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THE SURVIVAL FORECAST IN PATIENT WITH PNEUMONIA AND IMMUNITY DISORDERS ON A BACKGROUND OF THE ONCOHEMATOLOGICAL DISEASE

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ПРОГНОЗ ВЫЖИВАЕМОСТИ БОЛЬНЫХ ПНЕВМОНИЕЙ С НАРУШЕНИЯМИ ИММУНИТЕТА НА ФОНЕ ОНКОГЕМАТОЛОГИЧЕСКОЙ ПАТОЛОГИИ

ГУ «Днепропетровская медицинская академия МЗ Украины», Днепр, Украина

Цель исследования — определение факторов, обусловливающих выживаемость больных пневмонией на основе изучения комплекса клинико-лабораторных, анамнестических и иммунологических показателей больных пневмонией с нарушениями иммунитета на фоне онкогематологической патологии.

Независимыми предикторами, которые непосредственно влияли на выживаемость больных пневмонией на фоне онкогематологической патологии, были: грамотрицательные возбудители, количество эритроцитов и нейтрофилов, количество курсов химиотерапии и показатель иммунорегуляторного индекса. Коварианты благоприятного прогноза: количество курсов химиотерапии меньше 8; показатель количества эритроцитов больше $2{,}0 \cdot 10^{12}$/л; показатель иммунорегуляторного индекса больше 1,09. Коварианты неблагоприятного прогноза событий: количество курсов химиотерапии 8 и больше; наличие грамотрицательных возбудителей; показатель количества эритроцитов меньше $2{,}0 \cdot 10^{12}$/л; показатель иммунорегуляторного индекса меньше 1,09.

Анализ выживаемости больных пневмонией на фоне онкогематологической патологии с учетом ковариантов неблагоприятного развития событий доказал, что этот показатель в течение месяца будет составлять 30 %, при благоприятном прогнозе — 96 %.

Ключевые слова: пневмония, выживаемость, нарушение иммунитета, летальный исход.

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THE SURVIVAL FORECAST IN PATIENT WITH PNEUMONIA AND IMMUNITY DISORDERS ON A BACKGROUND OF THE ONCOHEMATOLOGICAL DISEASE

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The aim of the study: to determine the factors that cause the survival of patients with pneumonia, based on the study of complex, clinical and laboratory, anamnestic and immunological parameters of patients with pneumonia with immune disorders on the background of oncohematological pathology.

Materials and methods. To solve the problem, a computer database of the results of the examination of 811 patients with lesions of the broncho-pulmonary system on the background of oncohe-

matological pathology was created. The study was conducted in two stages in the haematological center "Multifunctional Clinical Hospital № 4", Dnipro, 2010–2016. The retrospective stage included the analysis of archival data of 535 cases of hospitalizations of patients with oncohematological pathology; prospective phase — a study of 276 cases of hospitalizations. Diagnosis of oncohematological diseases was determined according to generally accepted clinical and morphological criteria. The diagnosis of pneumonia was verified in accordance with the "Order of the Ministry of Health of Ukraine No. 128, March 19, 2007". We studied and analyzed the indices that characterizing the general condition of the patient; anamnestic information about the course of the main disease and peculiarities of the course of the broncho-pulmonary system disease in the dynamics. Features of infectious defeat of the bronchopulmonary system in the studied patients were studied regardless of the phase of the course of the underlying disease. The statistical processing of the research results was carried out using descriptive and analytical biostatistics methods implemented in software packages STATISTICA 6.1 (StatSoftInc., Serial No. AGAR909E415822FA); Microsoft Excel (Office Home Business 2KB4Y-6H9DB-BM47K-749PV-PG3KT). Median (Me) as a measure of the central tendency was used to describe the quantitative characteristics; interquartile scale ((25%, 75%) — 25 and 75 percentiles respectively, Q1 and Q3 — first and third quartiles) to describe the variation of attributes. In the statistical analysis of the results of the study, the non-parametric dispersion analysis of Kraskele-Wallis and the correlation analysis with the calculation of the Spirman rank correlation coefficients (c) were performed. Multiple comparisons were made with Bonferon and Holm. Methods for assessing survival of patients were used: analysis of lifetime tables and evaluation of Kaplan-Mayer's survival function with the construction of survival curves; logistic rank test with Yates correction for continuity; Cox proportional risk regression models were used too. Univariate and multiple analysis conducted; the ratio of risks was determined.

The results of the study showed that the survival rate of patients with pneumonia on the background of oncohematological pathology was determined by the factors that characterized the course of pneumonia, the course of oncological blood disease, indicators of immune reactivity.

Independent predictors influencing the survival of patients with pneumonia on the background of oncohematological pathology determined the indicators: gram-negative pathogens, the number of erythrocytes and neutrophils, the number of courses of HT and the immunoregulatory index. The covariates of the favorable forecast of events are defined: the number of HT courses is less than 8; not determined in the patient gram-negative pathogens; the number of erythrocytes more than $2.0 \cdot 10^{12}$/l; the immunoregulatory index is more than 1.09. Covariant of unfavorable forecast of events determined: number of chemotherapy courses 8 and more; the presence of gram-negative pathogens; the number of erythrocytes is less than $2.0 \cdot 10^{12}$/l; the immunoregulatory index is less than 1.09. Analysis of survival of patients with pneumonia with immunity disorders on the background of oncohematological pathology with covariates of unfavorable development of events, proved that the survival rate during the month will be 30%, with a favorable prediction of the development of events — 96%.

Prospects for further research. A promising further study of factors that affect lethality and cause survival of patients with pneumonia on the background of oncohematological pathology.

