

RISK OF DEATH FROM HYPERTENSION AMONG CHERNOBYL ACCIDENT LIQUIDATORS – NUCLEAR INDUSTRY WORKERS

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Abstract. *The aim of the study was to assess the radiation risk of death from hypertension in liquidators of the Chernobyl nuclear power plant accident consequences – workers of the nuclear industry – using doses from various types of irradiation.*

Materials and methods of the study. The study was conducted using data from the Industry Register of Persons exposed to radiation as a result of the Chernobyl accident – workers of the nuclear power industry. Information on 12659 liquidators (all male) was included in the analysis. 1327 of them got occupational radiation doses. Crude relative risks of death from hypertension were estimated for five dose groups using internal controls. Based on the stratified data file, a Poisson regression procedure was performed using the AMFIT module of Epicure program and the excess relative risk of death from hypertension was calculated and the nature of the dose-dependent excess relative mortality was investigated.

Results of the study and their analysis. Direct estimates of radiogenic risk of death from hypertension were obtained. No increase in mortality from hypertensive disease per unit dose was found for both the doses received during the liquidation of the Chernobyl accident consequences and for the total doses. The results of the study can be used in the development of radiation safety regulations for persons working with sources of ionizing radiation.

Key words: AMFIT, Chernobyl accident, EPICURE, hypertension, industry register, liquidators, nuclear industry workers, radiation, relative risk, risk of death, Rosatom State Corporation, study period

Conflict of interest. The authors declare no conflict of interest

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РИСК СМЕРТИ ОТ ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНИ У ЛИКВИДАТОРОВ ПОСЛЕДСТВИЙ АВАРИИ НА ЧЕРНОБЫЛЬСКОЙ АЭС – РАБОТНИКОВ АТОМНОЙ ПРОМЫШЛЕННОСТИ

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Резюме. *Цель исследования – оценка радиационного риска смерти от гипертонической болезни у ликвидаторов последствий аварии на Чернобыльской АЭС (ЧАЭС) – работников атомной промышленности с использованием доз от различных видов облучения.*

Материалы и методы исследования. Исследование проводилось с использованием данных Отраслевого регистра лиц, подвергшихся воздействию радиации в результате аварии на ЧАЭС – работников атомной промышленности. В анализ была включена информация о 12659 ликвидаторах (все – мужчины), 1327 из которых имели дозу профессионального облучения. Оценены грубые относительные риски смерти от гипертонической болезни для пяти дозовых групп с использованием внутреннего контроля. На основе файла стратифицированных данных проведена процедура Пуассоновской регрессии с использованием модуля AMFIT программы Epicure и рассчитана величина избыточного относительного риска смерти от гипертонической болезни, а также исследован характер дозовой зависимости избыточной относительной смертности.

Результаты исследования и их анализ. Получены прямые оценки радиогенного риска смерти от гипертонической болезни. Не обнаружено увеличения смертности от гипертонической болезни на единицу дозы как для дозовых нагрузок, полученных при ликвидации последствий аварии на ЧАЭС, так и для суммарных доз. Результаты исследования могут быть использованы при разработке регламентов радиационной безопасности лиц, работающих с источниками ионизирующего излучения.

Ключевые слова: AMFIT, EPICURE, авария на Чернобыльской АЭС, гипертоническая болезнь, Госкорпорация «Росатом», ликвидаторы – работники атомной промышленности, относительный риск, отраслевой регистр, период исследования, радиация, риск смерти

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Recently, there has been an interest in the impact of ionizing radiation on morbidity and mortality from non-oncologic somatic pathology. This is due to the emergence of a large body of clinical evidence of the damaging effects of radiation on the cardiovascular system.

At the same time, on the basis of data on survivors of the atomic bombing in Japan (LSS), it is shown that in the analysis of cardiovascular mortality, no statistically significant risk value was presented for any dose stratum of the total dose category relative to the control population (less than 0.2 Gy). And even the addition of additional corrective factors did not change this result [1]. Estimates of excess relative risk per Gy (ERR/Gy) corresponded to the level not exceeding the risk.

As for Russian liquidators of the Chernobyl NPP (ChNPP) accident consequences, there is a point of view that low dependence of population risks of somatic diseases on the value of radiation dose received in 30-km (30-km) ChNPP zone is connected with erroneous estimation of radiation exposure dose received by liquidators, and also with functional instability of diagnostic indicators change in time [2, 3]. According to data of Russian State Medical and Dosimetric Registry, excess relative risk of cardiovascular diseases (ERR/Zv) has a value of 0.4 – significantly different from zero, and of mortality from cardiovascular diseases is 0.2 – not significantly [4].

