Cancer incidence among the liquidators of the Chernobyl accident

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The work presents data on incidence of solid malignant neoplasms among liquidators of the Chernobyl accident which have been gathered in the Russian National Medical and Dosimetric Registry (RNMDR) from 1986 to the beginning of 1996. The RNMDR contains individual dosimetric data and results of annual medical check-ups of the liquidators living on the territory of Russia. The study involves male liquidators who had no oncological diseases before arrival to the 30-km zone and for whom the following information was available: confirmed dose of external irradiation, birth date, date of arrival to the 30-km zone, time spent in the 30-km zone, results of medical check-ups. The number of liquidators under study was 114504 persons, which is about 68% of all liquidators registered in the RNMDR. The average dose of the cohort that is considered is 108 mGy, the average age at the time of their first arrival in the 30-km zone is 34.3 year and the total number of person-years is 797781. The liquidators' cohort is briefly characterized, cancer incidence of liquidators is compared with that of the population of Russia as a whole by calculating standardized incidence ratio (SIR). SIRs with 95% confidence intervals for all solid malignant neoplasms and cancers of the digestive system were 1.23 (1.15; 1.31) and 1.11 (1.01; 1.24) respectively. Estimation of radiation risks for the same disease classes has revealed a statistically significant increase in cancer incidence with increase in external radiation dose of liquidators.

Introduction

After the Chernobyl accident in 1986 a system of collection, storage and verification of medical and dosimetric data on persons exposed to radiation as a result of the accident at the fourth reactor unit of the Chernobyl NPP was set up in Obninsk, Kaluga region [1]. After some organizational transformations [2], this system presently exists as the Russian National Medical and Dosimetric Registry (RNMDR).

The RNMDR database annually receives individual information from medical surveillance of the exposed persons including the liquidators residing in Russia. As of the beginning of 1996, 169372 liquidators were registered in the RNMDR.

By now a number of papers have been published in the CIS and abroad aimed at studying health effects and other consequences of the Chernobyl accident [3-11]. In particular, paper [11] presents estimates of morbidity and mortality among liquidators for a wide range of diseases and [3, 7, 8] - estimates of radiation risks.

However, these papers were either descriptive or considered influence of radiation and other factors on liquidators' health in a broad manner, for example, paper [7] presents estimates of radiation risks for various diseases, some of which are not traditionally regarded as radiogenic. An exception to the rule are specialized publications on relatively small groups of liquidators [12, 13].

One of the issues which has not been much publicized yet is the dependence of frequency of cancer diseases on the influence of radiation and other related risk factors on liquidators' health. On the other hand, malignant neoplasms are known to be radiogenic [14], which is confirmed by both clinical and radiation-epidemiological studies [15].

For example, the long-term study of the survivors of the atomic bombing of Hiroshima and Nagasaki in 1945 has shown growth in morbidity and mortality rates for malignant neoplasms with an increase in radiation dose [16].

Studies of large populations of those exposed to radiation or dealing with radioactive sources are under way in many developed countries: USA [17], Canada [18], UK [19] and others. To pool the available experience international collaborative projects have been carried out [20, 21].

The above studies help to elucidate the relationship between radiation, working conditions etc. and risk to develop or die from various diseases, primarily malignant neoplasms, for different groups of people professionally or otherwise affected by adverse factors, the principal of which is radiation. The levels of exposure considered were different. For the Japanese cohort [16] the dose range was rather wide including relatively high doses - more than 500 mGy, while for professionals in nuclear industry the doses were below 10 mGy [21]. From this standpoint the cohort of liquidators takes an interim position: the average dose for them is about 108 mGy [8, 22], which makes it particularly valuable for investigation.

This paper is devoted to a study of the incidence of solid cancer and risk estimation for liquidators of the Chernobyl accident and comparison of cancer incidence for liquidators with cancer incidence for the population of Russia as a whole. The paper may be considered as continuation of previous works [3, 7, 8, 23].

At the same time, it should be emphasized that due to objective and subjective reasons the results obtained cannot be considered as complete studies and are primarily indicative of the current amount of data in the RNMDR.