Key words: pneumonia, survival of patients, immunity disorders, lethal outcome, factors of poor prognosis.

Relationship of Work with Scientific Programs, Plans, Themes

This research work is a part of the planned comprehensive research work of the Department of Internal Medicine № 1 of the State Establishment "Dnipropetrovsk Medical Academy of Health Ministry of Ukraine""Studying the features of bronchopulmonary disease (chronic bronchitis, asthma, pneumonia) in the age aspect and develop schemes for integrated prevention and treatment", state registration N 0199U002120.

Introduction

The survival of patients is the most important integrated indicator of quality and effectiveness of medical care for the population. Most publications devoted to the survival of patients with oncohematological pathology are studies in which carried out a comparative analysis of the effectiveness of various medical diagnostic technologies, chemotherapy regimens (CTs) and their modifications for this indicator at different stages of treatment [1; 2; 9; 14; 18] or depending on the form of hemoblastosis [3]. Modern CT patterns, developed in accordance with the peculiarities of the pathogenesis of nosological forms of oncohematological pathology, to a large extent allow control of tumor progression and are the causes of the elongation of the life expectancy of such patients. Moreover, a significant threat to the lives of patients with hematological pathology are infectious complications (IC), including the leading role pneumonia and sepsis [17]. In studies devoted to the diagnosis of pneumonia in patients with immune disorders on the background of oncohematological pathology study microbiological features [16], peculiarities of the course and clinical picture [8]. Consequently, today attention is paid to the factors influencing the course of the underlying disease. Scientific studies that have examined the issue comprehensively virtually absent. Thus, despite the relevance of this problem in scientific publications, not enough attention is paid to determining the factors that determine the mortality and survival rate of patients with pneumonia

in patients with immune disorders on the background of oncohematological pathology.

The aim of the study: to determine the factors that cause the survival of patients with pneumonia, based on the study of complex, clinical and laboratory, anamnestic and immunological parameters of patients with pneumonia with immune disorders on the background of oncohematological pathology.

Materials and Methods

To solve the problem, a computer database of the results of the examination of 811 patients with lesions of the broncho-pulmonary system on the background of oncohematological pathology was created. The study was conducted in two stages in the haematological center "KZ multifunctional clinical hospital No. 4", Dnipro, 2010–2016. The retrospective stage included the analysis of archival data of 535 cases of hospitalizations of patients with oncohematological pathology; prospective phase — a study of 276 cases of hospitalizations. Diagnosis of oncohematological diseases was determined according to generally accepted clinical and morphological criteria [10]. The diagnosis of pneumonia was verified in accordance with the "Order of the Ministry of Health of Ukraine No. 128, March 19, 2007" [5]. We studied and analyzed the indices that characterizing the general condition of the patient; anamnestic information about the course of the main disease and peculiarities of the course of the bronchopulmonary system disease in the dynamics. Features of infectious defeat of the bronchopulmonary system in the studied patients were studied regardless of the phase of the course of the underlying disease. The statistical processing of the research results was carried out using descriptive and analytical biostatistics methods implemented in software packages STATISTICA 6.1 (StatSoftInc., Serial No. AGAR909E415822FA); Microsoft Excel (Office Home Business 2KB4Y-6H9DB-BM47K-749PV-PG3KT). Median (Me) as a measure of the central tendency was used to describe the quantitative characteristics; interquartile scale ((25%, 75%) — 25 and 75 percentiles respectively, Q1 and Q3 — first and third quartiles) to describe the variation of attributes. In the statistical analysis of the results of the study, the non-parametric dispersion analysis of Kraskele–Wallis and the correlation analysis with the calculation of the Spirman rank correlation coefficients (ρ) were performed. Multiple comparisons were made with Bonferon and Holm. Statistically significant was the value of the significance level $p<0.05$ (5%) [4]. An analysis of survival was conducted — an assessment of the likelihood that the patient will remain alive before a particular point after the start of treatment (in our case, until the end of inpatient treatment).

As the observation time for each patient using the time interval between the date of hospitalization for blood cancer against which there was pneumonia and the date of death or discharge from the hospital. Methods for assessing the survival rate of patients were: analysis of mortality table tables and Kaplan–Meier method survival estimation with the construction of survival curves that characterize the probability of surviving a certain moment of time after the onset of an initial event. The last method allows us to take into account the specificity of the time of life data, which is connected, first of all, with their incompleteness (censored data): patients during the observation may appear for one reason or another, that is, the real lifetime of such people is greater than the duration of their observation. The peculiarity of the data obtained in the study is the deviation of the distribution of life time from the normal law. In this regard, nonparametric criteria are used when comparing survival curves: for the characterization of the average life expectancy, the median survival rate was used with a 95% confidence interval (CI), which characterized the time point to which half (50%) of the population under study survives. To evaluate the probability of the difference in survival rates between the groups, a log-rank test with Yates correction for continuity was used [4]. Cox proportional-hazards regression models were used to analyze the influence of the investigated factors on survival, to evaluate the relationships between multidimensional continuous and binary variables with survival time values. An analysis of the impact of each individual indicator on the time from the beginning of the observation to the occurrence of the event (univariate analysis) and subsequent multiple analysis, which included all the indicators that, according to the previous analysis, influenced the occurrence of the event ($p<0.05$). The relation of risks (HR, HR risk atio) was defined, which is interpreted as the ratio of intensities in the Poisson regression. In such cases, the values above the unit indicate an increased risk, values below unit 1 are reduced risk, and unit levels indicate that there is no increased or reduced risk of reaching the endpoint [7].

