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Publication Date
1979
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PANCREAS

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January 1979
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Chapter V
Somatic Effects - Cancer
Pancreas

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This work was supported by the Office of Health & Environmental Research of the U.S. Department of Energy under contract No. W-7405-ENG-48 and the Environmental Protection Agency.
The NAS-BEIR report referred to cancer of the pancreas as one of a number of cancers reported to occur in excess in persons exposed to ionizing radiation; information on incidence in human populations was relatively limited, however. The 1969 ICRP Report listed the pancreas among organs of apparent, but uncertain, sensitivity to radiation carcinogenesis. This observation was based on preliminary data on reported excess mortality from pancreatic cancer among British radiologists who entered the practice of radiology before 1921 and among ankylosing-spondylitis patients treated with radiation. The pancreas was one of the heavily irradiated organs considered by Court-Brown and Doll in their survey of the ankylosing-spondylitis patients treated with radiation. The risk of pancreatic cancer at moderate radiation doses was difficult to assess, although it seemed likely that it was relatively low, for example, relative to the risk of leukemia induced under the same conditions of irradiation. There are no definitive experimental studies in animals on the radiation induction of cancer of the pancreas or other pancreatic tumors. However, pancreatic cancer was found in mice exposed to gamma irradiation, although not in sufficient numbers to establish its induction by radiation.
Radiotherapy for Benign Disease

The initial study of 14,554 ankylosing-spondylitis patients treated with irradiation found nine deaths from pancreatic cancer, compared with 3.78 expected according to population rates, or 5.2 (0.9-11.9)* excess cancer deaths in patients followed from 6 yr after the first irradiation treatment until January 1, 1960.

Furthermore, there were 12 observed deaths due to pancreatic cancer, compared with 5.71 expected, or an excess of 6.3 (1.2-13.7), in an incomplete followup of treated patients to January 1, 1963.

The most recent analysis by Doll and Smith, of 14,109 ankylosing-spondylitis patients who had received radiotherapy and who were later followed from the date of their first treatment until the year after their second treatment, if any, or until January 1, 1970, found a significant increase in deaths from cancer of the pancreas. The excess was 8.5 (1.2-17.0) cancer cases; or 18 deaths observed versus 9.49 expected (mean followup, 9.5 yr; all 9,10 deaths due to pancreatic cancer; 134,036 PY). In a subset of 6,838 patients observed for 6 yr or more after radiotherapy, with a mean followup of 17.3 yr, this estimate fell to 4.5 (-0.5 to 12.0) excess deaths from pancreatic cancer (12 deaths observed versus 7.47 expected). This is to be compared with no excess deaths due to cancer of the pancreas observed in 836 patients with ankylosing spondylitis (total, 1,021 patients in the series) not given x-ray therapy, with an average followup of 7.9 yr to January 1, 1968.

*Numbers in parentheses are 90% confidence intervals.
The values for this control series were one case of cancer of the pancreas observed versus $0.8$ expected.

There were six deaths observed versus $2.02$ expected during the first 6 yr after treatment; this suggested either that the minimal latent period for radiation-induced pancreatic cancer is less than 6 yr or that the treated disease had an associated risk of cancer of the pancreas. Complete followup of the patient group with ankylosing spondylitis not treated with radiation does not clarify this, in that one death from pancreatic cancer was observed versus $0.8$ expected from the second year after enrollment in the patient series until January 1, 1968. However, this figure is nevertheless consistent with an underlying risk some 2-3 times that expected according to population rates. Nevertheless, the pancreas was not prominent among tissues associated with excess mortality in the series of irradiated patients; the overall finding was 21 cancer deaths from all cancers versus 21.51 expected from the population rates.

If it is assumed that the mean radiation dose to the pancreas was approximately 90 rads* for the treatment group receiving only one course of radiotherapy, these data suggest an absolute risk of 0.70 (0.10-1.4) excess death from pancreatic cancer per 10 patients exposed per year per rad (PYR), assuming no minimal latent period, and an excess of 0.44 (-0.06 to 1.16) death per 10 PYR beginning 6 yr after treatment.

*See Appendix _____, p. _____.