Methods and materials

Cohort and radiation doses

The cohort of liquidators under study comprises 114504 persons and is a subgroup of the liquidators registered in the RNMDR (169372 persons as of the beginning of 1996). This subgroup includes male liquidators (females constitute 1% of the total number of liquidators) who had no cancer before their arrival to the 30-km zone and for whom the following data are available: birth date, date of arrival in the zone, period of time spent in the zone, results of medical check-ups and external radiation dose.

The term “ dose” means a documentary confirmed external radiation dose for each liquidator.

Dosimetric data can be divided into three major groups:

- absorbed dose obtained via an individual dosimeter;
- group dose assigned to members of a group working in the zone, based on readings of an individual dosimeter which was placed with one member of the group;
- itinerary dose which was estimated by dose rate in the zone and time spent by members of the group in the zone.

To verify dosimetric information certain steps were undertaken including efforts of the RNMDR specialists and projects involving independent experts from the European Community [13, 24].

Paper [22] examines in detail whether the RNMDR data are reliable. The analysis has revealed that the RNMDR contains an insignificant amount of unreliable dosimetric data.

The dosimetry issue remains a most critical one in managing the RNMDR.

Table 1 shows the distribution of liquidators by external radiation dose and Table 2 - distribution by age. The average age of liquidators at the time of their arrival in the Chernobyl zone is 34.3 years. The majority of liquidators (about 80%) took part in the recovery works in 1986-1987. The average period of work in the 30-km zone is 2.7 months, the average dose of liquidators from Russia is 108 mGy.

Table 1

Distribution of liquidators by external radiation dose

Dose group (mGy)	Number of liquidators
[0-50)	35898 (31.35%)
[5-100)	29470 (25.74%)
[100-150)	11685 (10.20%)
[150-200)	12940 (11.30%)
[200-250)	19755 (17.25%)
[250+)	4756 (4.15%)

Table 2

Distribution of liquidators by age at the moment of arrival to the 30-km zone

Age (years)	Number of liquidators
[15-20)	2180 (1.90%)
[20-25)	8905 (7.78%)
[25-30)	14097 (12.31%)
[30-35)	36323 (31.72%)
[35-40)	37116 (32.41%)
[40-45)	11587 (10.12%)
[45-50)	3294 (2.88%)
[50-55)	664 (0.58%)
[55-60)	263 (0.23%)
[60+)	75 (0.07%)

System of collection of medical information

The collection of data in the RNMDR is performed in the following way. Special Registry record papers [2] containing the information about health status of the liquidator under examination are filled in using unified medical protocols during annual medical check-ups in Central district hospitals and Regional oncological clinics. The papers filled in are verified and passed on to the regional level. On this level the data are recorded on magnetic media (floppy disks), verified and passed on to the Regional Center. The RNMDR encompasses 20 Regional Centers collecting information throughout Russia [2]. The information from the regional centers goes to the national level (Medical Radiological Research Center of RAMS, Obninsk) where it is checked and analysed. About 70-80% of liquidators registered in the RNMDR undergo annual check-ups as part of specialized screening programs. The group of doctors performing examination of liquidators necessarily includes an oncologist.

As a result, the RNMDR database includes individual medical-dosimetric information such as:

- general information about the liquidator: name, surname, birth date, address etc.;
- data related to participation in the recovery works at the Chernobyl NPP: date of arrival, period spent in the 30-km zone, external radiation dose etc.;
- information on health status: International Classification of Diseases codes (ICD-9 [25]) of diseases diagnosed after the Chernobyl accident, when and where the diagnosis was made.

The term “ cause of disease” is used here to denote the registration of the first oncological diagnosis since the liquidator’s arrival to the 30-km zone by a health-care institution.

The RNMDR database is annually updated with information from Regional Centers and from specialized Registries of the Defence Ministry of Russia, Ministry of Home Affairs, Federal Security Service, Ministry of Transport, Ministry of Nuclear Power and Industry. The liquidators’ cohort studied in the paper conforms to the data contained in the RNMDR database as of the beginning of 1996.

