Дослідження випадків раку серед довгожительок у Львівській області (Україна) протягом 1991–2019 роках

Наталія Кіцера[1, 2], Ярослав Шпарик[3], Орест Тріль[3], Зоряна Двуліт[4]

[1] *ДУ «Інститут спадкової патології НАМН України», м. Львів, Україна*
[2] *Івано-Франківський національний медичний університет, м. Івано-Франківськ, Україна*
[3] *Львівський онкологічний регіональний лікувально-діагностичний центр, м. Львів, Україна*
[4] *Національний університет «Львівська політехніка», м. Львів, Україна*

Вступ. Злоякісні пухлини є другою провідною причиною смерті у всьому світі.

Мета дослідження. Описати спектр злоякісних пухлин (ЗП) серед жінок-довгожителів у Львівській області (Україна) з бази даних протягом 1991–2019 років.

Матеріал і методи. Ми дослідили 444 жінки-довгожительки віком 90+ з діагностованими ЗП, що проходили лікування та перебували під спостереженням.

Результати. У 104 жінок (23 %) діагностовано ЗП I ступеня, II — у 142 (32 %), III — у 71 (10 %), IV — у 57 (13 %): інші злоякісні новоутворення шкіри (38,29 %), молочної залози (9,46 %), рак товстої кишки (6,98 %) та підшлункової залози (4,95 %). Діагноз підтверджено цитологічно — 169 (38,1 %), гістологічно — 139 (31,3 %). КТ та МРТ застосовувалися у рідкісних випадках у літніх жінок — 11 (2,5 %). Половина жінок (227 або 51,13 %) прожила менше 1 року після встановлення діагнозу. Решта — від 1 до 13 років.

Залежність між тривалістю життя після діагностики ЗП та типом лікування є слабкою (коефіцієнт Крамера K_φ= 0.112; критерій Пірсона K_P= 0.284). Виявлено, що залежність між тривалістю життя після встановлення діагнозу та віком пацієнтів на момент онкологічного діагнозу також є слабкою (коефіцієнт Крамера K_φ= 0.0933; критерій Пірсона K_P= 0.183). Залежність між тривалістю життя після діагностики та стадією раку є сильною (коефіцієнт Крамера K_φ= 0.163; критерій Пірсона K_P= 0.311).

Висновок. Агресивні протипухлинні методи лікування рідше використовуються у хворих на рак у віці 90+, що може бути однією з причин погіршення виживання через супутні захворювання та природні причини. Тривалість життя залежить від стадії ЗП, але не залежить від віку довгожителів та типу лікування.

Ключові слова: злоякісні пухлини, жінки-довгожителі, коефіцієнт Крамера, тривалість життя, Україна.

OPEN ACCESS

DOI 10.25040/ntsh2021.02.18

Адреса для листування: ДУ «Інститут спадкової патології НАМН України», вул. Лисенка, 31 а, Львів, Україна, 79008

E-пошта: nkitsera@gmail.com

Надійшла до редакції: 13.05.2021

Прийнята до друку: 5.07.2021

Опублікована онлайн: 29.12.2021

ORCID IDs
Наталія Кіцера: https://orcid.org/ 0000-0002-6617-9336
Ярослав Шпарик: https://orcid.org/ 0000-0003-2074-6320
Орест Тріль: https://orcid.org/ 0000-0003-0401-8796
Зоряна Двуліт: https://orcid.org/ 0000-0002-2157-1422

Конфлікт інтересів: автори декларують відсутність конфлікту інтересів.

Особистий внесок авторів
Концепція: Наталія Кіцера;
Збирання й аналіз даних: Ярослав Шпарик, Орест Тріль;
Написання: Наталія Кіцера, Зоряна Двуліт;
Редагування та затвердження остаточного варіанта: Наталія Кіцера, Ярослав Шпарик, Зоряна Двуліт.

Дозвіл комісії з біоетики щодо проведення досліджень: для цього дослідження непотрібний.

Фінансування: для цього дослідження непотрібне.

OPEN ACCESS

DOI 10.25040/ntsh2021.02.18

For correspondence: SI «Institute of Hereditary Pathology, National Academy of Medical Sciences of Ukraine», Lviv, Lysenko str. 31-a, Ukraine, 79008

E-mail: nkitsera@gmail.com

Received: May, 13, 2021

Accepted: July, 5, 2021

Published online: Dec, 29, 2021

ORCID IDs
Nataliya Kitsera: https://orcid.org/ 0000-0002-6617-9336
Yaroslav Shparyk: https://orcid.org/ 0000-0003-2074-6320
Orest Tril: https://orcid.org/ 0000-0003-0401-8796
Zoriana Dvulit: https://orcid.org/ 0000-0002-2157-1422

Disclosures: the authors declared no conflict of interest.

Author Contributions
Conceptualization: Nataliya Kitsera;
Results of study: Yaroslav Shparyk, Orest Tril;
Writing: Nataliya Kitsera, Zoriana Dvulit;
Review & editing: Nataliya Kitsera, Yaroslav Shparyk, Zoriana Dvulit.

Ethical approval: not required for this review.

Funding: this review did not require funding.

Research of cancer cases among long-lived women in Lviv region (Ukraine) during 1991–2019 years

Nataliya Kitsera[1, 2], Yaroslav Shparyk[3], Orest Tril[3], Zoriana Dvulit[4]

[1] SI «Institute of Hereditary Pathology, National Academy of Medical Sciences of Ukraine», Lviv, Ukraine
[2] Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine
[3] Lviv Oncological Regional Medical and Diagnostic Center, Lviv, Ukraine
[4] Lviv Polytechnic National University, Lviv, Ukraine

Cancer is the second leading cause of death worldwide.

