Renewal of epidemiological study design for Japanese nuclear workers cohort

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BACKGROUND

The public’s concern about low-dose radiation risk has grown since the March 2011 Fukushima nuclear accident. The Radiation Effects Association (REA) has studied a cohort of Japanese radiation workers since 1990 with a view to clarifying low-dose radiation risk, compiling a study report every five years. However, even in the latest analysis published in 2015, we could not offer a clear conclusion about low-dose radiation risk, because it is too small to isolate from other risk factors or it is distorted by confounders such as smoking.

The cohort of the fifth study consisted of 204,103 participants during the study period 1991–2010. Total person-years were 2.89 million, the mean follow-up was 14.2 years. At the end of follow-up, the mean age was 55.6 years old, the mean cumulative dose was 13.8 mSv, and the number of deaths was 20,519 (10.1%).

We investigated the insignificant negative excess relative risk (ERR) (-0.27%/10 mSv) for leukaemia. The ERR of 1.20 for all cancers before removing lung cancer decreased to 0.66 after removing lung cancer, which suggests that smoking might be a strong confounder in the association with radiation and all cancer mortality. Using a subset of the cohort consisting of 75,442 respondents from lifestyle surveys, we directly quantified the smoking effects, finding that the ERR decreased about 60%, from 0.92 to 0.36.

NEW STUDY DESIGN

We revamped the study design in 2015 and started a new study, an outline of which follows. The long-term goal of our cohort study is to investigate scientifically the low-dose radiation risk on health. To achieve this goal, we set a short-term target to establish a cohort of about 33,000 participants by 2018. The cohort should consist of several subgroups that are ideally homogeneous according to the characteristics of the participants but heterogeneous according to dose level, in order to enable a more explicit internal comparison. This will be attained by the matching method based on the participants’ characteristics of the highest-dose (50>mSv) subgroup.

Cancer morbidity will be taken as an end point along with cancer mortality, making use of the National Cancer Registry launched in 2016. At the same time, organ dose will be reconstructed from recorded dose.

To set up the new cohort, we are currently creating a process to obtain informed consent through an opt-in method, as well as conducting a workers’ lifestyle survey that includes possible confounding factors for all participants.
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Background
The public’s concern about low-dose radiation risk has grown since the March 2011 Fukushima nuclear accident. The Radiation Effects Association (REA) has studied a cohort of Japanese radiation workers since 1990 with a view to clarifying low-dose radiation risk, compiling a study report every five years. However, even in the latest analysis published in 2015, we could not offer a clear conclusion about low-dose radiation risk, because it is too small to isolate from other risk factors or it is distorted by confounders such as smoking.

Profile of the previous study cohort
Follow-up period: 1991-2010
Size: 204,103 male participants
Mean age at the end: 55.6 years old
Total follow-up: 2.9 million person-years
Mean follow-up: 14.2 years/person
Mean cumulative dose at the end: 13.8 mSv
Dose distribution: 65% participants <5mSv

Results of Risk Analysis
✓ Insignificant negative ERR for leukaemia.
✓ ERR of 1.20%/10mSv for all cancers excluding leukaemia before removing lung cancer decreased to 0.66 after removing lung cancer.
✓ Suggesting that smoking might be a strong confounder in the association with radiation and all cancer mortality.
✓ Using a subset of the cohort consisting of 75,442 respondents from lifestyle surveys, we directly quantified the smoking effects, finding that the ERR for all cancers excluding leukaemia decreased about 60%, from 0.92 to 0.36 by the adjustment of smoking.

Problems Faced
i. Unable to adjust smoking for all participants.
ii. In spite of the representativeness, extremely heterogeneous population depending on the dose.
iii. Low statistical power for detecting mortality risk.

New Study Design
We revamped the study design in 2015 and started a new study, an outline of which follows.

Long-term Goal: Main analysis to scientifically explore the low-dose radiation risk on health
20 years ahead

Follow-up of Cancer Morbidity and Mortality

Measures to problem iii

In every several years

0-5 mSv 5-10mSv ... 50mSv+
Dose level subgroups

Measures to problem ii

Short-term target: To set up a risk-detection oriented cohort of about 33,000 participants by 2018
Homogeneous according to the characteristics of the participants but heterogeneous according to dose level, in order to enable a more explicit internal comparison, by the matching method based on the participants' characteristics of the highest-dose subgroup.

Activities
In 2015/16
Obtaining informed consent through an opt-in method
Conducting a workers' lifestyle survey that includes possible confounding factors, especially smoking, drinking, hepatitis, cancer history and medical exposure, for all participants

Measures to problem i

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