Methods of analysis

For each person the time under risk to develop a disease of a particular class is calculated as a difference of dates T_1 and T_0, where T_0 is the time of arrival to the 30-km zone and T_1 is the first of the following dates: the date of the first diagnosis for the class of diseases under study, the date of the latest medical check-up and the date of death. The incidence rate used in the paper is defined as a ratio of the total cases of disease and the total time under risk which is measured in person-years.

In order to estimate the difference in cancer incidence among liquidators and the population of Russia as a whole, standardized incidence ratio (SIR) is calculated. Age-related incidence rates for the male population of Russia published in [26] were used in calculations.

To determine the dependence of incidence rates on the dose, individual data about liquidators have been grouped in a multidimensional table. In the present paper the data are divided into 10 strata by age ([15-20), [20-25), [25-30), [30-35), [35-40), [40-45), [45-50), [50-55), [55-60), [60+) years) and into 6 groups according to dose ([0-50), [50-100), [100-150), [150-200), [200-250), [250+) mGy).

Let i be the age group index and j be the dose group index.

Let Y_{ij} be the number of cases of diseases, P_{ij} - person-years, M_{ij} - the incidence rate in the stratum ij. In these terms M_{ij} for a given class of diseases can be defined as

$$M_{ij} = Y_{ij} / P_{ij} . \qquad (1)$$

It is reasonable to assume [27, 28] that Y_{ij} values are independent Poisson random values with mathematical expectation $E(Y_{ij}) = P_{ij}M_{ij}$. To determine the dependence of M_{ij} on the dose it is necessary to present M_{ij} in the form of a parametric function and its parameters are to be determined via maximisation of likelihood function

$$L = \Sigma\{Y_{ij} \ln(P_{ij}M_{ij}) - P_{ij}M_{ij}\}, \qquad (2)$$

where $M_{ij} = f(D_{ij})$ and D_{ij} is an average dose in ij stratum.

Simple functions are used in this paper

$$f(D_{ij}) = M_{i0} \exp(ad_{ij}), \qquad (3)$$

$d_{ij} = 0$ for $j = 0$ and $d_{ij} = 1$ for $j > 0$.

$$f(D_{ij}) = M_{i0} (1 + bD_{ij}). \qquad (4)$$

Function (3) is used to determine relative risk $RR = \exp(a)$, function (4) is used to determine significance of relative risk dependence on dose. The statistical test applied for these purposes is the test of ratios of likelihood maxima at zero hypothesis $b = 0$. The [0-50) mGy group was taken as a background dose group ($j = 0$).

AMFIT program [28] was used to estimate the parameters of function (3-4), perform statistical tests and determine confidence intervals.

Results

In the period under study from 1986 to early 1996, 983 cases of solid cancers (ICD-9 codes 140-165, 170-195) were diagnosed among the liquidators of the cohort under study, the total number of person-years was 797781. The most widespread among the liquidators are malignant neoplasms of the digestive system (ICD-9: 150-159) - 301 cases of diseases and malignant neoplasms of the respiratory system (ICD-9: 160-165) - 250 cases of diseases. Table 3 shows the values of SIR with 95% confidence intervals for these classes of malignant neoplasms and all solid tumors.

As is seen from Table 3 there is a statistically significant difference of SIR from unity for all solid tumors and for malignant neoplasms of the digestive system, which suggests an increased cancer incidence among liquidators for these classes of diseases as compared to the male population of Russia.

Table 4 contains estimates of radiation risks for all solid tumors and malignant neoplasms of the digestive and respiratory system. As was the case with SIR, a significant difference of relative risk ***RR*** from unity is observed for all solid tumors and malignant neoplasms of the digestive system. Table 4 also shows values of ***p*** corresponding to the test for linear trend in relative risk. For all solid tumors and malignant neoplasms of the digestive system, a statistically significant positive association of relative risk and external radiation dose has been noted.

Table 3

Observed and expected cases of the diseases under study

Disease class	**ICD-9**	**Observed cases**	**Expected cases**	**SIR**
Solid tumours	140-165; 170-195	983	800	1.23 (1.15;1.31)[a]
Malignant neoplasms of digestive system	150-159	301	271	1.11 (1.01;1.24)
Malignant neoplasms of respiratory system	160-165	250	247	1.01 (0.89;1.15)

[a] - 95% confidence intervals.