Aim of our study was to describe the spectrum of cancer among longlivers women in Lviv region (Ukraine) from database during 1991–2019.

Material and methods. We studied 444 longlivers women aged 90+ who were diagnosed of cancer, treated and followed-up.

Results. 104 women (23 %) were diagnosed cancer to stage I, II — 142 (32 %), III — 71 (10 %), IV — 57 (13 %): other malignant neoplasms of skin (38.29 %), breast (9.46 %), colon (6.98 %) and pancreas (4.95 %) cancer. Diagnosis was confirmed cytology — 169 (38.1 %), histology — 139 (31.3 %). CT and MRI were used in rare cases in older women — 11 (2.5 %). Half of the women (227 or 51.13 %) lived beyond 1 year after diagnosis. The rest is from 1 to 13 years.

The relationship between life expectancy after diagnosis of cancer and type of treatment is weak (Cramer ratio K_φ= 0.112; Pearson's criterion K_p= 0.284). Detected that the relationship between life expectancy after diagnosis and the age of patients at the time of oncologic diagnosis is weak too (Cramer ratio K_φ= 0.0933; Pearson's criterion K_p= 0.183). The relationship between life expectancy after diagnosis and stage of cancer is strong (Cramer ratio K_φ= 0.163; Pearson's criterion K_p= 0.311).

Conclusion. Aggressive anticancer treatments are less commonly used in cancer patients aged 90+, which may be one of the reasons for poorer survival due to comorbidities and natural causes. Life expectancy has relationship on the stage of the cancer, but does not have relationship on the age of the long-lived women and the type of treatment.

Keywords: cancer, long-lived women, Cramer ratio, life expectancy, Ukraine.

Introduction

Population aging poses a significant challenge to public health, both in social and health aspects. It is projected that by 2050, people aged above 60 will constitute 80 % of the whole population in the countries of medium and low income [1–2].

Cancer is the second leading cause of death worldwide, with an estimated 9.6 million lives lost in 2018 [2]. Many epidemiological studies study the characteristics of cancer in longlivers [1, 3–5]. In accordance with global trends, there are indications of increased cancer prevalence in Ukraine [6]. Although there are differences in cancer prevalence depending on age, region, rural/urban area, and reporting method (histologically confirmed or clinically diagnosed), cancer remains an important health issue in Ukraine [7–9]. Breast cancer and colon are most commonly diagnosed in older women in Ukraine [6].

Cancer is now widely recognized as a threat to global development. Lacks of situational analyses, prioritization, and budgeting have been identified as major obstacles in fighting cancer [10]. All of these require information on local cancer epidemiology [4; 11]. Aim of our study was to describe the spectrum of cancer among longlivers women in Lviv region from database over 29 years.

Material and methods

Our retrospective study included 444 longlivers women aged over 90 years living in cities and villages of Lviv region (Ukraine) diagnosed with cancer and considered in our study between 1 January 1991 and 31 December 2019 were considered for inclusion. This is a descriptive study of cancer among longlivers women who were born in 1901–1929. The data collected by each administrative district of Lviv region are then submitted to the database. Our database contains cases of various malignancies over 29 years. Mortality and treatment data were collected from electronic clinical notes, general practice records and public records.

To confirm or refute the existence of a relationship between life expectancy after oncologic diagnosis and other signs, were made three null hypotheses about the absence of such relationship, depending on the age of the patient, the stage of the disease, and the type of treatment.

To determine the relationship between life expectancy after diagnosis and the main factors that determine it used non-parametric methods of analysis. They are used to determine the statistical dependences in the study of the correlation of attributive features in the conjunction tables, the Pearson criterion (χ^2), the information test criterion, the Cramer ratio [12–13].

Results

In Lviv region (Ukraine) according to the Statistical office in January, 2018 population was 2 511 238 persons, including 1 320 689 women (52.6 %). The population more 90 years numbers 10 316 persons, in particular 8 111 (78.6 %) women [14].

The conducted research on the problem of cancer epidemiology among longlivers women in the Lviv region for the 29 studied years in the period from 1991 to 2019, made it possible to carry out structural analysis in different sections (method of confirmation of diagnosis, ICD-10-CM code, stage of disease, morphological type of diagnosis, type treatment, place of residence).

The frequency of distribution of longlivers women by habitat showed that about 71 % of these patients lived in cities, 29 % in villages. In terms of age categories, the largest share was in the interval of 90–92 years (approximately 60 % or 270 women), almost 29 % — aged 93–95. The remaining 11 % were women aged over 96. The median of age was 92,4±6.4.

The conducted research of diagnosed longlived women made it possible to distinguish and systematize their distribution by the codes of ICD by rating (TOP-10) in descending order, which is presented in the form of Table 1. It is worth noting that these were the 10 most frequently diagnosed and established 2/3 of the total sample (342 patients or 77.03 %), of which 207 women were 90–92 years old, and 100 — aged 93–95.

