hypocenter

Table 2. Mean Age of Examinees

Sex Dose (rad)	Male		Female		Total	
	Cases	Mean \pm S. D. (yrs)	Cases	Mean \pm S. D. (yrs)	Cases	Mean \pm S. D. (yrs)
0*	1329	58.0 \pm 13.7	2914	57.4 \pm 12.0	4243	57.6 \pm 12.6
1- 9	377	59.5 \pm 13.6	783	58.8 \pm 11.4	1160	59.0 \pm 12.2
10-49	339	60.9 \pm 14.5	794	60.8 \pm 11.6	1133	60.8 \pm 12.6
50-99	77	62.7 \pm 13.8	204	59.3 \pm 12.5	281	60.8 \pm 12.2
100-	127	59.2 \pm 13.2	244	58.9 \pm 12.1	371	59.0 \pm 12.5
Total	2249	58.9 \pm 13.9	4938	58.2 \pm 12.0	7188	58.4 \pm 12.6

* Including survivors were exposed at $\geq 3,000$ m from the hypocenter

health examinations at this clinic, approximately 20% have received more than one X-ray examination of the stomach during the study period.

RESULTS

1) Prevalence rate of gastric cancer

Of the 7,188 subjects who had received X-ray examination of the stomach, 43 were found to have gastric cancer. The prevalence rate by sex and exposure dose of gastric cancer was sought from among those who had undergone X-ray examination of the stomach (referred to hereafter as prevalence rate of gastric cancer) and is as shown in Table 3 and Fig. 1. In males it was 0.75% among the 1,329 subjects in the 0 rad control group, which increased linearly with dose, reaching 3.15% for the 127 subjects in the 100 rad and over group, which is 4.2-fold that of the 0 rad group ($P < 0.01$). The situation was similar for females being 0.31% for the 2,914 subjects in the 0 rad group,

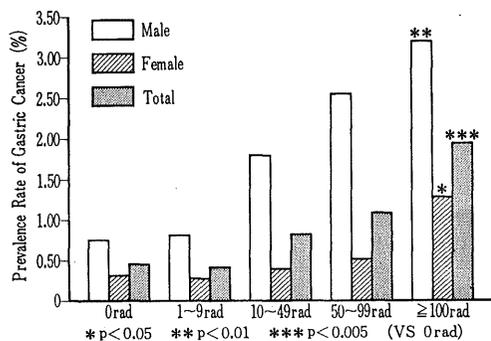


Fig. 1. Prevalence Rate of Gastric Cancer by Radiation Dose

which was less than one half of that for males, but it increased with the exposure dose, reaching 1.23% for the 244 subjects in the 100 rad and over group, which was 3.9-fold higher than that for the 0 rad group ($P < 0.05$). When all survivors were combined, the rate for those in the 100 rad and over group (371 subjects) was 4.2-fold higher than the 0.45% for the 4,243 subjects in the 0 rad group ($P < 0.005$). The mean age \pm S.D. for the gastric cancer cases was 63.6 \pm 9.0 for the 0 rad group, 66.6 \pm 8.9 for the 1 to 9 rad group, 67.4 \pm 7.3 for the 10 to 49 rad group, 69.0 \pm 8.3 for the 50 to 99 rad group and 66.0 \pm 6.6 for the 100 rad and over group. Further, it was 67.0 \pm 7.7 for the 24 cases in the groups excluding the 0 rad group.

2) Relative risk and 95% confidence limit in the prevalence rate of gastric cancer

The relative risk and 95% confidence limit in the prevalence rate for the various exposure dose groups as compared against the 0 rad group are as shown in Fig. 2. These values in males for the 1 to 9 rad group was 1.06 (0.28-4.00), 2.38 (0.84-6.72) for the 10 to 49 rad group, 3.52 (0.73-16.86) for the 50 to 99 rad group and 4.29 (1.29-14.22) for the 100 rad and over group. While for females, the values were 0.83 (0.17-3.96), 1.23 (0.32-4.66), 1.59 (0.19-13.16) and 4.02 (1.05-15.35) respectively, and for both sexes combined the values were 0.96 (0.35-2.64), 1.78 (0.79-4.01), 2.40 (0.69-8.36) and 4.28 (1.75-10.42) respectively. The values increased with dose in both sexes, and were significantly higher in the 100 rad and over group.

