II. BIOLOGICAL EFFECTS

Tumor Registries and Cancer Incidence Studies

KIYOHICO MABUCHI^{1,2)} AND MIDORI SODA³⁾

¹⁾Department of Epidemiology and

²⁾Departments of Epidemiology and Epidemiologic Pathology, Radiation Effects Research Foundation,
Hiroshima, 732 and

³⁾Department of Epidemiologic Pathology, Radiation Effects Research Foundation, Nagasaki 850, Japan

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A tumor registry is essential in the systematic collection and analysis of tumor data in a defined population. Population-based tumor registries have been in operation for more than 30 years in Hiroshima and Nagasaki. While the tumor registry data have previously been used for many site-specific cancer studies in atomic bomb survivors, overall analysis of tumor registry based cancer incidence data among the atomic bomb survivors has not been undertaken for some time. However, a recent improvement in the tumor registries has made it possible to analyze most recent cancer incidence data among the Life Span Study population. Preliminary analysis under way indicates a potential power of the data. There are a few methodological problems associated with the use of the incidence data, especially relating to consistency of data and migration. Several measures taken to resolve such problems are discussed.

INTRODUCTION

Cancer incidence data offer distinct advantages over mortality data. Being ascertained at the time of disease onset, incidence data provide a direct measure of risk of cancer as it occurs in members of the population. Incidence surveillance is also effective in documenting tumors with favorable prognosis such as cancers of the breast and thyroid which may not appear on death certificates. Furthermore, detailed medical data directly obtained from hospital records provide information needed for accurate and specific diagnosis. Such detailed information is not generally available from death certificate-based studies.

A tumor registry is essential in systematically collecting, managing and analyzing data relating to individual tumor cases on a population basis. More than 30 years ago, population-based registries were established in Hiroshima and Nagasaki. Cancer data derived from these registries in the early years were reported^{1,2,3)}. Later the tumor registry data were extensively utilized at RERF for a series of studies on specific sites of cancer. However, overall analysis of tumor registry incidence data for the LSS has not been undertaken since Life Span Study Report 9 (Part 3) on Nagasaki for 1959–78⁴⁾. Major improvements that have taken place in the last several years enable us to generate recent incidence data for the entire Life Span Study (LSS) sample.

Table 1. Indices of Reliability: Hiroshima and Nagasaki Tumor Registries vs. other registries

Area (Years)	Sex	Incidence* for all sites	% DCO	% HV	M/I
Hiroshima City (1978-80)	M	233.4	9	77	.63
	F	166.6	7	84	.49
Nagasaki City (1978-82)	M	258.1	7	67	.55
	F	166.0	7	67	.46
Osaka (1978-82)	M	242.9	25	58	.70
	F	150.9	22	63	.59
Miyagi (1978-82)	M	215.1	15	67	.67
	F	144.8	15	69	.60
Seattle, USA (1978-82)	M	313.1	1	93	.49
	F	264.0	1	94	.44

* World age-adjusted rate per 100,000

%DCO: Percentage of cases notified from a Death Certificate Only

%HV: Percentage of Histologically Verified cases

M/I: Ratio of mortality to incidence

POPULATION-BASED TUMOR REGISTRIES

The tumor registry was established in 1967 in Hiroshima and in 1958 in Nagasaki under the auspices of each city's medical association. The objective was to develop and maintain a source of information on tumors diagnosed in the community. Since the outset, ABCC-RERF has been responsible for the day-to-day operation including data collection, management and analysis. For case-finding and data collection, all physicians and hospitals in the city are requested by the medical association to report tumor cases to the registry. Reportable tumors include all malignant neoplasms, tumors of uncertain nature and selected benign neoplasms. One of the most important features of the Hiroshima and Nagasaki registries is that a great majority (about 80%) of cases are accessed by means of hospital visits. RERF field personnel visit most of the large hospitals in the area, and abstract detailed information from hospital records.