Results and Discussion

Of the 881 patients who had been diagnosed with IU in the

background of program treatment: 270 (33.29%) patients had bronchitis (1 group); in 162 (19.98%) patients (group 2) — pneumonia without severe pulmonary complications and with a positive conclusion of pneumonia; in 112 (13.81%) — severe pneumonia with complications (bilateral lung disease, pleurisy, hemoptysis, respiratory failure) with positive completion of pneumonia (group 3); in 267 (32.92%) — pneumonia with a lethal consequence (group 4).

Of the total number of hospitalizations: 258 patients were the main primary illness, which was 31.81%; hospitalized because of pneumonia — 98 patients, which was 12.08%; Hospitalized patients due to the need to conduct HT in accordance with the stage and form of oncological disease of the blood — 455 patients, which was 56.10%.

Characteristics of patients in the study group on oncohematological diseases was as follows: patients with chronic lymphocytic leukemia — 152 (18.74%), chronic myeloid leukemia — 80 (9.86%); myeloma (MH) — 116 (14.3%), acute leukemia (AL) — 184 (22.69%) (of which acute lymphocytic leukemia is 92 (11.34%), acute myeloid leukemia — 80 (9.86%), subleukemic myelosis — 10 (1.23%), acute monoblast leukemia — 2 (0.25%)); aplastic anemia (AA) — 83 (10.23%), Valdenstrem disease (VD) — 47 (5.8%), lymphoma — 46 (5.67%), myelodysplastic syndrome — 33 (4.07%), erythremia — 31 (3.82%), skin's melanoma — 7 (0.86%), idiopathic thrombocytopenic purpura — 24 (2.96%), lymphoproliferative diseases — 4 (0.49%), and others — 8 (0.98%) (thrombosis, hemorrhagic vasculitis, lymphosarcoma, extracellular plasmacytoma). The ratio of women to men is 2 : 3.

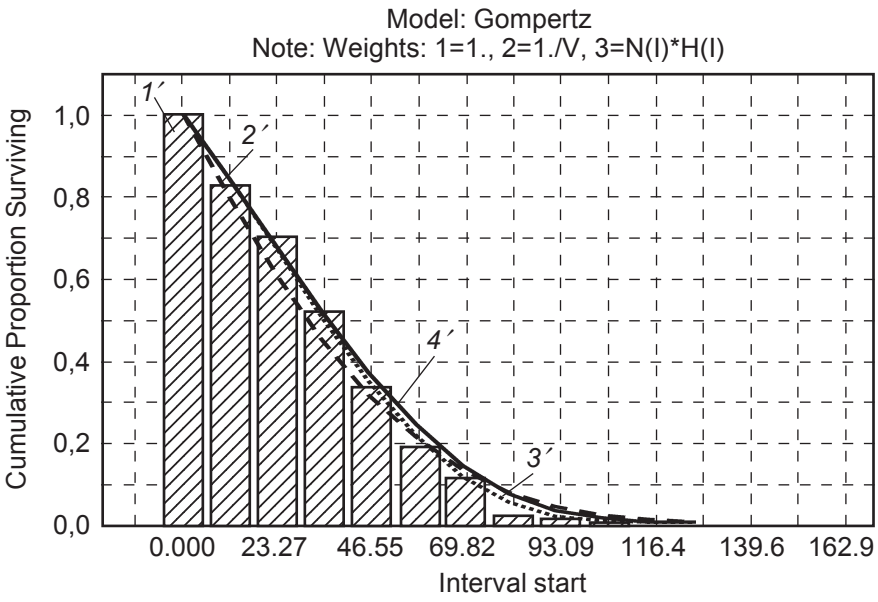

Fig. 1. Estimates of the theoretical distribution of the survival function (according to the criterion χ^2 for the model 1 — p=0.001; 2 — p=0.029; 3 — p=0.079); *1´*— observed; *2´*— Weight 1; *3´*— Weight 2; *4´*— Weight 3

An estimate of the theoretical distribution of the survival function is presented in Fig. 1

The evaluation of the theoretical distribution of the survival function has shown that the most suitable family of distributions for the data obtained by the study groups is the distribution of the Gompertz: in this distribution there is no significant difference from the observed values in the evaluation of parameters, fitting in the third way (corresponding to weight 3) shows satisfactory agreement with the data (by criterion χ^2 — p=0,079). Thus, by statistical methods, we have determined that the distribution of Gompertz fully describes the survival function of patients in study groups.

The curve of overall survival of patients with pneumonia on the background of oncohematological pathology, which is based on the Kaplan–Meier method is presented in Fig. 2.

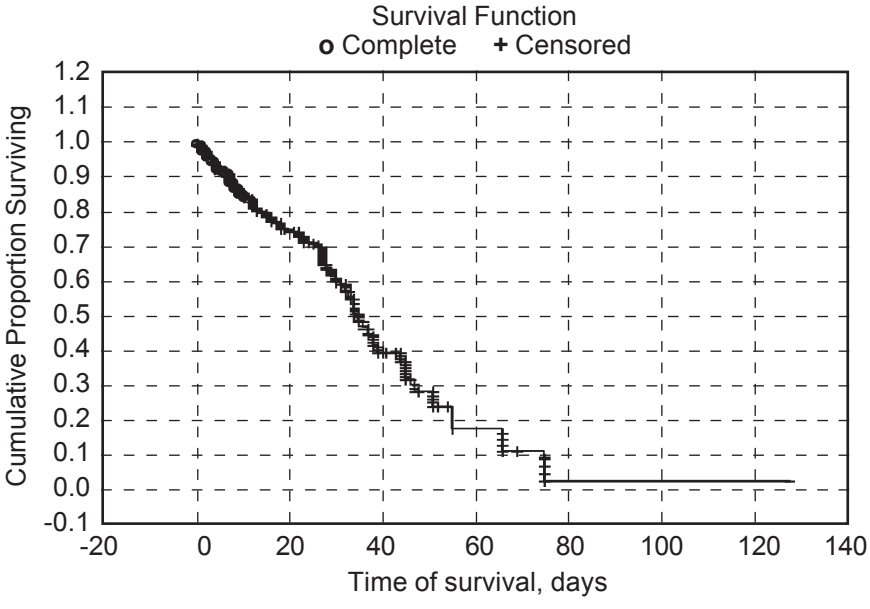

Fig. 2. Total cumulative survival for patients with pneumonia on the background of oncohematological pathology

