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SCIENTIFIC APPROACH TO RADIATION-INDUCED CANCER RISK

TOMOTAKA SOBUE

Surveillance Division, Center for Cancer Control and Information Services, National Cancer Center, Tokyo, Japan

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Abstract: When evaluating cancer risk of low-dose radiation, it is difficult to distinguish the actual effect from that of chance, bias, and confounding as they become relatively large. This is why the relation between radiation doses of less than 100 mSv and cancer risk is considered unknown. Based on data of atomic bomb survivors in Hiroshima and Nagasaki, the cancer risk at 100 mSv is calculated at 1.05 times. On the other hand, the risk ratio for the relation between passive smoking and lung cancer is estimated at approximately 1.3 and judging the actual effects faced difficulties. It is almost impossible for epidemiology research alone to show that the risk ratio of 1.05 is the actual effects of radiation. The ICRP estimation, “exposure to 100 mSv increases cancer risk by 0.5%”, has been frequently cited, however, it is not a simple excess lifetime risk of death. It will be more appropriate to indicate a value with clear definition to people in general, such as excess lifetime risk of death or excess lifetime risk of morbidity rather than the value obtained from such complicated process. Radiation epidemiology equally uses ratio and difference to indicate degrees of risk increase. Difference largely changes depending on effects of background factors whereas ratio is often relatively stable. Therefore the use of ratio would be more appropriate when comparing other cancer risk factors.

EFFECTS OF LOW-DOSE RADIATION ON CARCINOGENESIS

Radiation-induced cancer risk has been estimated mainly on the basis of the followup survey for atomic bomb survivors in Hiroshima and Nagasaki. At doses of 100-200 mSv or higher, an almost linear increase of solid cancer risk has been observed as radiation doses increase. However, it is unknown whether there is a link between radiation and cancer risk when the doses are less than 100 mSv. This is not because of the absence of data on low-dose radiation. In the cohort of atomic bomb survivors in Hiroshima and Nagasaki, the majority of them were exposed to doses less than 100 mSv and the greater number of cancers occurred in the group with doses less than 100 mSv. The problem is that small magnitude of effects caused by low-dose radiation led to effects of chance, bias, and confounding to become relatively large. This made it difficult to distinguish the actual effects of low-dose radiation.

Chance is created in any epidemiological survey and it is necessary to increase the number of subjects to control such chance. The required number of subjects can be obtained from the expected effect size. Where the power of the test is 80%, the significance level, 5%, and the risk ratio, 1.1 times, the required number of subjects will be 6,000. For 1.01 times, it will be 620,000. For 1.001 times, that will be 60,000,000. However, increasing the number of subjects does not remove bias and confounding effects but often makes control harder to overcome.

Bias is divided broadly into two categories. One is selection bias (selection of biased subjects) and the other is information bias (measurement error in individual radiation doses or carcinogenesis). For example, when a cohort is set 10 years after the exposure, risk can be measured only in the group excluding those who died. As a result, the risk is possibly underestimated. In addition, bias could not be created when selecting all people who had been exposed within 2.5 km from ground zero for the investigation but it could be created when...
sampling from those who had been exposed 2.5 to 10 km from ground zero. For the estimation of individual radiation doses, a survey interview was conducted for the survivors who had been exposed within 2 km from ground zero but not for those beyond that distance. An estimation error possibly remained with regards to individual radiation doses. The only way to control bias is thoughtful implementation of research for not creating bias.

Confounding is a phenomenon which shows a spurious relationship between radiation and cancer when such relationship is examined. This phenomenon occurs as the distribution of the third risk factor is uneven (e.g. A high-dose exposure group includes many smokers.). Confounding factors such as smoking or drinking have been investigated through questionnaires in the cohort study on workers (which is underway for 200,000 workers) engaged in the nuclear power plants in Japan. The result has revealed that the higher the cumulative doses of a group become, the larger the number of heavy smokers included in the group becomes. In addition, the 10-year tracing result (analysis without adjusting with confounding factors) indicated the relationship between cumulative doses and death rate from smoking-related cancers such as esophageal cancer, liver cancer and lung cancer. It has thus confirmed the need of adjustment with confounding factors.

A convex curve above a straight line at 150 to 300 mSv is observed when examining the details of relationship between radiation doses and solid-cancer risk in the low-dose region of the trace data for Hiroshima and Nagasaki1). It would be more appropriate to consider that this was generated by bias of the radiation-dose estimation or by confounding created by residents who had been a certain distance away from ground zero, rather than by chance. Removing subjects who had been more than 3 km away from ground zero from analysis requires more consideration as cancer occurred 5% more than those within 3 km with zero dose of radiation.

Bias and confounding effects cannot be totally controlled even when epidemiological research on cancer risks of low-dose radiation is carried out with an increased number of subjects. It is therefore necessary to examine the risks together with research on other mechanisms.

**COMPARISON OF CANCER RISK CAUSED BY RADIATION AND OTHER RISK FACTORS**

Data of Hiroshima and Nagasaki indicates that exposure of 1 Sv increases cancer risk by 1.5 times. When a linear relation is applied to radiation doses and cancer risk, cancer risk at 100 mSv is relevant to 1.05 times. This ratio is considerably small when comparing with the risk ratio generally obtained from cancer-risk factors. The risk ratio of those which have a specific relationship, such as in hepatitis C and liver cancer, or asbestos and mesothelioma, becomes as large as ten or higher. For smoking and lung cancer, or Helicobacter pylori and gastric cancer, the ratio is between five and ten due to their relatively strong association. Generally, when examining a risk ratio of a new risk factor, the ratio is within 1.5 to 2.0 and it is difficult to exactly evaluate ratios that are below 1.5, even for properly designed epidemiological researches. The estimated risk ratio for the relation between passive smoking and lung cancer is approximately 1.3 which took a number of globally carried out researches before reaching this conclusion of causal relationship. Therefore, it is almost impossible for a high quality research alone to show statistical significance for the risk ratio of 1.05. On the other hand, even with a small risk ratio, the value of population attributable risk percentage (an indicator which shows the size of impact on the whole society) can become large when exposed subjects account for a high percentage (The risk ratio of passive smoking is approx. 1.3 and the number of people who are exposed to smoking is larger than that of active smoking.). It is always necessary that the balance with other risk factors is taken into account when considering cancer risks of low-dose radiation.

**THE MEANING OF ICRP ESTIMATION, “EXPOSURE TO 100 mSv INCREASES CANCER RISK BY 0.5%”**

The ICRP estimation, “exposure to 100 mSv increases cancer risk by 0.5%”, has been frequently cited by the media. This means that fatal cancer will increase by 0.5% among 100 people who are exposed to 100 mSv but it does not mean that the number of fatal cancers will increase by 1.005 times. As ICRP Publication 103 describes the calculation process2, it is not a simple excess lifetime risk of death but the value is a result of 1) estimating the lifetime cancer risk, 2) applying the dose and dose-rate effectiveness factor (assume it is two), 3) transfer risk across population, 4) calculating each nominal risk factor, 5) adjusting fatality, 6) adjusting QOL, and 7) adjusting years of life lost. However, it will be more appropriate to indicate a value with clear definition to people in general, such as excess
lifetime risk of death or excess lifetime risk of morbidity rather than the value obtained from the above complicated process.

While general epidemiology often uses ratio to indicate the degree of risk increase, radiation epidemiology equally uses ratio and difference. A difference largely changes depending on effects of background factors whereas a ratio is often relatively stable even with different background factors. The use of ratio will be more appropriate than difference when informing degrees of radiation-induced risk increase with comparison to other risk factors.

REFERENCES