This approach to cancer registration, termed "active" and employed by most of the well-known American tumor registries, results in a high quality of registry data. To evaluate the quality of data and hence the reliability of registration, two numerical indices are commonly used. These are (i) the proportion of cases registered with histologically verified diagnosis (histologically verification, HV) and (ii) the proportion of cases registered for which only information from the death certificate is available (death certificate only, DCO). At the present time, the Hiroshima

Table 2. Major Characteristics of Tumor and Tissue Registries Hiroshima and Nagasaki

	Hiroshima		Nagasaki		
	Tumor Registry	Tissue Registry	Tumor Registry	Tissue Registry	Pref. Cancer Registry
Year started	1957	1973	1958	1974	1985
Target Population	Hiroshima City (pop = 1,000,000)	Hiroshima Pref. (pop = 2,800,000)	Nagasaki City (pop = 450,000)	Nagasaki City & vicinity (pop = undefined)	Nagasaki Pref. (pop = 1,600,000)
Responsible Authority	City Med. Assoc.	Pref. Med. Assoc.	City Med. Assoc.	City Med. Assoc.	Pref. Health Dept.
Reportable cases	1. All malignancies 2. Selected benign tumors	Both malig. & benign tumors with histol. Dx.	1. All malignancies 2. Selected benign tumors	Malig. & benign tumors, tumor-like lesions with histol. diagnosis	1. All malignancies 2. Selected benign tumors
No. of new cases accessed each year	2,100	5,500 (malig.)	1,200	5,500 (malig., benign. & tumor-like)	4,000 (excl. City)
No. of new LSS cases/year	170	130 (malig.)	90	60 (malig.)	30
Case-finding & data acquisition method	1. Hospital record abstraction 2. Supplemented by notification & mortality data	1. Visitation to hospitals & pathology labs 2. Storage of pathology slides	1. Hospital record abstraction 2. Supplemented by notification & mortality data	1. Visitation to hospitals & pathology labs 2. Storage of pathology slides	1. Voluntary notification 2. Supplemented by hospital visitation & death certificates

and Nagasaki registries have an HV rate in excess of 70% and a DCO rate of less than 9%, which make them among the best in Japan and comparable to many internationally established tumor registries (Table 1)⁵.

RERF also supports tissue registries to which tissue-diagnosed tumor cases, both benign and malignant, in the Hiroshima and Nagasaki area are reported along with tumor tissue slides. The tissue registries, started in 1973 under the auspices of the Hiroshima Prefectural Medical Association and the Nagasaki City Medical Association, serve as an important supplemental data source for case-finding and provide materials for pathology review. Recently, a prefecture-wide cancer registry also administered by RERF was started in Nagasaki, adding another source of cancer incidence data.

Major characteristics of the tumor and tissue registries in Hiroshima and Nagasaki are summarized (Table 2).

CANCER INCIDENCE AMONG A-BOMB SURVIVORS

It is important to realize that maintaining good population-based tumor registries in Hiroshima and Nagasaki is requisite for attaining a high-quality cancer incidence database for various cohorts of A-bomb survivors, a majority of whom reside in the Hiroshima and Nagasaki area. As shown in Table 2, from 5% to 10% of cancer cases accessed by various registries in Hiroshima and Nagasaki are members of RERF's LSS cohort.

One of the reasons that caused the delay in overall analysis of tumor registry incidence data for the LSS and other cohorts has been the difficulty in data collection in Hiroshima. However, this problem has been resolved during the last several years and cases from all major hospitals in Hiroshima have been updated.