The median survival rate for the examined patients was 36.0 (CI 34.0–39.0) days in total; the 25th percent survival rate was 19.0 days; the 75th percent survival rate was 51.0 days. At the time of the analysis, the cumulative survival rates for the examined patients in general for the analyzed period were: the probability of living ≥1 month was 61.32% (95% CI 56.73–65.91); ≥ 2 months — 17.38% (95% CI 9.88–24.88); ≥ 4 months — 2.21% (95% CI 0–6.32).

Cumulative survival of patients 1, 2, 3 and 4 groups with pathology of the broncho-pulmonary system on the background of oncohematological pathology is presented in Fig. 3.

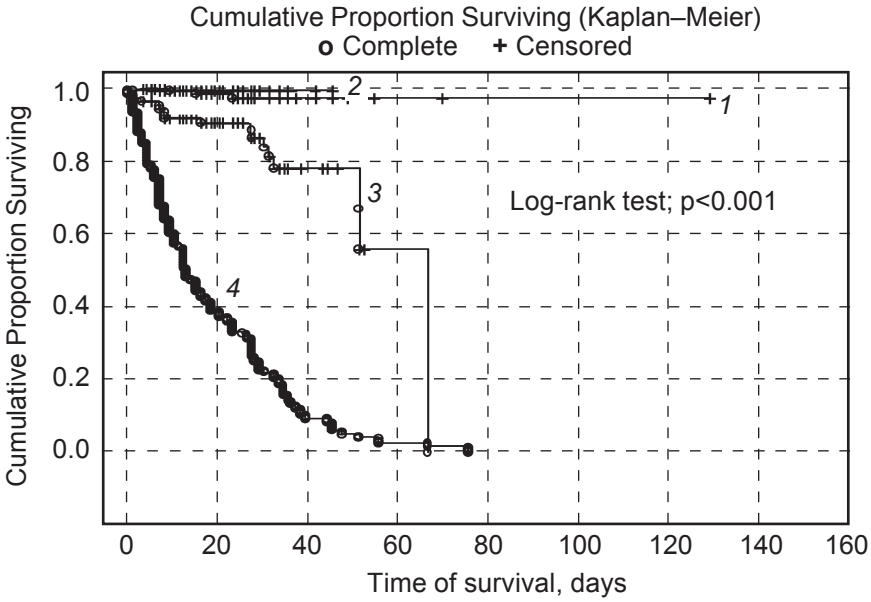

Fig. 3. Total cumulative survival for patients with pneumonia on the background of oncohematological pathology: *1* — group 1; *2* — group 2; *3* — group 3; *4* — group 4

The conducted analysis of survival of patients with pneumonia on the background of oncohematological pathology generally concerned mainly patients 3rd and 4th group, as for patients in the 1st and 2nd groups of the study during the observation, survival was almost 100%: in 1 group of patients — 98.89%, in the 2nd — 99.38%. This fact allows us to conclude that the overall cumulative survival for patients in general characterizes, basically, the survival of patients with severe pneumonia, including pneumonia with severe complications.

The overall survival of patients with pneumonia on the background of oncohematological pathology, depending on the stage of the underlying disease according to the Ann-Arbor classification is presented in Fig. 4

In the analysis of cumulative survival for the Ann-Arbor classification, significant differences between the groups were determined (log-rank test, p<0.001). For patients with stage I of oncohematological disease, according to the Ann-Arbor classification, the total cumulative survival for 1 month was 66.1% (95% CI 55.95–76.25); for patients with stage II — 61.9 (95% CI 54.63–69.17); for patients with the III stage — 57.4 (95% CI 48.91–65.89); for patients with the IV stage — 18.1 (95% CI 2.2–34.0). Consequently, the higher stage of the Ann-Arbor classification was, the overall cumulative survival rate of the patients was less.

Cumulative survival of patients with pneumonia on the background of oncohematological pathology, depending on the degree of neutropenia presented in Fig. 5 and in Table 1.

Analysis of the survival rate of patients with pneumonia in the background of oncohematological pathology, depending on the degree of neutropenia showed that the probability of the onset