Table 4

Relative risk (*RR*) for the studied class of diseases with 95% confidence intervals

Disease class	***RR***	***P***[a]	**Comment**
Solid tumours	1.2 (1.04; 1.39)	0.01	***RR*** increases with dose
Malignant neoplasms of digestive system	1.68 (1.25; 2.25)	0.02	***RR*** increases with dose
Malignant neoplasms of respiratory system	1.07 (0.8; 1.42)	0.24	No significant effect

[a] - test for linear trend.

Discussion

The system of collection, storage and verification of medical and dosimetric data on liquidators of the Chernobyl accident which was established in 1986 has made it possible to accumulate a large body of factual material about their health status, received doses and so on. The collected individual data include, among other things, information on cancer incidence among liquidators which became the subject of our analysis.

The analysis of the available information has shown that oncological diseases of the digestive and respiratory systems are most widespread among liquidators. For these classes of diseases and for all solid cancers SIR values were derived. The male population of Russia was used as a standard. Estimates of SIR for all solid cancers (SIR = 1.23 with 95% CI (1.15; 1.31)) and cancers of the digestive system (SIR = 1.11 with 95% CI (1.01; 1.24)) are significantly different from unity. This is indicative of an increased incidence of these classes of diseases among liquidators as compared with the male population of Russia, according to official statistical data [26]. This fact can be attributed to different reasons. e.g., to the difference in the system of collecting medical information used in the RNMDR and when preparing official statistical data on cancer in Russia. It is reasonable to assume that deeper and more systematic medical check-ups of liquidators as compared to conventional health care procedures in Russia, can lead to higher detectability of cancer among liquidators.

The estimates of relative risk, as with SIR, have a statistically significant difference from unity for all solid cancers (RR = 1.2 with 95% CI (1.04; 1.39)) and all cancers of the digestive system (RR = 1.68 with 95% CI (1.25; 2.25)). These classes of diseases have also shown a statistically significant positive trend as a function of external radiation dose of liquidators.

One of the difficulties in interpreting the obtained coefficients of relative risk is that they are rather high for the dose range under study. Extrapolation of risks derived for the Japanese cohort of the atomic bombing survivors [16] to the doses of the order of 100 mGy will give a lower relative risk in comparison with the results of the present work. It should be noted, however, that the analysis of cancer incidence among liquidators is based on the follow-up of 10 years, whereas for the Japanese cohort data on cancer incidence became available only ten years after exposure. According to the results in [16], the relative risk for solid cancers decreases with time after exposure. The decrease in risk is particularly dramatic for people who were younger than 20 at the time of bombing. For those who were older at the time of exposure no decrease is observed. It might be assumed, however, that in earlier periods the dependence of relative risk on time for 20-40 year-olds could have a similar trend for an increase in relative risk with the decrease in the period of time since exposure. Such a hypothesis will probably partly explain the discrepancy between the results of the present work and results of the analysis based on the Japanese cohort, as the overwhelming majority of liquidators were 20-40 years old at the time of their arrival to the 30-km zone and the cohort has been followed up for less than 10 years. Yet, this is just a hypothesis and to confirm or disprove it additional studies are required going beyond the scope of this work.

Conclusion

Based on the analysis of medical and dosimetric information about liquidators of the Chernobyl accident collected during the period from 1986 to the beginning of 1996 by the Russian National Medical and Dosimetric Registry, relative risks for different classes of oncological diseases have been estimated and cancer incidence in liquidators and the population of Russia as a whole were compared.

In general, for all solid tumors and malignant neoplasms of the digestive system, the incidence rate is higher for the liquidators’ cohort under study as compared with the male population of Russia. For the same class of cancers a statistically significant increase in relative risk of incidence with external radiation dose among liquidators has been observed.

The results obtained should be considered as qualitative. Further follow-up of the liquidators’ cohort is to help reduce uncertainties in the quantitative interpretation of these results.

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