The highest frequency occurred in the diagnosis of C44 (other malignant neoplasms), which was found in 170 (38 %) women of the total sample, 23.87 % of which were women aged 90–92, and every tenth was aged 93–95. Due

Table 1

Distribution of longlivers women by age and most commonly observed ICD-10 codes in Lviv region (West Ukraine), 1991–2019

№	Code of ICD-10	Diagnosis of malignant neoplasms	Years								All	
			90–92		93–95		96–98		99–101			
			n	%	n	%	n	%	n	%	n	%
1	C44	Other malignant neoplasms of skin	106	23.87	46	10.36	16	3.60	2	0.45	170	38,29
2	C50	Breast	23	5.18	16	3.60	2	0.45	1	0.23	42	9,46
3	C18	Colon	17	3.83	9	2.03	3	0.68	2	0.45	31	6,98
4	C25	Pancreas	11	2.48	8	1.80	2	0.45	1	0.23	22	4,95
5	C16	Stomach	13	2.93	6	1.35	1	0.23	0	0.00	20	4,50
6	C34	Bronchus and lung	9	2.03	4	0.90	1	0.23	1	0.23	15	3.38
7	C20	Rectum	8	1.80	4	0.90	0	0.00	0	0.00	12	2,70
8	C67	Bladder	6	1.35	5	1.13	0	0.00	0	0.00	11	2,48
9	C00	Lip	8	1.80	1	0.23	1	0.23	0	0.00	10	2.25
10	C56	Ovary	6	1.35	1	0.23	1	0.23	1	0.23	9	2,03
Total			207	46.62	100	22.52	27	6.08	8	1.80	342	77.03

attention should be paid to the fact that more than a third of patients have non-melanoma skin conditions, which are mostly not prognostically serious diseases and therefore in most countries are not included in onco-epidemiological projects and examinations [15].

From the total sample (444 women), one third of diagnoses were 5 ICD codes of cancer (C50 breast, C18 colon, C25 pancreatic, C16 stomach, C34 lung and bronchial). The most common breast cancer was C50 in women aged 90–92. As a result of this cancer, it was generally diagnosed for 42 women who are long-lived, that is, in every tenth patient. The pancreatic C25 (22 females) and stomach cancer C16 (20 females) were also characterized by the highest prevalence among women aged 90–92.

In the TOP-10 diagnoses for women aged 90+, the last 4 places ranked those diseases that were also diagnosed in 42 patients.

Among 444 women met only14 diagnoses of malignant neoplasm (C05 — palate, C07 — parotid gland, C15 — esophagus, C17 — small intestine, C21 — anus and anal canal, C31 — accessory sinuses, C32 — larynx, C40 — bone and articular cartilage of limbs, C41 — bone and articular cartilage of other and unspecified sites, C52 — vagina, C71 — brain, C77 — secondary and unspecified malignant neoplasm of lymph nodes, C81 — Hodgkin lymphoma, C94 — other leukemias of specified cell type) with 1 case. On 2 cases were established on 5 diagnoses of malignant neoplasm (C02 — other and unspecified parts of tongue, C08 — other and unspecified major salivary glands, C23 — gallbladder, C48 — retroperitoneum and peritoneum, C79 — secondary malignant neoplasm of other and unspecified sites).

After systematization of data we made the following conclusions:

- 104 women or 23 % of the whole sample applied to stage I cancer. One third of the subjects who accounted for the largest proportion had stage II cancer — 142 (32 %). The third stage was diagnosed in 71 (10 %) cases. 70 patients were not accurately established the stage of the disease. 57 (13 %) women over the age of 90 applied for stage IV;
- half of the women (227 or 51.13 %) lived beyond 1 year after diagnosis. The rest is from 1 to 13 years. Up to 2 years after diagnosis — 95 (21.4 %). One in ten women lived for another 3 years. More than 10 years have passed since the diagnosis of 5 women (Table 2).

Two main methods of confirming the diagnosis — cytologic — 169 (38.1 %) cases and histologic — 139 (31.3 %) cases. CT and MRI were used in rare cases in older patients — 11(2.5 %).

Table 2

Life expectancy of longlivers women after diagnosis and stage of cancer in Lviv region (West Ukraine), 1991–2019

Years	Stage										All	
	I		II		III		IV		Not set			
	n	%	n	%	n	%	n	%	n	%	n	%
Up to 1 year	44	9.91	60	13.51	41	9.23	44	9.91	38	8.56	227	51.13
1	14	3.15	37	8.33	15	3.38	11	2.48	18	4.05	95	21.40
2	11	2.48	16	3.60	7	1.58	1	0.23	6	1.35	41	9.23
3	8	1.80	7	1.58	2	0.45	1	0.23	3	0.68	21	4.73
4	10	2.25	8	1.80	3	0.68	0	0.00	3	0.68	24	5.41
5	9	2.03	6	1.35	1	0.23	0	0.00	2	0.45	18	4.05
6	1	0.23	3	0.68	2	0.45	0	0.00	0	0.00	6	1.35
7	2	0.45	0	0.00	0	0.00	0	0.00	0	0.00	2	0.45
8	2	0.45	2	0.45	0	0.00	0	0.00	0	0.00	4	0.90
9	1	0.23	0	0.00	0	0.00	0	0.00	0	0.00	1	0.23
10	1	0.23	1	0.23	0	0.00	0	0.00	0	0.00	2	0.45
11	1	0.23	1	0.23	0	0.00	0	0.00	0	0.00	2	0.45
12	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
13	0	0.00	1	0.23	0	0.00	0	0.00	0	0.00	1	0.23
Total	104	23.42	142	31.98	71	15.99	57	12.838	70	15.77	444	100.00

If we analyze the life expectancy of the patients and the age at which the diagnosis was made, almost half (45.5 %) of the patients were aged 90–92; 130 women had a diagnosis date of 92–93, 67 patients were 94–95 years old (Table 3).

Nearly 8 % had long-lived patients aged 96 to 97 years, and 2.5 % were over 98 years of age. Almost one in four patients (98 people) aged 90 to 91 died from dying within 1 year, 14 % died by 2 years; 15 % of women, aged 92–93, also did not live to 1 year. Moreover, with increasing age, the proportion of those who did not live to 1 year decreased. The same tendency was observed in the index of life expectancy at intervals of 1–2, 3–4, 5–6 and more than 6 years. The pattern of distribution of life expectancy after diagnosis and the age of patients demonstrates this feature. For all age intervals except those over the age of 98, there was a decrease in life expectancy over time. That is, most of them died without living even 1 year after diagnosis.

