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**“Risk of Death among Children of Atomic Bomb Survivors after 62 Years of Follow-up: A Cohort Study”**

Eric J. Grant, Kyoji Furukawa, Ritsu Sakata, Hiromi Sugiyama, Atsuko Sadakane, Ikuno Takahashi, Mai Utada, Yukiko Shimizu, Kotaro Ozasa

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**Study Findings**

We did not observe any association of mortality in the children of the atomic bomb survivors with parental (either paternal or maternal) radiation exposure from the atomic bombings.

**Explanation**

We conducted a study of the relationship between parental radiation exposure and the patterns of cancer and non-cancer deaths among children conceived after the bombings in the F1 mortality cohort of the Radiation Effects Research Foundation (RERF).

1. Study purpose

Radiation-induced hereditary effects have been detected in many species, but no clear epidemiological effects have been demonstrated in humans. This mortality study of children conceived by the survivors of the atomic bombings includes follow-up data since 1946, serving as an important resource in the search for hereditary effects of radiation exposure in humans.

2. Study methods

In this prospective cohort study (a follow-up study of a fixed population), we assessed 75,327 children of atomic bomb survivors in Hiroshima and Nagasaki and unexposed controls who were born between 1946 and 1984 and followed up until December 31, 2009. Analyses were conducted using parental gonadal radiation doses from the atomic bombings. The primary health effects endpoint was death due to cancer or non-cancer disease, based on death certificates. We analyzed deaths over the full follow-up period, divided into the period between birth and until age 20 years and the period at and after age 20. Analyses were performed using <sup>\*</sup>Cox proportional hazards regression, and <sup>\*</sup>hazard ratios (HR) were reported.

<sup>\*</sup>Cox proportional hazards regression: Is a statistical methodology, developed by Sir David Cox in the 1970s, to estimate the risk (or hazard) of the occurrence of an event. In this case, we estimated the hazard of death. The word “proportional” in the title is used because the hazard of those exposed to an agent is assumed to be proportional to those unexposed to the agent.

<sup>\*</sup>hazard ratios (HR): The hazards are compared as a mathematical ratio. In this study, if the ratio is 1.0, then the hazard of death is not associated with parental radiation exposure.

3. Study results

(1) Demographics:

Median follow-up was 54.3 years (<sup>\*</sup>inter-quartile range: 45.4–59.3). A total of 5,183 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 gonadal dose was 264 mGy (<sup>\*</sup>SD 463).

\*inter-quartile range: The inter-quartile range describes the range from the 25<sup>th</sup> percentile to the 75<sup>th</sup> percentile. This statistic is often reported in combination with the ‘median’ (50<sup>th</sup> percentile).

\*SD: The standard deviation (SD) is a measure of the spread of the data and is often used in combination with the mean value.

(2) Relationship between mortality and parental exposure:

No association was detected between maternal gonadal radiation exposure and risk of death caused by cancer in the children (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 (HR: 0.973 [0.849–1.115]; p = 0.69). Similarly, paternal exposure had no effect on deaths caused by cancer (HR: 0.815 [0.614–1.083]; p = 0.14) or deaths caused by non-cancer disease (HR: 1.103 [0.979–1.241]; p = 0.12). Analyses of the period birth until age 20, and the period at and after age 20 also showed no association between parental exposure and mortality in the children.

\* Confidence interval (95% CI): The confidence interval means that if the experiment were repeated 100 times, the “true value” of the hazard ratio would be within each experiment’s reported confidence interval 95% of the time. Or stated another way, if the confidence interval that we derived from our data does not contain the “true” value, then an event has occurred that had a 5% probability of happening by chance.

(3) Other findings:

Those born in the decade immediately after the bombings had higher non-cancer death rates than those born in later decades regardless of parental exposure, but parental age at exposure or time between parental exposure and childbirth had no effect on risk of death.

**Study significance**

Based on RERF research results, late effects of ionizing radiation exposure include increased mortality risks in those exposed directly to the atomic bombs. Theoretical models of the transgenerational effects of radiation exposure predict more disease based on genetic alterations in the children of people exposed to radiation. However, children of people directly exposed to the atomic bombs in Hiroshima and Nagasaki had no indications of deleterious health effects after 62 years of follow-up. Epidemiological studies complemented by sensitive molecular biologic techniques are needed to understand the overall effects of preconception parental exposure to ionizing radiation on children and are being pursued at RERF.

**The Radiation Effects Research Foundation** has studied A-bomb survivors and their offspring in Hiroshima and Nagasaki for more than 60 years. RERF’s research achievements are considered the principal scientific basis for radiation risk assessment by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and for recommendations regarding radiation protection standards by the International Commission on Radiological Protection (ICRP). RERF expresses its profound gratitude to the A-bomb survivors and survivors’ offspring for their cooperation in our studies.

<sup>§</sup>*The Lancet Oncology* delivers essential original research, expert review, and candid commentary in the field of clinical oncology and also provides breaking news to give context and perspective on today’s most important medical advances across the broad spectrum of oncology. (Impact factor for 2014: 24.725)