According to the data of Ukrainian researchers, in spite of the fact that clinical characteristics of the functional state of cardiovascular system and concomitant diseases in the liquidators were almost similar to those observed in the control group, the beginning of hypertensive disease in this contingent came earlier – at 55.9 years – against 59.8 years in the control group [5]. It was also shown that in the persons who took part in the liquidation of the Chernobyl accident at the age of 40 and older at the time of the accident, irradiation in low doses caused the development of hypertensive disease. The mortality rate in these persons with higher radiation doses was significantly higher ($p < 0.05$) than in persons with lower radiation doses. The main causes of mortality from circulatory system diseases in the studied cohorts were cerebro-vascular diseases, arterial hypertension, diseases of arteries, arterioles and capillaries [6, 7].

Also of interest are estimates from national registries of nuclear power workers and uranium ore miners (Germany). According to NRRW (England) and their German colleagues, estimates of ERR/Gy for cardiovascular mortality do not differ significantly from zero, which also corresponds to the data of T.V. Azizova on the cohort of “Mayak” Industrial Association workers [8-12].

M.P. Little presented the results of the IARC/HS estimates on the LSS cohort data for cardiovascular disease mortality, which were 0.17 (0.08-0.26) – [13]. An analysis of IARC data from a study of nuclear-cycle worker mortality in 15 countries yielded lower estimates for morbidity in selected nosologies (coronary heart disease, hypertension, heart attacks, embolisms) that were generally close to zero. His analysis of morbidity data of Chernobyl accident liquidators yielded the following results for ERR/Zv: hypertension, 0.26;

coronary heart disease, 0.41; other cardiovascular pathologies, 0.26. Except for the latter, the first 2 coefficients were significantly different from zero. In the work on meta-analysis of data presented by researchers from many countries, the ERR/Zv value for death from coronary heart disease was 0.10 [14].

Great work on the analysis of mortality data for employees of nuclear-cycle enterprises was carried out by E. Cardis and co-authors [15]. The risk of death from all diseases, excluding cancer, was 0.24 per 1 Sv; for cardiovascular diseases it was 0.09 per 1 Sv. For both coefficients, the confidence interval includes zero.

Unfortunately, the studies presented above were made using data on doses of a single type of exposure and therefore their results cannot be reliable. In this connection, it is relevant to carry out studies to assess the risk of radiation-induced diseases or death from them using total doses from different types of irradiation.

The aim of the study was to assess the radiation risk of death from hypertensive disease in the liquidators of the Chernobyl accident consequences – workers of the nuclear industry – using doses from various types of radiation.

Materials and research methods. The data on employees of enterprises and organizations of the State Corporation “Rosatom” who participated in liquidation of consequences of the Chernobyl accident were used in the work. The analysis included information on 12,659 liquidators (male) registered in the Industry Register of the persons exposed to the Chernobyl NPP accident and having data on verified external radiation doses. The average age of the liquidators at the time of participation in the liquidation of the Chernobyl accident consequences was 36.6 years; 80% of the liquidators were in the 30-40 age group.

At present, due to the fact that none of the medical dosimetric registers meet the requirements of Radiation Safety Norms of 1999 – availability of total radiation dose to calculate radiation risk – there is no possibility to perform correct studies on risk assessment for radiation-induced diseases at low doses on existing registers both in our country and abroad.

Rosenergoatom OJSC provided the State Research Center – Federal Medical Biophysical Center named after A.I. Burnazyan of the Federal Medical and Biological Agency (FMBA of Russia) with the data on occupational radiation doses to main production workers at 10 NPPs who were under individual dosimetry control and who participated in the liquidation of the Chernobyl accident consequences. Data on occupational radiation doses of Balakovo, Beloyarsk, Bilibino, Kalinin, Kursk, Leningrad, Novovoronezh, Rostov and Smolensk NPP workers are included in the development.

In addition, data on occupational radiation doses to employees of enterprises and organizations of ROSATOM were obtained from healthcare institutions of the Federal Medical and Biological Agency of Russia.

Occupational exposure doses were presented by years of their work with radioactive substances and ionizing radiation sources, starting from the first year of work and ending

in 2015. Cumulative doses were also calculated, which were linked to the accident liquidators included in the Industry Register.

The data on external radiation doses among the liquidators during their stay in the 30-km ChNPP zone are presented in Table 1.

Table 2 shows some characteristics of the generalized database of the Register by 5 dose groups — both by doses at the Chernobyl NPP and by total doses. The groups were formed from an approximately equal number of persons and taking into account the radiation doses received.