In the study of the types of treatment, the following were used: refused, hormone-therapy, general, not subject to treatment, non-specific, radiotherapy, chemo-therapy and surgery (Table 4). Data were given on the types of treatment for 339 (76.4 %) of 444 women, and for the remaining 105 (23.6 %) women no information was available. Among these 339 patients, there were 36 women or 10.62 % who refused treatment and 5 or 1.47 % who were not treated. For half of this sample

Table 3

Life expectancy for longlivers women, depending on age at diagnosis in Lviv region (West Ukraine), 1991–2019

Years	Age										All	
	90–91		92–93		94–95		96–97		more than 98			
	n	%	n	%	n	%	n	%	n	%	N	%
Up to 1 year	98	22.07	66	14.86	38	8.56	21	4.73	4	0.90	227	51.13
1–2	62	13.96	39	8.78	21	4.73	8	1.80	6	1.35	136	30.63
3–4	20	4.50	14	3.15	7	1.58	3	0.68	1	0.23	45	10.14
5–6	17	3.83	5	1.13	1	0.23	1	0.23	0	0.00	24	5.41
More than 6	5	1.13	6	1.35	0	0.00	1	0.23	0	0.00	12	2.70
Total	202	45.50	130	29.28	67	15.09	34	7.66	11	2.48	444	100.00

surgery was used, chemotherapy was intended for 14 patients, and half of them survived up to 1 year. One in five long-lived patients received radiotherapy and 44 (12.98 %) patients received symptomatic treatment. The longest patient has undergone 13 years of radiotherapy. Hormone therapy were prescribed for 7 patients. The majority of those who didn't live to 1 year were those who had surgery. Most longlivers women lived the least time (up to 2 years) — 231 persons (78.14 %) or 2/3 of the total number of patients. However, 91 (11.5 %) longlivers women lived to 5 years. Five women (1.47 %) have lived for ten years or more since cancer was diagnosed.

Three null hypotheses (with a probability of 0.95) for the independence of the relations between the longevity of women with longevity and their oncological diagnosis have been put forward: 1) type of treatment of the patient; 2) stage of cancer; 3) women age.

A sample distribution of the sign «A» was obtained depending on «B«. To test the independence of signs «A» and «B» let's test the null hypothesis. Non-parametric methods of analysis are proposed to evaluate the relationships between attribute attributes. Qualitative data is presented in the form of a statistical table, which can be used to calculate the frequency and proportions of the presented feature categories. To this end, we use conjunction tables to illustrate relationships. The estimation of the interconnection density is based on the deviations of the frequencies of the conditional and unconditional distributions, that is, the deviations of the actual frequencies n_{ij} from the theoretical ones N_{ij}.

The absolute value of these deviations is characterized by the statistical criterion calculated χ^2:

$$\chi^2 = \sum\sum \frac{(n_{ij} - N_{ij})^2}{N_{ij}}, \qquad (1)$$

where n_{ij} — the actual frequencies,
N_{ij} — theoretical frequencies.

Theoretical frequencies are calculated by the formula:

$$N_{ij} = \frac{N_i \cdot N_j}{n}, \qquad (2)$$

n — number of observations.

Only 339 of the 444 women surveyed were taken to examine the relationship between attributional traits, namely life expectancy

Table 4

Life expectancy for longlivers women, depending on the type of treatment in Lviv region (West Ukraine), 1991–2019

Years	Type of treatment																All	
	Surgery		Radio-the-rapy		Refused		General (symptom-atic)		Chemo-therapy		Non-specific (herbal)		Hor-mone-therapy		Not subject to treatment			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Up to 1 year	79	23.3	23	6.78	14	4.13	19	5.60	7	2.06	5	1.47	2	0.59	4	1.18	153	45.13
1	33	9.73	15	4.42	11	3.24	9	2.65	5	1.47	2	0.59	3	0.88	0	0.00	78	23.01
2	15	4.42	9	2.65	3	0.88	3	0.88	1	0.29	1	0.29	2	0.59	0	0.00	34	10.03
3	10	2.95	4	1.18	2	0.59	2	0.59	0	0.00	0	0.00	0	0.00	0	0.00	18	5.31
4	12	3.54	7	2.06	1	0.29	2	0.59	0	0.00	0	0.00	0	0.00	0	0.00	22	6.49
5	9	2.65	4	1.18	2	0.59	0	0.00	1	0.29	0	0.00	0	0.00	1	0.29	17	5.01
6	3	0.88	1	0.29	1	0.29	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	5	1.47
7	1	0.29	0	0.00	1	0.29	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	2	0.59
8	1	0.29	1	0.29	1	0.29	1	0.29	0	0.00	0	0.00	0	0.00	0	0.00	4	1.18
9	1	0.29	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	0.29
10	2	0.59	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	2	0.59
11	1	0.29	1	0.29	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	2	0.59
12	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
13	0	0.00	1	0.29	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	0.29
Total	167	49.26	66	19.47	36	10.62	36	10.62	14	4.13	8	2.36	7	2.06	5	1.47	339	100.00

after diagnosis and type of treatment. This is because 339 women were treated and 105 women were missing information. According to the data (sign «A» means type of treatment, among them — refused (A1), hormone-therapy (A2), general (A3), not subject to treatment (A4), non-specific (A5), radiotherapy (A6), chemo-therapy (A7) and surgery (A8); sign «B» identify life expectancy after diagnosis — < 1 year (B1), 1 (B2), 2 (B3), 3 (B4), 4 (B5), 5 (B6), 6 (B7), > 6 (B8)), we calculate the values of theoretical frequencies for each cell in the table. As a result, we obtain a conjunction table of theoretical frequencies of distribution. We find the value of the statistical criterion χ^2 for verifying A's independence from B. The significance of the connection is made on the basis of a comparison of the theoretical value χ^2 with the critical one χ^2. If χ^2*calculated* > χ^2critical, then relation is essential, and vice versa. In other words, if $\chi^2 < \chi^2$ critical, then the hypothesis of random distribution is rejected.