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Atomic-Bomb Survivors, Hiroshima and Nagasaki

The most recent survey of the Atomic-bomb life span study mortality data on survivors in Hiroshima and Nagasaki contains little suggestion of a firm relationship between radiation dose and the induction of pancreatic cancer. However, cancer of the pancreas is often poorly diagnosed, on to death certificates in Japan, and death certificates are commonly completed before autopsy findings become known. A search of the tumor registries maintained by the city medical associations of Hiroshima and Nagasaki has, nevertheless, revealed suggestive evidence of an increasing trend in the induction of pancreatic cancer with increasing radiation dose, among members of the life span study during the period 1954-1970. For the two cities combined, the estimated linear trend was \( 0.18 \pm 0.15 \) excess case of pancreatic cancer per 10 PYR (karma) \((p = 0.09)\). For a ratio of organ dose to kerma dose of 0.37 for the two cities combined, for an RBE of 1, the excess cancer risk is \( 0.49 \pm 0.41 \) per 10 persons per year per rad. For the two cities separately, however, the trend toward an increased incidence of cancer of the pancreas appears in the Nagasaki survivors, but not in the Hiroshima survivors; the risk estimate for the Nagasaki survivors was \( 0.33 \pm 0.21 \) excess cancer per 10 persons exposed per year per rad kerma \((p = 0.04)\). For a ratio of organ dose to kerma dose of 0.40* for Nagasaki exposure, for an RBE of 1, the estimate is \( 0.83 \pm 0.53 \) excess cancer death per 10 persons per year per rad. For the Hiroshima survivors, it was \( 0.04 \pm 0.22 \) excess cancer per
persons exposed per year per rad kerma \( (p = 0.37) \); conversion factors for kerma dose for RBE factors up to 5 do not improve the accuracy of this estimate. These estimates of excess cancer-induction rate are subject to bias, in the sense that the known atomic-bomb survivors, or survivors known to have been heavily exposed, may receive more thorough diagnostic medical attention than would other persons under normal circumstances. The conclusion may be drawn, however, that, although the life span study data for the 24-yr followup period after exposure to September 1, 1974, by themselves do not suggest a firm radiation effect, the data do lend plausibility to the epidemiologic evidence from the ankylosing-spondylitis patient series.

**Occupational Exposure**

Pancreatic cancer is one of the two cancers reported by Mancuso, Stewart, and Kneale, and confirmed by other analysts of the same material to be associated with cumulative radiation-badge dose among nuclear workers at the Hanford Works. Doubling-dose estimates based on proportional mortality analyses and assuming a linear dose response are extremely low, from 7 to 13 rem, and a population-based data analysis yields a formal absolute risk estimate of about 10 excess deaths per 10 persons exposed per year per rem. However, although the various analyses of these data confirm that the observed association of pancreatic cancer mortality with cumulative badge dose is unlikely to be an artifact of the original analysis, there remains considerable doubt that these data give an accurate
representation of the relationship between radiation dose and 
pancreatic cancer. Both exposed and nonexposed workers showed 
higher-than-expected SMRs with respect to cancer of the pancreas, 
which has been linked to chemical exposures. Further, and more 
complete, studies of cancer risk and exposures to radiation and 
other potential carcinogens among nuclear workers are needed. The 
preliminary findings from the Hanford study suggest the existence 
of an increased risk of pancreatic cancer among nuclear workers that 
may or may not be causally related to radiation, but these data appear 
to offer only limited information about the dose-response relation 
between this cancer and radiation.

Radiotherapy for Malignant Disease

Excess mortality from pancreatic cancer (seven cases observed 
versus 2.85 expected) has been reported in 925 patients who survived 
5 yr or more after radiotherapy for carcinoma of the cervix. Pan-
creatic carcinoma has been reported in patients treated with radiation 
for lymphoma. Dose estimates are not available for the reliable 
assessment of excess risk in these radiotherapy patients.

Conclusions

New data from the British survey of ankylosing-spondylitis 
patients treated with radiation tend to confirm and refine the 
elier observations of an increased radiation risk of cancer of 
the pancreas. The most recent report of the atomic-bomb life span 
study of Japanese survivors has suggested a radiation dose-response 
relationship for pancreatic cancer, but this is not apparent from
death-certificate information. A recent study of proportional mortality among workers at the Hanford nuclear plant suggested that workers in the nuclear industry may be at increased risk of pancreatic cancer. Nevertheless, pancreatic cancer continues to be an especially difficult malignancy to study for possible radiation carcinogenesis. Thus far, the only three positive studies have given widely varied risk estimates. This may be explained, at present, on the basis of inaccuracy of death-certificate diagnoses, ascertainment bias, inaccurate or incomplete dosimetry, and the possible association of radiation with other carcinogens and environmental pollutants. It appears, primarily from the series of ankylosing-spondylitis patients, and the life span study data on atomic-bomb survivors, that it is likely that the increase in pancreatic-cancer induction rate may be attributable to exposure to radiation. The induction rate per rad appears to be low, but this is not known with certainty.
REFERENCES


This report was done with support from the Department of Energy. Any conclusions or opinions expressed in this report represent solely those of the author(s) and not necessarily those of The Regents of the University of California, the Lawrence Berkeley Laboratory or the Department of Energy.

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