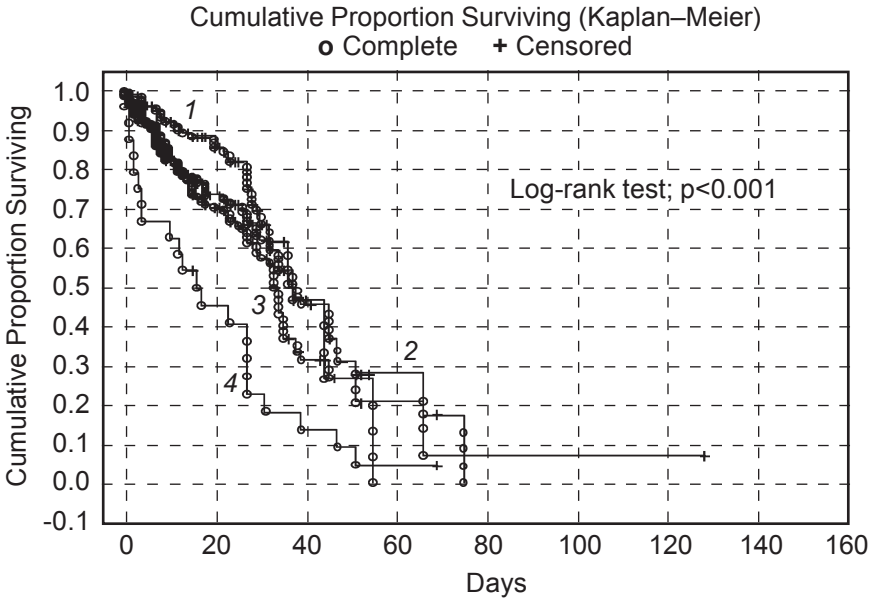

Fig. 4. Cumulative survival of patients with pneumonia on the background of oncohematological pathology, depending on the stage of the underlying disease according to the Ann-Arbor classification: *1* — I stage; *2* — II stage; *3* — III stage; *4* — IV stage

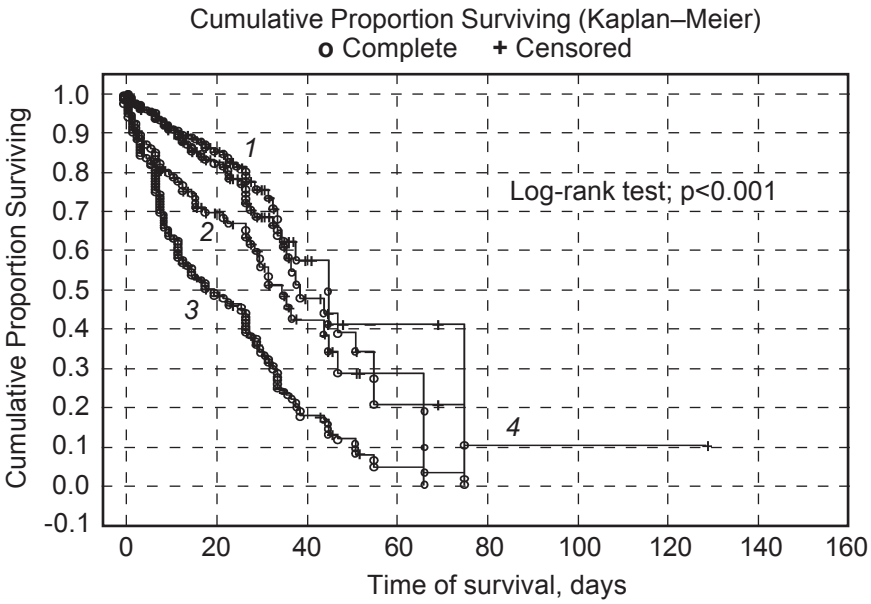

Fig. 5. Cumulative survival of patients with pneumonia in the background of oncohematological pathology, depending on the degree of neutropenia: *1* — 1 stage; *2* — 2 stage; *3* — 3 stage; *4* — 4 stage

Table 1

Cumulative survival of patients with pneumonia in the background of oncohematological pathology, depending on the degree of neutropenia

Survival by individual groups	Total cumulative survival during 1 month		Median survival	
	%	95% CI	days	95% CI
Without neutropenia	68.5	59.74–77.26	40.0	36.0–56.0
Neutropenia 1 st.	75.5	67.58–83.42	46.0	36.0–76.0
Neutropenia 2 st.	59.8	49.2–70.4	36.0	30.0–46.0
Neutropenia 3 st.	35.6	27.54–43.66	19.0	14.0–28.0
log-rank test, p<0.001				

of the lethal consequence of pneumonia within one month is highest in patients with neutropenia of grade 3: the median surviving bridge was 19.0 days (95% CI 14.0–28.0)) and significantly differed from the indicator of other groups (log-rank test, p<0.001). The survival rate of patients with neutropenia of grade 2 was 36.0 days (95% CI 30.0–46.0)); the survival rate of patients with neutropenia of grade 1 was 46.0 days (95% CI 36.0–76.0)). Consequently, with an increase in the degree of neutropenia, the possibility of survival in the patient was less.

It should be noted that the group of patients without neutropenia for survival did not differ from the group of patients with neutropenia of 1 degree (p=0.326).

Factors influencing survival of patients were determined by analyzing Cox proportional risks with the definition of BP as coarse (uncorrected) based on the analysis of the individual effects of each factor (univariate analysis) and corrected BP by means of multiple analysis. The results of the analysis (adjusted and coarse Risk Ratio Indicators) in determining the factors influencing the survival of patients with pneumonia in the background of oncological pathology (survival predictors) by the proportional Cox risk model are presented in Table. 2.

All the analyzed parameters (see Table 2) were associated with an increased risk of a lethal outcome of pneumonia in a univariate analysis (p<0.001). According to the results of the multiple analysis of proportional Cox intensities, the independent predictors of the lethal outcome of pneumonia were determined: the number of HT courses, gram-negative pathogens, glycemia, wet wheezing, pulse

Table 2

Factors for predicting the survival of patients with pneumonia in the background of oncohematological pathology according to the proportional Cox risk model

Predictors of survival	Kind of analysis of proportional intensity of Cox					
	univariant			multiple		
	RR rude	95% CI	p	RR adjusted	95% CI	p
Gram-negative pathogens (presence)	4.32	3.17–5.90	< 0.001	2.12	1.49–3.01	< 0.001
Courses HT “8 and more”	2.46	1.95–3.1	< 0.001	1.50	1.16–1.95	0.002
Hemoptysis (presence)	2.29	1.7–3.07	< 0.001	1.27	0.89–1.81	0.183
Glycemia	2.75	2.13–3.54	< 0.001	1.34	1.0–1.77	0.047
Neutropenia 3 st.	2.77	2.19–3.52	< 0.001	1.35	0.86–2.09	0.189