The estimated value of statistics is 29.717.

The theoretical value χ^2 depends on the significance level α and the number of degree of freedom of the tables of the intersection.

According to the table χ^2— distribution we find:

$$\chi^2 \text{ crit } (0{,}05;\ 49) = 67.50481,$$

where v = (r-1) (s-1) = (8-1) (8-1) = 49 — is the number of degree of freedom.

The critical area: $\chi^2_{calculated} > \chi^2$crit. Since the calculated value χ^2 does not fall into the critical range, the independence hypothesis is accepted with a probability of error of 0.05.

We apply the information criterion χ_I^2 for testing this hypothesis of independence of features.

$$\chi_I^2 = 2\sum\sum n_{ij} \ln\frac{n_{ij}}{N_{ij}}, \qquad (3)$$

χ_I^2=37.5.

Critical area when testing the specified hypothesis: $\chi_I^2 > \chi_I^2$ *table* = 67.50481

Since χ_I^2 = 37.5 and does not fall into the critical range, the hypothesis is accepted with a probability of error of 0.05.

Let's determine the closeness of the relationship using the coefficients of conjugation. To do this, we calculate the Cramer coupling coefficient and the Pearson coupling criterion. The values of the coefficients vary from 0 to 1. If the coefficients are 0, then the link is missing, if 1, then the link is functional.

The Cramer ratio is calculated by the formula:

$$K\varphi = \sqrt{\frac{\chi^2}{n\cdot\min[r-1;s-1]}}, \qquad (4)$$

$$K\varphi = \sqrt{\frac{29.717}{339\cdot\min[8-1;8-1]}} = 0.112\cdot$$

Pearson's creterion is calculated by the following formula:

$$K_P = \sqrt{\frac{\chi^2}{\chi^2+n}} \qquad (5)$$

The calculated value of this coefficient is:

$$K_P = \sqrt{\frac{29.717}{29.717+339}} = 0.284$$

The calculated values of the coefficients K_φ and K_P we can conclude that the connection between «A» and «B» is weak. The relationship between life expectancy after diagnosis and type of treatment is weak. Null hypothesis is confirmed. The first hypothesis that there is a link between life expectancy and the type of treatment of patients is rejected.

Let's test the second hypothesis, the independence of life expectancy of female patients from the stage of cancer. According to the data (sign «A» means stage of cancer, among them — stage I (A1), stage II (A2), stage III (A3), stage IV (A4), not set (A5); sign «B» identify life expectancy after diagnosis — < 1 year (B1), 1–2 (B2), 3–4 (B3), 5–6 (B4), > 6 (B5)) (fig.1).

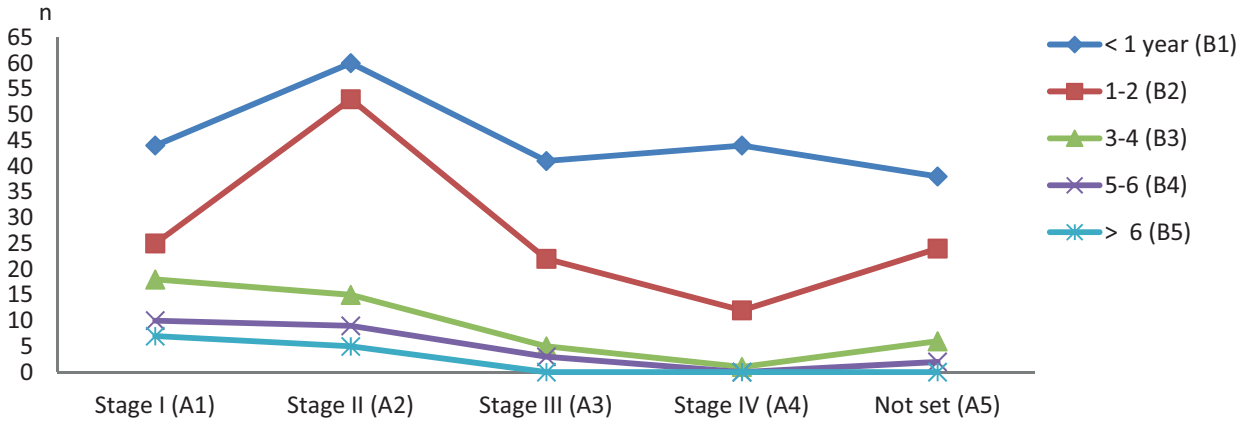

Figure 1. Life expectancy for women who are longlivers, depending on the stage of cancer in Lviv region (West Ukraine), 1991–2019

The calculated value of statistics χ^2 is 47.441.

According to the table χ^2 — distribution we find:

$$\chi^2 \text{ crit } (0{,}05;\ 16) = 26.29623,$$

where v = (r-1) (s-1) = (5-1) (5-1) = 16 — is the number of degree of freedom.

The critical area $-\chi^2_{calculated} > \chi^2$crit. As the calculated value χ^2 falls in the critical range, the independence hypothesis is rejected with a probability of error of 0.05.