3) Gastric cancer prevalence rate by age at time of exposure

Table 3. Prevalence Rate of Gastric Cancer by Radiation Dose

Sex Dose (rad)	Male			Female			Total		
	Examinees	Gastric Cancer		Examinees	Gastric Cancer		Examinees	Gastric Cancer	
		Cases	%		Cases	%		Cases	%
0	1329	10	0.75	2914	9	0.31	4243	19	0.45
1-9	377	3	0.80	783	2	0.26	1160	5	0.43
10-49	339	6	1.77	794	3	0.38	1133	9	0.80
50-99	77	2	2.60	204	1	0.49	281	3	1.07
100-	127	4	3.15**	244	3	1.23*	371	7	1.89***
Total	2249	25	1.11	4938	18	0.36	7188	43	0.60

* $P < 0.05$ ** $P < 0.01$ *** $P < 0.005$ VS Orad

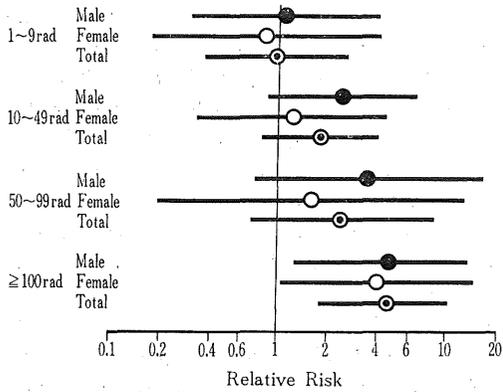


Fig. 2. Relative Risk and 95% Confidence Limit Interval for Prevalence Rate of Gastric Cancer by Dose Group vs 0 rad

The subjects were divided into two groups, 20 to 34 and 35 and over, on the basis of their ages at time of exposure. Comparison of prevalence rates by 10^5 person years at risk for each exposure dose group is shown in Table 4 and Fig. 3. In males, the prevalence rate was 32.9 per 10^5 person years at risk for those in the 0 rad group whose ages at time of exposure were 20 to 34, while it was 30.5 for those 35 and over, indicating that there was no difference between the two age groups. In all of the other exposure dose groups also, the prevalence rate tended to be higher in the 20 to 34 year age group than those 35 and over,

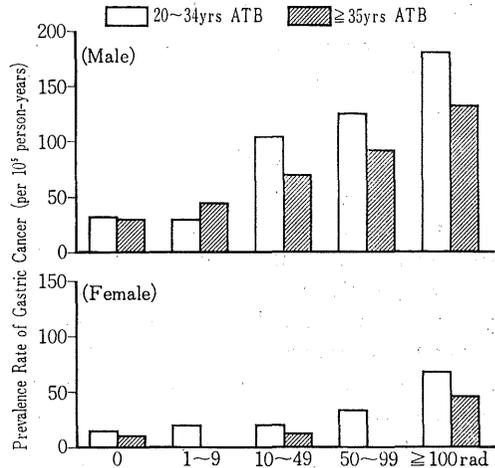


Fig. 3. Comparison of Prevalence Rate of Gastric Cancer (per 10^5 person-years) between Survivors 20-34 yrs and 35 yrs at Time of Bomb (ATB)

but the difference was largest in the 100 rad and over group. A similar trend was noted for the females, but generally the prevalence rate was low rendering it impossible to make adequate review. Further, there were 3 cases of gastric cancer whose ages at time of exposure had been under 19, but the number of cases was too small rendering the analysis by dose impossible.

DISCUSSION

The effects of radiation exposure on the

Table 4. Number of Person Years and Prevalence Rate of Gastric Cancer (10^5 person-years) by Age at Time of Bomb

Dose (rad)	Sex Age ATB (yrs)	Male			Female			Total		
		Number of person-years	Gastric Cancer		Number of person-years	Gastric Cancer		Number of person-years	Gastric Cancer	
			Cases	/10 ⁵ PYR		Cases	/10 ⁵ PYR		Cases	/10 ⁵ PYR
0	20-34	12148	4	32.9	39453	6	15.2	51601	10	19.4
	35-	13099	4	30.5	19828	2	10.1	32927	6	18.2
1-9	20-34	3382	1	29.6	10141	2	19.7	13523	3	22.2
	35-	4271	2	46.8	6909	0	0	11180	2	17.9
10-49	20-34	2817	3	106.5	10533	2	19.0	13350	5	37.5
	35-	4320	3	69.4	8338	1	12.0	12658	4	31.6
50-99	20-34	795	1	125.8	2676	1	37.4	3471	2	57.6
	35-	1077	1	92.9	2030	0	0	3107	1	32.2
100-	20-34	1090	2	183.5	3038	2	65.8	4128	4	96.9
	35-	1512	2	132.3	2244	1	44.5	3756	3	79.9