End of Table 2

Predictors of survival	Kind of analysis of proportional intensity of Cox					
	univariant			multiple		
	RR rude	95% CI	p	RR adjusted	95% CI	p
Wet wheezing (presence)	2.97	2.32–3.8	< 0.001	1.44	1.1–1.88	0.008
Pulse rate, in min.	1.04	1.04–1.05	< 0.001	1.02	1.01–1.03	< 0.001
Leukocytes, $\cdot 10^9$/l	0.74	0.67–0.81	< 0.001	0.93	0.79–1.08	0.325
Hemoglobin, g/l	0.98	0.98–0.98	< 0.001	1.0	0.99–1	0.008
Erythrocytes, $\cdot 10^{12}$/l	0.48	0.42–0.55	< 0.001	0.69	0.58–0.81	< 0.001
Thrombocytes, $\cdot 10^9$/l	1.0	1.0–1.0	< 0.001	1.0	1.0–1.0	0.461
Lymphocytes, %	0.94	0.92–0.95	< 0.001	0.98	0.96–1.01	0.144
B CD19, %	0.89	0.85–0.94	< 0.001	0.99	0.91–1.09	0.981
T CD19, %	1.04	1.02–1.05	< 0.001	1.0	0.98–1.02	0.955
CD4, %	0.94	0.92–0.95	< 0.001	0.96	0.92–1.01	0.085
CD4/CD8=1,09	0.19	0.12–0.3	< 0.001	2.90	1.09–9.23	0.050
CD56, %	0.79	0.75–0.83	< 0.001	1.0	0.9–1.13	0.881
IgG, g/l	0.8	0.72–0.89	< 0.001	0.93	0.81–1.05	0.246
NST-stimulated test, unit.	0.94	0.92–0.96	< 0.001	0.98	0.95–1.0	0.067
Number of neutrophils, $\cdot 10^9$/l	0.53	0.44–0.64	< 0.001	0.98	0.95–1.0	0.131

rate, hemoptysis, the number of red blood cells, hemoglobin, the number of lymphocytes, platelets, neutrophils, cellular immunity indexes absolute values, indicators of humoral immunity, immunoregulatory index (see Table 2).

Independent predictors of the lethal outcome of pneumonia are given in Table 3.

A meaningful (p<0.001) proportional Cox survival model was constructed, based on the obtained data on independent factors in the prognosis of survival of patients with pneumonia on the background of oncohematological pathology. This model included the following predictors (significance level p<0.01): HT courses "8 and more" presence of gram-negative pathogens, erythrocyte count, immunoregulatory index (CD4/CD8) (Table 4). Other independent predictors were not included in the model because of insignificant influence on Wald's statistics.

The probability of the endpoint (the patient's death) according to the Cox regression

Table 3

Indicators of survival of patients with pneumonia in the background of oncohematological pathology, depending on certain predictors of the lethal outcome of pneumonia

Survival by individual groups	Total cumulative survival during 1 month, %		Median of survival	
	%	95% CI	days	95% CI
CHT more than 8 courses (log-rank test, p<0.001)				
No	72	66.79–77.21	45.0	37.0–52.0
Yes	42.1	34.57–49.63	28.0	28.0–30.0
Gram-negative pathogens (log-rank test, p<0.001)				
No	83.6	77.43–89.77	67.0	45.0–67.0
Yes	43.6	37.76–49.44	28.0	27.0–31.0
Glycemia (log-rank test, p<0.001)				
No	75.7	69.66–81.74	52.0	40.0–76.0
Yes	44.7	38.37–51.03	29.0	28.0–33.0
Wet wheezing (log-rank test, p<0.001)				
No	66.6	61.33–71.87	40.0	38.0–48.0
Yes	28.9	20.26–37.54	16.0	13.0–23.0
Pulse rate > 92 (log-rank test, p<0.001)				
No	74.6	68.99–80.21	46.0	40.0–56.0
Yes	31.8	25.04–38.56	19.0	14.0–24.0
Erythrocytes = 2 (log-rank test, p<0.001)				
No	77.4	71.52–83.28	52.0	38.0–76.0
Yes	32.1	25.81–38.39	19.0	15.0–24.0
CD4/CD8 ≤ 1,09 (log-rank test, p<0.001)				
No	—	—	—	—
Yes	39.1	25.03–53.17	28.0	16.0–33.0

Table 4

The regression model of Cox proportional risks of the influence of independent factors of the prognosis of the risk of a lethal outcome of patients with oncohematological diseases on the background of which there was a pneumonia

Factors	Regression coefficient β	Standard error β	Wald's χ^2	p-value χ^2 Wald's	RR	95% CI
HT courses "8 and more" (x_1)	0.535	0.123	18.98	0.001	1.71	1.34–2.17
presence of gram-negative pathogens (x_2)	1.071	0.163	43.14	<0.001	2.92	2.11–4.02
Erythrocyte (x_3)	-0.521	0.071	53.99	<0.001	0.59	0.52–0.68
CD4/CD8 (x_4)	-0.725	0.247	8.64	0.003	0.48	0.30–0.79

model of proportional risk is modeled as follows:

$$H(t) = H0(t) \cdot \exp(\beta_1 \cdot x_1 + \beta_2 \cdot x_2 + \beta_3 \cdot x_3 + \beta_4 \cdot x_4), \quad (1)$$

where β1–β4 — regression coefficients; x_1–x_4 — predictive variables presented in the Table 4; H0 (t) is the basic danger at time t representing the risk of death for a patient with a value of 0 for all predictive variables.