We apply the information criterion χ_I^2 for testing this hypothesis of independence of features.

$$\chi_I^2 = 54.14.$$

Critical area for testing this hypothesis: $\chi_I^2 > \chi_I^2\,table = 26.29623$

Since χ_I^2 = 54.14 and falls into the critical range, the hypothesis is rejected with a probability of error of 0.05.

The coefficients of conjugation.

$$K\varphi = \sqrt{\frac{47.441}{444 \cdot \min[5-1;5-1]}} = 0.163.$$

Pearson Mutual criterion:

$$K_P = \sqrt{\frac{47.441}{47.441 + 444}} = 0.311$$

After calculated values of the coefficients K_φ and K_P we can conclude that the relationship between «A» and «B» is strong. The relationship between life expectancy after diagnosis and stage of cancer is strong. Null hypothesis is rejected. The alternative hypothesis that there is a link between life expectancy of female patients from the stage of cancer is confirmed.

Let's test the third hypothesis, the independence of life expectancy of female patients from the age at which they were diagnosed. According to the data (sign «A» means the age at which they were diagnosed, among them — 90–91 (A1), 92–93 (A2), 94–95 (A3), 96–97 (A4), >98 (A5); sign «B» identify life expectancy after diagnosis — < 1 year (B1), 1–2 (B2), 3–4 (B3), 5–6 (B4), > 6 (B5)).

The calculated value of statistics χ^2 is 15.443.

According to the table χ^2 — distribution we find:

$$\chi^2 \text{ crit } (0{,}05;\ 16) = 26.29623,$$

where v = (r-1) (s-1) = (5-1) (5-1) = 16 — is the number of degrees of freedom.

The critical area $-\chi^2_{calculated} > \chi^2$crit. Since the calculated value χ^2 does not fall into the critical range, the independence hypothesis is accepted with a probability of error of 0.05.

We apply the information criterion χ_I^2 for testing this hypothesis of independence of features.

$$\chi_I^2 = 17.91.$$

Critical area for testing this hypothesis: $\chi_I^2 > \chi_I^2 table = 26.29623$

Since $\chi_I^2 = 17.91$ and does not fall into the critical range, the hypothesis is accepted with a probability of error of 0.05.

The Cramer ratio is:

$$K\varphi = \sqrt{\frac{15.443}{444 \cdot \min[5-1;5-1]}} = 0.0933$$

Pearson Mutual criterion:

$$K_P = \sqrt{\frac{15.443}{15.443+444}} = 0.183$$

According to the calculated values of the coefficients K_φ and K_P we can conclude that the connection between «A» and «B» is weak. The relationship between life expectancy after diagnosis and the age of patients at the time of oncologic diagnosis is weak. Null hypothesis is confirmed. The first hypothesis that there is a link between life expectancy of female patients from the age at which they were diagnosed is rejected.

Discussion

In 2019, there were 1 014 352 patients with oncology on the register of oncological clinics of Ukraine, including 657 424 women. Leading place in the structure of patients is occupied by non-melanoma of skin (17.1 %), breast (23.1 %), uterine corpus (12.2 %) and cervix (8.4 %) of the uterus, as well as colorectal cancer (8.1 %) [6].

We found in our region that the prevalence of colorectal cancer is increasing in the elderly women. Our data agree with the researchers from United Kingdom of Great Britain [16].

Research results in Lviv region (West Ukraine) are updated on an annual basis. In this article we focus on changes over the past decade and present the most recent research results based on the cancer registry and vital registration data to estimate the burden of cancer in Lviv region from 1991 to 2017. The data cover the Lviv region and contain at least some estimates of cancer survival based on the population of 2.5 million people in the region, including 8111 female longlivers [14].

In our study, the majority of women — 71 % lived in the city, and only less than a third in the village, and our data are consistent with the data of Chinese scientists [17].

In Ukraine, people over the age of 75 make up 21.6 % of sick women. And in the age structure of mortality it is, accordingly, 29.2 % [6]. That is, malignant neoplasms in the older age group are slightly more likely to cause death. This may be due to the fact that patients with older cancer are more likely to receive suboptimal treatment (often due to the presence of concomitant pathology) [18–20]. Because in old age it is often impossible to perform biopsies for medical reasons or do a CT scan due to patient non-transportability, patients are diagnosed with cancer clinically.

These findings highlight health risks among female longlivers in Ukraine. Our analysis shows that cancer has become a major health problem and there are significant issues related to the treatment and care of such patients [11; 21].

This is even more true for the group of longlivers women from Lviv region (West Ukraine), in which a significant part of patients did not receive treatment 41 (12.1 %). In the group of longlivers people analyzed by us, special treatment (surgery and chemotherapy) was received by 53.4 % (181 women). But, apparently, these data are actually lower, because the deterioration of health in this group is more often due to «age changes» or common diseases, due to which the detection of malignant disease, and even more so the diagnosis is not clarified. The same features of the treatment of older women are pointed out by other scientists [22].

It should be borne in mind that such patients cannot always be prescribed specific treatment for safety reasons. In our study, refusal from treatment ranks third after surgery and radiotherapy. Among the 339 female longlivers, about whose survival we were able to gather reliable information, 55.16 % lived for five years or more, which coincides with other studies, where this indicator was 50–70 % [21].

Despite being cancer the most common disease in many populations, cancer incidence data are very important. Statistics on the incidence of malignant tumors are quite well developed not only in some countries but also around the world. Among the indicators analyzed, morbidity in different age groups is important, in particular among long-lived.

