Risk of death among children of atomic bomb survivors after 62 years of follow-up: a cohort study

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Lancet Oncol 2015; 16: 1316–23

Published Online September 15, 2015 http://dx.doi.org/10.1016/S1470-2045(15)00209-0

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Summary

Background No clear epidemiological hereditary effects of radiation exposure in human beings have been reported. However, no previous studies have investigated mortality into middle age in a population whose parents were exposed to substantial amounts of radiation before conception. We assessed mortality in children of the atomic bomb survivors after 62 years of follow-up.

Methods In this prospective cohort study, we assessed 75 327 singleton children of atomic bomb survivors in Hiroshima and Nagasaki and unexposed controls, born between 1946 and 1984, and followed up to Dec 31, 2009. Parental gonadal doses of radiation from the atomic bombings were the primary exposures. The primary endpoint was death due to cancer or non-cancer disease, based on death certificates.

Findings Median follow-up was 54·3 years (IQR 45·4–59·3). 5183 participants died from disease. The mean age of the 68 689 surviving children at the end of follow-up was 53·1 years (SD 7·9) with 15 623 (23%) older than age 60 years. For parents who were exposed to a non-zero gonadal dose of radiation, the mean dose was 264 mGy (SD 463). We detected no association between maternal gonadal radiation exposure and risk of death caused by cancer (hazard ratio [HR] for 1 Gy change in exposure 0·891 [95% CI 0·693–1·145]; p=0·36) or risk of death caused by non-cancer diseases (0·973 [0·849–1·115]; p=0·69). Likewise, paternal exposure had no effect on deaths caused by cancer (0·815 [0·614–1·083]; p=0·14) or deaths caused by non-cancer disease (1·103 [0·979–1·241]; p=0·12). Age or time between parental exposure and delivery had no effect on risk of death.

Interpretation Late effects of ionising radiation exposure include increased mortality risks, and models of the transgenerational effects of radiation exposure predict more genetic disease in the children of people exposed to radiation. However, children of people exposed to the atomic bombs in Hiroshima and Nagasaki had no indications of deleterious health effects after 62 years. Epidemiological studies complemented by sensitive molecular techniques are needed to understand the overall effects of preconception exposure to ionising radiation on human beings.

Funding Japanese Ministry of Health, Labour and Welfare, US Department of Energy.

Introduction

Children of radiation-exposed parents are predicted to have higher rates of mendelian and multifactorial genetic diseases. However, no clear epidemiological effects have been shown in the first filial (F1) generation of people after parental radiation exposure.[1–3] Concerns of possible deleterious effects among children conceived after parental exposure to the atomic bombs in Hiroshima and Nagasaki led to the creation of the atomic bomb survivors F1 mortality cohort. Previous reports on this cohort have not noted increased cancer incidence or cancer mortality.[4–8] Despite these findings, surveillance has continued as scientific interest and public attention have remained focused on the health effects of ionising radiation. Questions to be answered include the dangers of diagnostic radiography among children, the full effects of the Fukushima nuclear power plant disaster, and germline mutations that could be passed to following generations.

With nearly 63 years of follow-up, the F1 mortality cohort is the longest running study of children born to parents exposed to ionising radiation and has an instrumental role in establishing long-term health effects of parental radiation exposure. This report updates the radiation risks of death caused by cancer and non-cancer diseases among the children of the survivors of the atomic bombings up to 2010 and includes 10 additional years of follow-up since the last report.[8]

Methods

Study design and participants

This study uses a prospective cohort design. Children conceived after the atomic bombings and born in Hiroshima and Nagasaki were identified via city birth records or by active recruitment at city offices where pregnant women could apply for supplemental rice allowances. Parents were interviewed or matched to a master list of survivors based on the 1950 Japanese National Census to determine parental exposure status. All singleton children with one or both parents within 2 km of the hypocentres were included (n=16 869). Comparison groups consisting of children born to one or both parents resident in the city before and after the bombing but neither closer than 2·5 km to the hypocentres (n=18 450), and both parents outside of the cities at the time of the bombing (n=16 738) were matched

Research in context

Evidence before this study

Since 1927, hereditary effects of radiation exposure have been reported in many species. Concerns that parental radiation exposure would have deleterious health effects on human beings led to the creation of a cohort study of children conceived after the atomic bombs in Hiroshima and Nagasaki.