In the structure of total doses received by the liquidators of the Chernobyl accident consequences while working in the 30-km zone and during their professional activities, 48% were doses up to 100 mSv; 6% of the liquidators had doses higher than 500 mSv.

Table 3 provides information on the average, minimum and maximum external radiation doses received by the liquidators at various work sites.

The study calculated the 95% confidence interval of the indicators.

The applied statistical software package EPICURE (AMFIT module), widely used in modern radiation and epidemiological practice, was used for risk assessments based on age-, dose-, and other groups of data [16]. The methodology of radiation risk assessment is implemented in this package. The AMFIT program is a recognized standard for radiation and epidemiological studies. Radiation risk assessments among the personnel of ROSATOM enterprises and organizations were performed using this program. The model of excess relative risk in general form is presented by formula 1:

$$\lambda_d = \lambda_0 \times (1 + \beta \times d) \quad (1)$$

where λ_d — is the incidence rate; λ_0 — is the spontaneous incidence rate; β — is the excess relative risk; d is the radiation dose.

Таблица 1/ Table No. 1

Дозы внешнего облучения у ликвидаторов (мужчины и женщины) последствий аварии на ЧАЭС

Provision of Liquidators (Men and Women) of the Consequences of the Chernobyl Accident with Data on External Exposure Doses

Годы въезда в 30-км зону Years entrance to the 30-km zone	Число ликвидаторов, чел. Amount liquidators, people	В том числе с дозой, чел./% Of these there is a dose, people/%	Среднее значение дозы, мЗв Average value, mSv
1986–1990	18450	12698/68,8	55,3
1986	10790	7276/67,4	74,8
1987	4738	3365/71,0	33,1
1988	1868	1389/74,4	25,7
1989	798	571/71,6	16,8
1990	266	97/36,5	11,9

Дозы внешнего облучения у ликвидаторов (мужчины) последствий аварии на ЧАЭС

Provision of Liquidators (Men) of the Consequences of the Chernobyl Accident with Data on External Exposure Doses

Дозовая группа – ЧАЭС Dose group – ChNPP	Число ликвидаторов, чел. Number of liquidators, people	Средняя доза, мЗв Average dose, mSv	Дозовая группа – проф. Dose group – professional	Число ликвидаторов, чел. Number of liquidators, people	Средняя доза, мЗв Average dose, mSv
0,1–4,9	2864	2,23	0,1–5,9	2922	2,6
5,0–12,9	2237	7,95	6,0–16,7	2222	10,3
13,0–35,1	2490	21,70	17,0–48,8	2468	30,4
36,0–98,8	2516	62,30	49,0–120,5	2482	80,3
99,0–1478,5	2552	181,80	121–1985,6	2565	228,4

The likelihood function is constructed based on the assumption that the number of cases is an independent Poisson random variable.

The results of the study and their analysis.

To calculate the relative radiation risk of mortality from hypertension among the liquidators of the Chernobyl accident consequences using the AMFIT program the data were divided into 5 dose groups obtained during the liquidation of the Chernobyl accident and the total dose (Tables 4, 5).

Formula 2 was used to estimate the reliability of the relative radiation risk of mortality:

$$\log RR (SE) = \sqrt{(1/r_1 + 1/r_2 - 1/N_1 - 1/N_2)} \quad (2)$$

where r_1, r_2 — number of cases in the control and current strata; N_1, N_2 — number of person-years in the control and current strata.

Due to the small values of relative risk, all values of point risks do not reliably exceed 1, which makes it impossible to make parallel comparisons. At the same time, according to the data in Tables 4 and 5, the relative risk values for mortality from hypertension have some tendency to increase inversely.

The results of radiation risk assessment using the AMFIT program for different dose loads are given in Table 6. The excess relative risk was not detected both in the case of taking into account only doses received in Chernobyl, and in the case of total doses.

The case of a uniform expansion of the dose range — the addition of occupational exposure doses in each stratum — leads to a shift of the regression line of the risk curve to the right along the axis of dose values. In the empirical control problem, this automatically leads to a reduction in excess risk. In the case of unequal addition of dose loads by strata — an increase in doses due to occupational exposure only for 1327 people out of 12659 — the "risk" response can be paradoxical.

Discussion

As noted by a number of authors, there are different approaches to explaining the pathogenesis of the development of cardiovascular diseases in the long-term period [17]. Some authors consider the role of chronic emotional stress exclusively. Others argue that the damaging effect of ionizing radiation does not depend on human consciousness and in case of uniform irradiation of the organism is manifested at the cellular-molecular level in all organs and tissues without exception [18]. Apparently, the prognostic significance in the development of cardiovascular diseases in liquidators of the concept of disintegrative syndrome as a non-specific radiation syndrome in contrast to acute or chronic radiation disease considered as a specific radiation syndrome is a priority.