In recent decades, life expectancy has increased, and the number of older people has increased. According to the WHO classification, people over the age of 90 belong to the category of «long-lived» (age 90+). The WHO classification is used in the analysis of statistics on morbidity and mortality from malignant tumors, but the statistics of these indicators in the 90+ group are limited due to the small number of long-lived people. American authors have analyzed in detail the cancer statistics in the elder people [23]. Our report refers to the group of long-lived according to the WHO classification (more 90+). This group is less than 0.5 % of the total population, but is important for analysis because it can be the basis for important conclusions about differences in carcinogenesis in different age groups.

According to the Cancer Registry of Ukraine [6], the incidence of cancer (excluding non-melanoma malignant skin neoplasms) among women gradually increases with age (is the maximum in 2018). Apparently in the group of long-lived (90+ years) we can expect an even greater reduction in morbidity. This phenomenon is explained by two main reasons:

1) Insufficient diagnosis due to the presence of severe comorbidities, reduced basic functional indicators, which does not allow to apply adequate diagnostic measures, social isolation. The same reasons explain the relatively lower percentage of morphological confirmation of the diagnosis (a significant proportion of tumors of internal organs are diagnosed only by clinical and radiological methods). The importance of this factor is confirmed by the fact that studies on detailed postmortem autopsy in the elderly often find undiagnosed lifelong undiagnosed tumors [24–25].

2) Decreased incidence of cancer in old age may reflect less genetic susceptibility or the effects of the natural aging process, which contribute to the inhibition of tumor growth [26].

If we analyze the changes in the structure of the five most common malignancies depending on age, it can be noted that women with age increase the incidence of colorectal cancer and breast cancer (instead, the incidence of cervical and ovarian cancer) [6]. The most common malignant tumors among women aged 90+ in the Lviv region were non-melanoma skin tumors, and the rest (in decreasing frequency) — colorectal cancers, breast cancer, pancreas, stomach, lung. This list differs slightly from the statistics of patients in the United States, where breast cancer, colorectal cancer, lung and pancreatic cancer [23] are the most common. This can be explained by the difference in the dynamics of smoking among women (in particular, the higher incidence of lung cancer in the US) and the peculiarities of the cancer epidemiology in Ukraine (relatively high incidence of gastric cancer), while in the US this type of cancer is not among the ten most common. morbidity or mortality).

Aggressive anticancer treatments (including extensive surgery and infusion chemotherapy) are less commonly used in cancer patients aged 90+, which may be one of the reasons for poorer survival than in younger age groups [27–28]. Life expectancy has relationship on the stage of the cancer, but does not have relationship on the age of the long-lived women and the type of treatment. Until now, elderly patients (especially those with comorbidities) are rarely included in clinical trials that study the treatment of malignancies, which narrows the evidence base for treatment recommendations [29]. In addition, the lower survival in this group is due to comorbidities and natural causes. In conclusions:

1. Our retrospective study included 444 longlivers women from Lviv region (Ukraine) aged over 90 diagnosed with cancer during 1991–2019. The median of age was 92,4±6.4 years, 71 % of longlivers women lived in cities and the remaining 29 % lived in villages.
2. Most often, during these 29 years, longlivers women had other malignant neoplasms of skin (38.29 %), breast (9.46 %), colon (6.98 %) and pancreas (4.95 %) cancer.
3. The relationship between life expectancy after diagnosis of cancer and type of treatment

is weak (Cramer ratio K_φ = 0.112; Pearson's criterion K_p = 0.284). Null hypothesis is confirmed. The first hypothesis that there is a link between life expectancy and the type of treatment of patients is rejected.

4. The relationship between life expectancy after diagnosis and stage of cancer is strong (Cramer ratio K_φ = 0.163; Pearson's criterion K_p = 0.311).
5. Detected that the relationship between life expectancy after diagnosis and the age of patients at the time of oncologic diagnosis is weak (Cramer ratio K_φ = 0.0933; Pearson's criterion K_p = 0.183).

Aggressive anticancer treatments (including extensive surgery and infusion chemotherapy) are less commonly used in cancer patients aged 90+, which may be one of the reasons for poorer survival due to comorbidities and natural causes. Life expectancy has relationship on the stage of the cancer, but does not have relationship on the age of the long-lived women and the type of treatment.