development of gastric cancer are being studied by animal experiments⁹, gastric cancer mortality rates^{5,11} and tumor registry data¹⁰, but few analyses have been made on gastric survey results based on many cases. In 1972, we reported on the results of a 7-year gastric cancer survey on A-bomb survivors 40 years old and over living in Hiroshima City. Comparison of the results was made by exposure distance and it was noted that the prevalence rate of gastric cancer was high in the proximally exposed⁴. In this study the number of survivors who had undergone X-ray examination of the stomach during the 10-year and 5-month period from November 1972 to March 1982 selected as subjects totalled 7,188 persons, of whom RERF had available estimated exposure dose (T65DR) on 3,369 and those who had been directly exposed to the bomb at a distance beyond 3,000 m and thus were estimated to have received 0 rad numbered 3,819. The gastric cancer prevalence rate was sought by exposure dose. The total number of survivors who had undergone general examination during this time at our clinic was approximately 75,000 of whom about 20% received X-ray examination of the stomach. As a difference in gastric cancer prevalence rate was noted by age, comparison of the mean age was made by exposure dose, but no major difference could be demonstrated. Check was made of the ratio of gastric survey subjects within the RERF Life Span Study sample, and it was found that it was about the same for all exposure groups who had received 10 rad and over. The basis for diagnosis of gastric cancer was histological examination in 95.3%. Thus, this tabulation is highly worthy from the standpoint of diagnosis.

The gastric cancer prevalence rate increased with dose. In the 100 rad and over group, the prevalence rate in both males and females was significantly high being 3.15% which was 4.2-fold higher than that for the 0 rad group for the former, and was 1.23% or 3.9-fold higher than that for the 0 rad group in the latter. When the male-female ratio was 1:1 for the 0 rad group, the gastric cancer prevalence rate was 0.53%, and as about 20% of the general examination recipients underwent X-ray examination of the stomach, the gastric cancer prevalence rate of all survivors was estimated as

0.11%. The nation-wide gastric cancer detection rate for 1980 has been reported to be 0.13% which approximates over rate for the 0 rad group. Further, when review is made by exposure dose of the relative risk and 95% confidence limit for the gastric cancer prevalence rate at 0 rad, the values are significantly high being 4.29 (1.29-14.22) for males and 4.02 (1.05-15.35) for females. As described above, it is obvious that the gastric cancer prevalence rate is high in the high dose exposed group of 100 rad and over. The mean age of the gastric cancer case was lowest for the 0 rad group, while it tended to be high for other exposure groups. This tendency agreed well with the analysis made by Hamada¹¹ based on autopsy cases. It is felt that there is a considerably long latent period before radiation induced cancers develop. Kato et al.⁵ also reported that the gastric cancer mortality rate based on analysis of death certificates was significantly high among those exposed to high doses of 200 rad and over. With the recent progress in medicine, gastric cancer is being detected earlier and noteworthy advances are being made in treatment. The 5 years and over survival rate of surgical cases is reported to be in excess of 50%^{8,7}. Of the 192 cases of gastric cancer detected by us at this clinic, 32.3% were early cancer and the 5-year survival rate was over 90%. Even when the advanced cancers were included, the 5-year survival rate was 46.1%⁴ which is very good. It is felt that analysis based on prevalence rate is better than that based on mortality rate. Wakabayashi et al.¹⁰ in their analysis on tumor registry data in Nagasaki made comparison of the 0 rad and 100 rad groups and reported that the prevalence rate was high in the 100 rad group, but that there was no difference in mortality rate, and made a point of the difference between the two rates. When seeking prevalence rates, it is necessary to perform examination on a large number of cases with the same degree of precision. However, from the standpoint of examination facilities, there is a limit to the number of examinations that can be performed. Therefore, it is felt a comprehensive study should be made covering all aspects such as mortality rate, tumor registry and prevalence rate. According to Sekine et al.⁸ the incidence rate of gastric cancer for Nagasaki and Hiroshima in-

creases with exposure dose in both sexes, with the rate being significantly high in the 100 rad and over group. Further, their study by age at time of exposure showed that the rate is larger among those aged 30 and under who had been exposed to high doses, which agreed with the findings of Kato et al.⁵⁾ and us. It is said that radiation induced cancers develop after the individual reaches the cancer predilection age and that there is a considerable time lag between exposure to onset of disease. Our current tabulation represents findings of over the past ten years. When the age of survivors at the mid-point of the survey, that is, 1977, is considered, the ages of those who were 20 to 34 at the time of exposure would be 52 to 66, and the majority of those 19 and under would be 50 and under. The mean age \pm standard deviation (S. D.) of the cancer cases excluding the 0 rad group was 67.0 ± 7.7 . The future gastric cancer prevalence rate of those 35 and over would probably not increase greatly, but it is presumed that there will be an increase in those whose age at time of the bomb was 20 to 34. Further, as those 19 and under at the time of exposure have not yet reached the cancer predilection age, review was not possible, but as it can be assumed that their prevalence rate will increase, it is hoped that health management efforts be further strengthened.

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