Added value of this study

This study is the longest study of children born to parents with substantial exposure to ionising radiation. This study contributes an additional 10 years of follow-up to the last report and now totals nearly 63 years of follow-up. More than 20% of the cohort is aged 60 years or older. We recorded no effect of parental radiation exposure on risk of death from cancer and non-cancer disease.

Implications of all the available evidence

Although radiation-induced mutations might have been passed to the children of the atomic bomb survivors, parental exposure does not seem to have discernible effects on the children's mortality rates. This finding accords with predictions based on doses of parental radiation and induced mutation rates.

by year of birth, sex, and city. After the Life Span Study cohort of atomic bomb survivors was established in 1958,[9] all singleton children born to a member of the cohort exposed within 10 km were automatically added to the F1 mortality cohort (n=23 270). Thus, the F1 mortality cohort includes a high percentage of all children born to proximally exposed atomic bomb survivors in Hiroshima or Nagasaki.

Date of entry was the child's date of birth and the exit date was the date of death or Dec 31, 2009 (the last year of complete follow-up data). The earliest entry date was May, 1946 (10 months after the bombing) and the latest entry year was 1984 when births effectively ceased as the survivors aged. The Radiation Effects Research Foundation's Human Investigation Committee approved the study.

Procedures

Data about a parent's exposure were obtained via one or more interviews and from census data. During the active recruitment period, expectant parents were interviewed. In 1950, the Japanese national census included a supplemental attachment to identify atomic bomb survivors. From this master list, survivors still living in Hiroshima or Nagasaki were interviewed to assess their exposure.[10] Using the collected exposure information, we calculated parental radiation doses using Dosimetry System 2002, which provides gonadal γ and neutron dose estimates based on distance from the bomb, shielding conditions, body orientation, and age at exposure.[11] Doses were adjusted to remove known dose errors.[12] We used a weighted gonadal dose (γ+10×neutron) to account for the greater biological effectiveness of neutrons, which is consistent with current estimates for neutron quality factors and has been traditionally used for the atomic bomb studies.[13] The dosimetry system can be used to calculate arbitrarily small doses; to create dose categories, weighted gonadal doses of less than 1 mGy were truncated to 0 mGy for all analyses (for 4643 mothers and 2764 fathers). There were roughly 4000 mothers and 3000 fathers for whom a dose could not be assigned, primarily because of complex shielding conditions for which the dosimetry system could not calculate a dose. Many of these people were at locations where a substantial dose could have been expected; they were included in the study but modelled with special consideration. There were also roughly 8000 mothers and 8000 fathers whose whereabouts were unknown at the time of the bombing and were assumed to be not in the city.

Outcomes

The primary cause of death was the outcome of interest and was assessed from death certificates. Causes of death were classified with the WHO International Classification of Diseases (ICD). We analysed deaths caused by non-cancer diseases (ICD-9 codes 1–100, 210–799), and those caused by cancers (ICD-9 codes 140–208) including haemopoietic cancers (ICD-9 codes 204–208).[14] We censored deaths caused by external causes (ICD-9 codes 800–998) or unknown causes (ICD-9 code 999). Participants lost to follow-up were censored at the last contact date. We assessed vital status using the compulsory Japanese family registry system, which provides almost complete ascertainment of vital status for Japanese nationals.

Statistical analysis

We estimated hazard ratios (HRs) and 95% CIs for cancer and non-cancer disease deaths using proportional hazards methods.[15,16] We postulated that risk of death would increase with parental radiation exposure. The primary timescale was attained age. The primary exposures were separately modelled paternal and maternal gonadal radiation doses in weighted Gy. We estimated the effects of exposure using categorical dose groups (0, 1–49, 50–149, 150–499, ≥500 mGy, and unknown) and with a continuous log-linear response model to estimate the HR at 1 Gy. Parents not in the city at the time of the bombing were assigned 0 Gy dose and we included an indicator representing this exposure group. The statistical reference group was children born to a parent who was in the city at the time of the bombing but with an estimated dose of zero (those located about 3·5–10 km from the hypocentres). Parents with an unknown dose were represented with an indicator