References

1. Arem H, Loftfield E. Cancer Epidemiology: A Survey of Modifiable Risk Factors for Prevention and Survivorship. Am J Lifestyle Med. 2018; 12 (3): 200–210. DOI: 10.1177/1559827617700600
2. WHO. Cancer key facts. Geneva: WHO; 2018. https://www.who.int/news-room/fact-sheets/detail/cancer.
3. Legrand R, Manckoundia P, Nuemi G, Poulain M. Assessment of the Health Status of the Oldest Olds Living on the Greek Island of Ikaria: A Population Based-Study in a Blue Zone. Curr Gerontol Geriatr Res. 2019; 2019: 8194310. DOI: 10.1155/2019/8194310. eCollection 2019.
4. Hotta S, Kameyama H, Shimada Y, Yamada S, Tanaka K, Tajima Y et al. A Case of Long-Term Survival in a Patient with Ascending Colon Cancer and Synchronous Multiple Liver Metastases after Multimodality Therapy Including Multiple Hepatectomy. Gan To Kagaku Ryoho. 2018;45(13): 2464–2466.
5. Presley C J, Dotan E, Soto-Perez-de-Celis E. Jatoi A, Mohile SG, Won E et al. Gaps in nutritional research among older adults with cancer. J Geriatr Oncol. 2016; 7 (4): 281–292.
6. Bulletin of National Cancer Registry of Ukraine. Cancer in Ukraine, 2018–2019. V.21. http://www.ncru.inf.ua/publications/BULL_21/index_e.htm
7. Evaluation of data quality at the National Cancer Registry of Ukraine. Ryzhov A, Bray F, Ferlay J, Fedorenko Z, Goulak L, Gorokh Y et al. Cancer Epidemiol. 2018;53:156-165. DOI: 10.1016/j.canep.2018.02.002.
8. Situation of older women in Ukraine (2014). Analytical report/ http://www.un.org.ua/en/
9. Grybach S.M., Polishchuk L.Z, Chekhun V.F Analysis of the survival of patients with breast cancer depending on age, molecular subtype of tumor and metabolic syndrome.Exp Oncol. 2018; 40 (3): 243–248.
10. Morrow M., Petruolo O. Breast Cancer in Elderly Women. Principles and Practice of Geriatric Surgery. 2017. 1–25. DOI: https://doi.org/10.1007/978-3-319-20317-1_63-1
11. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2017: A Systematic Analysis for the Global Burden of Disease Study. Global Burden of Disease Cancer Collaboration, Christina Fitzmaurice, Degu Abate, Naghmeh Abbasi et al. JAMA Oncol. 2019; 5(12): 1749–1768. DOI: 10.1001/jamaoncol.2019.2996
12. Bakhrushin VE .Methods of data analysis. A textbook for students. Zaporizhzhya: KPU, 2011. 268 p. [in Ukrainian].
13. The encyclopaedic companion to medical statistics / ed. by Brian S. Everitt and Christopher R. Palmer; with foreword R. Horton. 2nd ed.2011. 516 p. ISBN: 978-0-470-68419-1.
14. Population of Ukraine. http://lv.ukrstat.gov.ua/ukr/
15. Cancer Incidence in Five Continents. Ferlay J, Kraywinkel K, Rous B, Znaor A. Chapter 3: Classification and coding. https://ci5.iarc.fr/CI5-XI/PDF/Chapter %203.pdf
16. Ng O, Watts E, Bull CA, Morris R, Acheson A, Banerjea A. Colorectal cancer outcomes in patients aged over 85 years Ann R Coll Surg Engl. 2016; 98 (3): 216–221. DOI: 10.1308/rcsann.2016.0085
17. Huang Y, Dai H, Song F, Li H, Yan Y, Yang Z et al. Preliminary effectiveness of breast cancer screening among 1.22 million Chinese females and different cancer patterns between urban and rural women. Sci Rep. 2016; 6: 39459. DOI: 10.1038/srep39459
18. Chargari C, Moriceau G, Auberdiac P, Guy J-B, Assouline A, Tinquaut F et al. Feasibility of Radiation Therapy in Patients 90 years of Age and Older: A French Multicentre Analysis. Eur J Cancer. 2014; 50 (8): 1490–1497. DOI: 10.1016/j.ejca.2014.02.012.
19. Suhag V, Sunita BS, Vats P, Singh S, Jain M, Vashisht R. Radiotherapy and geriatric cancer patients: A

single institute experience. Indian J Med Sci. 2019; 71 (1): 28–34.
20. Hurria A, Soto-Perez-de-Celis E, Allred JB, Cohen HJ, Arsenyan A, Ballman K. Functional Decline and Resilience among Older Women Receiving Adjuvant Chemotherapy for Breast Cancer. J Am Geriatr Soc. 2019; 67 (5): 920–927.
21. Allemani C, Weir HK, Carreira H, Harewood R, Spika D, Wang X-S et al. Global surveillance of cancer survival 1995–2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet. 2015; 385 (9972): 977–1010. DOI: 10.1016/S0140-6736(14)62038-9
22. Mandelblatt JS, Cai L, Luta G, Kimmick G, Clapp J, Isaac C et al. Frailty and Long-term Mortality Of Older Breast Cancer Patients: CALGB 369901 (Alliance). Breast Cancer Res Treat. 2017; 164(1): 107–117. DOI: 10.1007/s10549-017-4222-8.
23. DeSantis CE, Miller KD, Dale W, Mohile SG, Cohen HJ, Leach CR et al. Cancer statistics for adults aged 85 years and older, 2019. CA Cancer J Clin. 2019; 69 (6): 452–467.
24. Pavlidis N, Stanta G, Audisio RA. Cancer prevalence and mortality in centenarians: a systematic review. Crit Rev Oncol Hematol. 2012; 83 (1): 145–152.
25. Stanta G, Campagner L, Cavallieri F, Giarelli L. Cancer of the oldest old. What we have learned from autopsy studies. Clin Geriatr Med. 1997; 13 (1): 55–68.
26. Amin A.R.M, Karpowicz PA, Carey TE, Arbiser J, Nahta R, Chen ZG et al. Evasion of anti-growth signaling: a key step in tumorigenesis and potential target for treatment and prophylaxis by natural compounds. Semin Cancer Biol. 2015; 35 Suppl: S55–S77. DOI: 10.1016/j.semcancer.2015.02.005
27. Mohile SG, Dale W, Somerfield MR, Schonberg MA, Boyd CM, Burhenn PS et al. Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Chemotherapy: ASCO Guideline for Geriatric Oncology. J Clin Oncol. 2018; 36 (22): 2326–2347. DOI: 10.1200/JCO.2018.78.8687
28. Schwartz RM, Ornstein KA, Liu B, Alpert N, Bevilacqua KG, Taioli E. Change in Quality of Life after a Cancer Diagnosis among a Nationally Representative Cohort of Older Adults in the US. Cancer Invest. 2019; 37(7): 299–310. DOI: 10.1080/07357907.2019.1645160
29. Mohile SG, Hurria A, Cohen HJ, Rowland JH, Leach CR, Arora NK, Canin B et al. Improving the Quality of Survivorship for Older Adults with Cancer. Cancer. 2016; 122 (16): 2459–2568. DOI: 10.1002/cncr.30053.