Another significant development that has taken place was a new effort initiated jointly by the Hiroshima and Nagasaki registry teams to establish a common tumor registry database for the LSS. The objective was to achieve uniformity and consistency in the handling of registry data from the two cities. An intensive effort was undertaken by the registry staffs from the two cities to consciously standardize diagnostic criteria and data handling procedures. The registry staff reviewed all documents for all cancer patients who have been accessed during the last 30 years. The documents reviewed included not only tumor and tissue registry records but also other records such as autopsy protocols, surgical pathology reports, Adult Health Study's medical charts, and records from previous site-specific cancer studies. For cases with ambiguous or inadequate information, hospital records were re-visited. To ensure consistency, staffs from the two cities met on a monthly basis to review samples of case materials and to discuss cases presenting difficulty in coding. A common set of coding rules, modeled after the US SEER (Surveillance, Epidemiology and End Results) program, was developed and used under the guidance of the registry physicians and pathologist. The effort resulted in the updating of cancer incidence data through 1987 for the LSS sample. The analysis of this data set is now in progress.

Figure 1 presents the number of incidence cases resulting from the above effort among members of the LSS population in comparison with cancer deaths reported during 1958–1985.

Fig. 1. Number of Cancer Incidence Cases Compared with Cancer Deaths, 1958-1985

Noteworthy is the number of incidence cases which total nearly 10,000 (excluding those who were not in the city at the time of the bombing). This is almost twice the number of mortality cases which total about 5,800. Proportional excesses in incidence over mortality cases are striking for such sites as the breast, thyroid, skin, mouth and pharynx, uterus (mostly cervix), and urinary tract (mostly bladder). There also is a marked increase in the number of cases (almost 2,000) for cancer of the digestive tract, reflecting the high background incidence of cancer of the stomach and liver in Japan. How the increased number of cases together with improved precision in diagnosis affect risk assessment is of special interest.

METHODOLOGICAL ISSUES

Different from the mortality surveillance based on a single source of information, the ascertainment of incidence cases relies on a wide range of sources. These sources may represent the different nature of cases, providing information of variable diagnostic accuracy. To ensure consistency, therefore, special care must be exercised to collect cases from all possible sources and to collect and process data in a systematic manner. This is the reason why the special effort was made to achieve consistency as described earlier.

Another issue relate to the ascertainment of cancer cases among individuals who moved out of the Hiroshima and Nagasaki area. The catchment areas of the Hiroshima and Nagasaki registries are limited to the two prefectures, focusing on the cities of Hiroshima and Nagasaki. Accordingly, incidence data are not obtained when the place of residence has changed to outside the two prefectures. Adult Health Study (AHS) data and LSS mail survey data show migration of approximately 20% of the living LSS subjects out of Hiroshima and Nagasaki around 1980 and the migration rate is especially high among young survivors. At the present time, cancer

data on the migrants are obtained only through the nation-wide mortality surveillance.

The considerable number of migrants raises questions concerning the ascertainment of the numerator as well as the denominator, the numerator being the tumor cases of specific interest and the denominator being the population (at risk) from which the cases come. Possible sources of tumor information for migrants include cancer registries operating in various parts of Japan, particularly in large cities such as Osaka and Nagoya where many migrants are known to live. To determine the population at risk, it will be necessary to know when migrants left the Hiroshima and Nagasaki area and also, if other area-wide tumor registries are to be used for case ascertainment, when they moved into other ascertainment areas. For this purpose, an effort is underway to establish an address data base which contains data on residential history for individual subjects from various sources (e.g. AHS records, mail surveys, A-bomb handbooks).

In the analysis currently undertaken of the 1958-87 incidence data, statistical methods are used to adjust for migration in estimating cancer risk. Since the AHS data enable us to estimate the proportion of subjects living outside the area for a given demographic as well as exposure category, this can be used to compute estimated person-years at risk for various strata, which then are used for adjustment for migration. A similar method was employed in a previous breast cancer incidence study⁶). Since migration has not been found to correlate with radiation dose, relative risk estimates are not expected to be influenced by such adjustment. It is expected, however, the excess risk estimated on the basis of cancer incidence data will be greater than that obtained from mortality data, as demonstrated from the previous analysis⁴).

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