At present, total radiation doses received by workers both at Chernobyl and during their main job, as well as medical and natural doses of exposure, are of particular relevance

Таблица 2 / Table No. 2

Таблица 3 /Table No. 3

Распределение доз облучения у ликвидаторов в зависимости от места их работы, мЗв

Distribution of Radiation Doses among Liquidators Depending on the Place of Work, mSv

Место получения дозы A place receiving dose	Средняя доза Average dose	Минимальная доза Minimum dose	Максимальная доза Maximum dose
ЧАЭС/ChNPP	55,2	0,1	1478,50
Предприятия Госкорпорации «Росатом» Enterprises of the State Corporation "Rosatom"	180,8	0,1	1832,40
Взвешенная сумма доз Weighted sum of doses	70,5	0,2	1847,72

Таблица 4 /Table No. 4

Значения стратифицированных показателей смертности от гипертонической болезни (на 1000) и ОР для ликвидаторов (мужчины) последствий аварии на ЧАЭС – работников предприятий и организаций Госкорпорации «Росатом» (дозы ЧАЭС)

Values of Stratified Mortality Rates from Essential Hypertension (per 1000) and RR for Liquidators of the Consequences of the Chernobyl Accident, Men - Employees of Enterprises and Organizations of the State Corporation "Rosatom" (Doses of the Chernobyl NPP)

Средняя доза, мЗв Average dose, mSv	Смертность (на 1000) (МКБ 10: I10-I15.9) Mortality (per 1000) (ICD 10: I10-I15.9)	ОР/RR
2,23	1,21	1,00
7,95	0,84	0,70
21,70	1,32	1,09
62,30	1,11	0,92
181,00	0,89	0,74

in risk analysis. The available results of worldwide dosimetry studies also indicate that exposure to the A-bomb cannot be reliably assessed unless medical X-ray doses are fully included in these long-term assessments [19].

For the first time we obtained the results on the assessment of the risk of exposure from the combined dose of two types of exposure. However, the process of collecting complete information is currently in its infancy, and it will be shown in the future how much consideration of medical and natural doses is needed in population risk analysis.

The liquidators in the distant terms of observation after the liquidation of the accident consequences need medical care aimed at the prevention and treatment of such most common and socially significant diseases as cardiovascular diseases.

The results we obtained can be used in the development of radiation safety regulations.

The uniqueness of the liquidator cohort for obtaining direct estimates of the risk of distant effects of radiation ex-

Таблица 5 /Table No. 5

Значения стратифицированных показателей смертности от гипертонической болезни (на 1000) и ОР для ликвидаторов (мужчины) последствий аварии на ЧАЭС – работников предприятий и организаций Госкорпорации «Росатом» (дозы ЧАЭС + профессиональные)

Values of Stratified Mortality Rates from Hypertension (per 1000) and OR for Liquidators (Men) of the Consequences of the Chernobyl Accident - Employees of Enterprises and Organizations of the State Atomic Energy Corporation Rosatom (Doses of ChNPP + Professional)

Средняя доза, мЗв Average dose, mSv	Смертность (на 1000) (МКБ 10: I10-I15.9) Mortality (per 1000) (ICD 10: I10-I15.9)	ОР RR
2,6	1,24	1,00
10,3	1,04	0,84
30,4	1,25	1,00
80,3	0,97	0,78
228,4	0,91	0,74

Таблица 6 /Table No. 6

Оценка радиационных рисков смертности от гипертонической болезни с использованием программы АМФИТ для различных дозовых нагрузок, ИОР/Зв

Estimate of the radiation risks of mortality from hypertension using the AMFIT program for various dose loads (ERR/Sv)

Тип дозы Dose type	ИОР/Зв ERR/Sv	ДИ (95%) CI (95%)
ЧАЭС доза /Chernobyl dose	-0,28	-2,3–2,0
Суммарно с профдозой In total with the professional dose	-0,31	-1,37–1,52

posure at low doses indicates the need for surveillance of this population. Further research involves increasing the statistical power of the analysis by extending the follow-up period, as well as working to reduce uncertainties in dose estimates and to improve the completeness and quality of epidemiological data.

Conclusion

1. Evaluation of the calculation of the risk of death from hypertension using data on the doses of different types of exposure showed no difference in the results obtained.

2. No increase in the risk of death from hypertension was noted with increasing dose.

3. To reliably assess the risk of radiation-induced diseases or death from them it is necessary to create a medical and dosimetric register of nuclear industry workers with data on the doses of all types of exposure — occupational, accidental, medical, natural.

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