Based on this, the ratio of risks is calculated by the formula:

$$\text{Ln}(H(t) / H0(t)) = \beta_1 \cdot x_1 + \beta_2 \cdot x_2 + \beta_3 \cdot x_3 + \beta_4 \cdot x_4. \quad (2)$$

Risk Ratio (RR) is the degree of risk associated with each variable (an independent predictor) when fixing all other variables. For a dichotomous variable (1 is an existing risk factor, 0 is absent), the risk ratio 1 means that the patient's risk of death is the same regardless of whether he has the relevant characteristic or not.

RR for more than 1 indicates an increased risk for patients with this characteristic; less than 1 — at reduced risk. If the factor is continuous, then the value of BP is the instantaneous relative risk of an event at any time for a person with an increase of 1 in the predictor's value compared to another person, since the two values are the same for all other covariates. In general, RR is the final value of the increased risk for each unit or the level of growth of the predictor variable [4]. Regression coefficients (beta-weights) are the weights for each variable in the equation. Positive coefficients of regression with predictive variables indicate an increase in risk and deterioration of the forecast when they are present. Negative regression factors mean a more favorable prognosis for patients with higher variables. In our study, it was determined that predictors of "8 courses of HT and more" and gram-negative pathogens are positive regression coefficients. Their presence in patients determines the increase in the risk of death and, thus, the deterioration of the prediction of survival. Negative coefficients of regression in our study were determined: the number of red blood cells and the immunoregulatory index. This means that with an increase in these indicators for patients, a more favorable prognosis is determined.

Thus, based on the received regression model of Cox proportional risks with the determined independent predictors, the probability of dying during the first month after hospitalization for a patient with pneumonia in the background of oncohematological pathology is greater by 1.71 times with the number of courses HT "more than 8"; in the presence of a patient with gram-negative pathogens of pneumonia — greater 2.92 times. Conversely, the survival rate of patients with pneumonia in the background of oncohematological pathology is statistically significantly increased with an increase in the number of erythrocytes and immunoregulatory index. Adjusted RR for erythrocytes is 0.64 (95% CI 0.55–0.74), for the immunoregulatory index (CD4/CD8) — 0.48 (95% CI 0.30–0.79).

The basic integral death risk function can be used to calculate the probability of survival S (t) for any case at time t:

$$S(t) = \exp(-H_0(t) \cdot PI), \quad (3)$$

where PI — prognostic index

$$PI = x_1 \cdot \beta_1 + x_2 \cdot \beta_2 + x_3 \cdot \beta_3 + x_4 \cdot \beta_4. \quad (4)$$

Survival curve of patients with pneumonia background of oncohematological pathology for covariate adverse events: number of courses HT 8 and more; the presence of gram-negative pathogens; the number of erythrocytes — $2.0 \cdot 10^{12}$/l; the index of immunoregulatory index (CD4/CD8) — 1.09, is shown in Fig. 6.

When constructing the survival curve of patients with pneumonia with immunity disorders on the background of oncohematological pathology for covariate adverse events: with the number of courses HT of 8 and more; the

presence of gram-negative pathogens; an indicator of the number of erythrocytes less than $2.0 \cdot 10^{12}$/l; the value of the index of immunoregulatory index is less than 1.09, it is determined that survival of patients with pneumonia with immunity disorders on the background of oncohematological pathology during the month will be 30%.

The curve of cumulative survival of patients with pneumonia with immunity disorders on the background of oncohematological pathology with the number of courses of HT less than 8; not defined in the patient gram-negative pathogens; the number of erythrocytes more than $2.0 \cdot 10^{12}$/l; the immunoregulatory index more than 1.09, is presented in Fig. 7.

When constructing the survival curve of patients with pneumonia with immunity disorders on the background of oncohematological pathology with a favorable prognosis of the development of events (with the number of courses of HT less than 8; not determining the patient gram-negative pathogens, the number of erythrocytes = $2.0 \cdot 10^{12}$/l, the values of the immunoregulatory index (CD4/CD8)=1.09), the survival rate of patients with pneumonia for the month will be 96%.

In the study among the independent predictors of survival of patients with pneumonia are the number of red blood cells and hemoglobin levels. Some scholars also testify that there is a probable relationship between the clinical manifestations of anemic syndrome and survival rates in patients with chronic lymphocytic leukemia. A decrease in hemoglobin to less than 100 g/l is associated with a decrease in the median of overall survival to 93 days versus 160 days in patients with hemoglobin levels greater than 100 g/l

