Leukemia, Lymphoma, and Multiple Myeloma Incidence in the LSS Cohort: 1950–2001

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Summary. Leukemia was one of the first late health effects of radiation exposure observed among the atomic bomb survivors, initially appearing in the late 1940s. Several Atomic Bomb Casualty Commission/Radiation Effects Research Foundation studies have reported a highly significant radiation-associated excess risk for leukemia, although the evidence for increased risks of lymphoma and myeloma are less clear in the Life Span Study (LSS) cohort. As this cohort ages, the number of incident leukemia and lymphoma cases continues to increase. The current analyses update the incidence risk estimates with a particular focus on how the radiation-associated excess risk varies with age at exposure, gender, and attained age or time since exposure. Consideration is also given to characterization of curvature in the leukemia dose response.

Key words Leukemia incidence · Atomic bomb survivor · Radiation · Temporal pattern

Introduction

A marked radiation-related increase in leukemia incidence was apparent within 5 years of the bombings of Hiroshima and Nagasaki. The excess risk appeared to reach a peak in the mid-1950s and is generally believed to have declined since that time [1]. The most recent detailed report on the risks of radiation-induced leukemia and lymphoma in the Life Span Study (LSS) cohort of atomic bomb survivors considered the nature of the risks for the period from 1950 to 1987 [2]. This study

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aims to extend the follow-up through the end of 2001 using cases from the Hiroshima and Nagasaki Tumor Registries, validated by available information from the Leukemia Registry (1950–1987) through the end of 2001. One goal of the current study is to investigate whether simpler statistical models can describe the radiation at least as well as those used in the earlier analyses. In this chapter, we provide a short description of the new risk models used in the new analyses and briefly outline the nature of the excess relative risk (ERR) model for all leukemias as a group. Additional details on the leukemia excess risk and the risks for other lymphohematopoietic malignancies will be presented elsewhere.

Material and Methods

The LSS consists of a cohort of Japanese residents in Hiroshima or Nagasaki born before August 1945 and whose members were alive on October 1, 1950. The cohort currently includes 93,741 people (atomic bomb survivors) who were within 10 km of the hypocenters at the time of the bombings and 26,580 people who were not near the cities at the time of the bombings. Cases of leukemia, lymphoma, and multiple myeloma were identified from the Leukemia and Tumor Registries. Details on the registries are given in Mabuchi et al. [3] and Preston et al. [2]. By the end of 2001, there were 488 cases of leukemia, 542 of lymphoma, and 179 of multiple myeloma. Cases were eligible for analysis if they were a first-primary cancer diagnosed after October 1, 1950, among cohort members (including those who were not in the city at the time of the bombings), with dose estimates. There were 360 eligible leukemia cases, 434 lymphomas, and 134 multiple myelomas among 113,000 people, with 3,610,000 person-years of follow up (after allowing for migration).

Radiation effects on the leukemia, lymphoma, and multiple myeloma incidence rates were investigated using Poisson regression models. Both ERR and excess absolute rate (EAR) models were considered. The general forms of the models used in the study were these:

$$\text{ERR: Total Risk} = B(c, s, b, a)[1 + \text{ERR}(d, s, e, a)]$$

$$\text{EAR: Total Risk} = B(c, s, b, a) + \text{EAR}(d, s, e, a)$$

where $c =$ city, $s =$ gender, $b =$ birth year, $a =$ attained age, $d =$ radiation dose, $e =$ age at bombing, and $B(c, s, b, a)$ is the background risk for the people with zero radiation exposure. Radiation dose was estimated using Dosimetry System 2002 (DS02) weighted bone marrow dose. Various dose–response functions, such as linear, linear-quadratic, and threshold models, were examined. The risks were estimated using the AMFIT module of the Epicure risk modeling software.

In the previous LSS leukemia report (1994), radiation effects were described using EAR models in which the risk varied with time since exposure and gender.