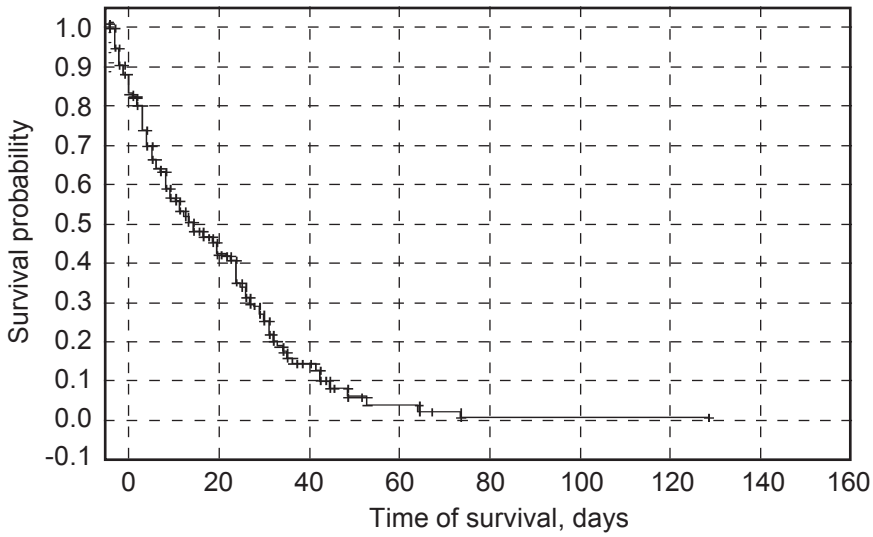

Fig. 6. Cumulative survival of patients with pneumonia with immunity disorders on the background of oncohematological pathology at: number of HT courses 8 and more; the presence of gram-negative pathogens; the number of erythrocytes ≥ $2.0 \cdot 10^{12}$/l; values of CD4/CD8 ≤ 1.09

[6]. In a recent study, regarding survival rates of patients depending on nosological forms of oncohematological pathology, it was determined that survival of patients with chronic forms is higher compared to acute leukemias [3]. In the same study, the age of patients is also considered as a factor affecting the mortality rate. Patients with oncohematologic pathology have immunity disorders, which deepen the inflammatory reaction in pneumonia. Thus, the state of the immune response can affect the course of the disease and determine the prognosis. In the study, the following data were obtained: the parameters of cellular and humoral immunity are independent predictors of survival of patients with pneumonia on the background of oncohematological diseases. Since the development of IC and pneumonia

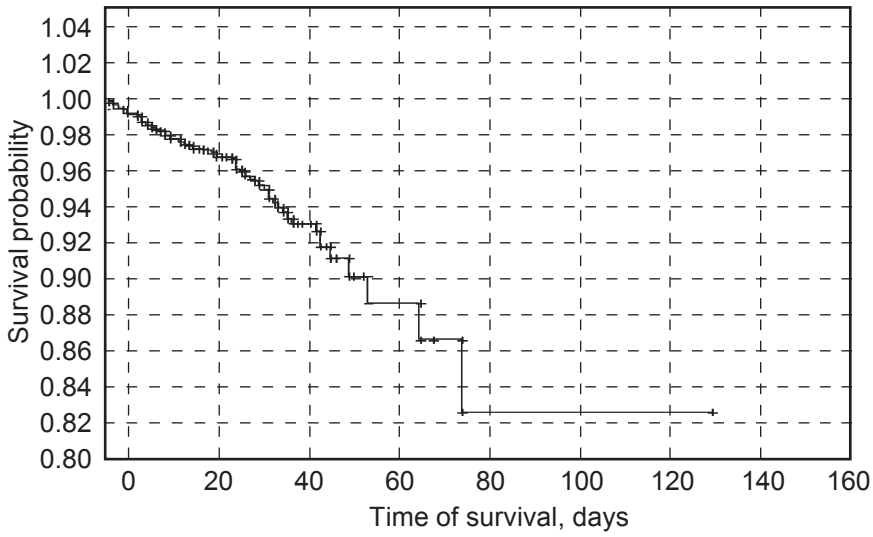

Fig. 7. Cumulative survival of patients with pneumonia with immunity disorders on the background of oncohematological pathology with the number of courses HT less than 8; not defined in the patient gram-negative pathogens; the number of erythrocytes ≥ $2.0 \cdot 10^{12}$/l; values of CD4/CD8 ≥ 1.09

in patients with background of oncohematological disease is often associated with neutropenia, it was logical to include this indicator for the analysis of relationships with fatalities. The results of the study prove the connection between the number of neutrophils and the survival rate of patients with pneumonia. The obtained data coincide with the data of other authors [13]. Authors studying the course of pneumonia in patients on the background of oncohematological pathology emphasize that it has certain features depending on the main oncological blood disease [11] and the etiological factor [12]. In the study on a sufficient amount of material, it has been determined that the number of HT courses preceding the onset of pneumonia and gram-negative pathogens of pneumonia has been identified as independent survivors.

Conclusions

1. The results of the study showed that the survival rate of patients with pneumonia on the background of oncohematological pathology was determined by the factors that characterized the course of pneumonia (the presence of gram-negative pathogens, hemoptysis), the course of oncological blood disease (the number of courses of HT preceding pneumonia, anemia, glycemia, leukopenia, neutropenia, thrombocytopenia), as well as indicators of immune reactivity (lymphocytopenia, indicators of cellular and humoral immunity in absolute numbers, immunoregulatory index).

2. Independent predictors influencing the survival of patients with pneumonia on the background of oncohematological pathology determined the indicators: gram-negative pathogens, the number of erythrocytes and neutrophils, the number of courses of HT and the immunoregulatory index. The covariates of the favorable forecast of events are defined: the number of HT courses is less than 8; not determined in the patient gram-negative pathogens; the number of erythrocytes more than $2.0 \times \times 10^{12}$/l; the immunoregulatory index is more than 1.09. Covariant of unfavorable forecast of events determined: number of chemotherapy courses 8 and more; the presence of gram-negative pathogens; the number of erythrocytes is less than $2.0 \times \times 10^{12}$/l; the immunoregulatory index is less than 1.09.

3. Analysis of survival of patients with pneumonia with immunity disorders on the background of oncohematological pathology with covariates of unfavorable development of events, proved that the survival rate during the month will be 30%, with a favorable prediction of the development of events — 96%.

Prospects for further research. A promising further study of factors that affect lethality and cause survival of patients with pneumonia on the background of oncohematological pathology.

Ключові слова: пневмонія, виживаність, порушення імунітету, летальний кінець.

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