

Original Article

Factors for evaluating the progress of chronic tonsillitis based on multifactor regression analysis

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Abstract

The aim is to propose an approach to predicting the risk of progression of chronic tonsillitis in patients based on multivariate regression analysis for timely, convenient, and accurate diagnosis with subsequent selection of effective treatment and preventive measures in ENT departments (otolaryngology departments). A number of 100 patients with various forms of chronic tonsillitis, whose average age was 37 years, and 51 women and 49 men, were examined according to a specially developed questionnaire to predict the risk of ChT progression. The most probable indicators of chronic tonsillitis progression were selected to build a multivariate regression model for predicting the risk of ChT progression, 13 probable factors of the ChT progression were analyzed, and 9 factors were used to build a multivariate regression model. Histogram of the residual deviations is distributed symmetrically, approaching the curve of the normal distribution of the residuals and the absence of systematic deviations from the normal-probability straight line, so we conclude that the statistical hypothesis that their distribution conforms to the normal distribution law is not rejected. The residuals relative to the predicted values are scattered chaotically, which indicates the absence of dependence on the predicted values for the risk of chronic tonsillitis progression. The coefficient of determination was calculated, which is 0.8258, which claims that 82.58% of the factors are considered in the prediction model of the risk of chronic tonsillitis progression. The coefficient of determination indicates how well the obtained observations confirm the mathematical model. The proposed multivariate regression model that considers the risk factors for the ChT progression makes it possible to predict potential meta tonsillar complications and the possibility of timely disease prevention.

Keywords: chronic tonsillitis, progress, multivariate regression analysis.

Introduction

For today, chronic tonsillitis (ChT) is the most common among all ENT pathologies. According to the literature, from 12.5% to 22.1% of the population suffers from chronic tonsillitis, which is from 22% to 40% among all chronic pathologies of the ENT organs [1–3]. The main feature of chronic tonsillitis is a progres-

sive course with a high probability of developing a few metatonsillar complications [2, 4]. Since the palatine tonsils (PT) take an active part in the formation of local and humoral immunity, it is not surprising that together with ChT, immunological pathology associated with it begins to develop – myocarditis, endocarditis, rheumatoid arthritis, rheumatism, glomerulonephritis, vasculitis [3, 5–7]. This indicates that the inflammatory



process that develops in Waldeyer's tonsillar ring zone is a chronic, constantly acting source of toxic effects on the body and disrupts its homeostasis. This is why treating chronic tonsillitis as a focal infection is an important component in preserving human health as a whole [8, 9].

However, the choice of the optimal and correct treatment method for this disease continues to be the number one issue among otolaryngologists since there are no clearly defined and classified forms or stages of the disease [1].

According to the classification used in Ukraine for decades, L.A. Lukovsky (1941, 1955, 1966) distinguishes between compensated, subcompensated, and decompensated chronic tonsillitis. If conservative treatment is used for the first two forms, then surgical intervention is the method of choice for the decompensated form [10]. However, the problem is that sometimes, it is difficult to draw a clear line between the mentioned forms.

Today, the methods of integral assessment of a patient's condition according to clinical and laboratory criteria, including immunological ones, are increasingly used. This is based on individual clinical and laboratory parameters expressed in points [11, 12].

One of the modern and fairly accurate methods of forecasting the progression of various diseases, including ChT, is the construction of a multivariate regression model, which includes several predictors that may cause the progression of the inflammatory process and the development of metatonsillar complications [13].

Approaches to building multivariate regression forecasting models in medicine are considered in the works of Musiienko V. et al. (2021) and Musiienko V. et al. (2022) [13–15].

The work aims to propose an approach to predicting the risk of progression of chronic tonsillitis in patients based on multivariate regression analysis for timely, convenient, and accurate diagnosis with subsequent selection of effective treatment and preventive measures in ENT departments (otolaryngology departments).

Material and methods

Study design and patients

We examined 100 patients aged 18 to 70, including 51 women and 49 men, with a diagnosis of chronic tonsillitis, who were undergoing outpatient treatment in the surgical department of the polyclinic of communal noncommercial enterprise "City Clinical Hospital

No. 3" under Ternopil City Council. The average age of the patients was 37 years, and the disease duration varied between 5–8 years.

All patients signed an informed consent to participate in the study. The research was conducted in compliance with all moral and ethical principles, considering the World Medical Association Declaration of Helsinki and after receiving the approval of the ethics commission at I. Horbachevsky Ternopil National Medical University (minutes no. 74 dated September 1, 2023).

Each patient underwent a comprehensive clinical and laboratory examination, which included anamnesis collection, oropharyngeal examination, general blood test with formula, rheumatic tests (Antistreptolysin-O (ASL-O), C-reactive protein (CRP), rheumatoid factor (RF).

According to a specially developed questionnaire for assessing the prediction of the level of progression of chronic tonsillitis, all patients were surveyed, which included 13 risk factors for the progression of ChT: age, gender, sanitation of the oral cavity, level of ASL-O, CRP, RF, ESR level, presence of leukocytosis (according to WBC differential), hyperemia of the palatal arches, the presence of caseous detritus in the lacunae of the PT, the condition of the submandibular lymph nodes, body temperature, smoking, and their gradation was established from numerical values.

The construction of a prognostic model for the risk of ChT progression was carried out using multivariate regression analysis. The statistical processing of the obtained research results was done using the statistical package Statistica 10.0 and the table editor Microsoft Excel 2019.

Results

The creation of a mathematical model using the method of multivariate regression analysis of the risk prediction of the ChT progression, which considers the most informative factors and variants of their severity, makes it possible to predict the progress of this disease. The obtained results make it possible to assess the disease's progress and choose the most optimal and effective methods of treatment and prevention of this pathology.

One hundred patients with various forms of chronic tonsillitis, whose average age was 37 years, and 51 women and 49 men, were examined according to a specially developed questionnaire to predict the risk of ChT progression.

The most probable indicators of chronic tonsillitis progression were selected to build a multivariate regression model for predicting the risk of ChT progression. With the help of multivariate regression analysis, 13 probable factors of the ChT progression were analyzed: age, gender, sanitation of the oral cavity, the level of ASL-O, CRP, RF, ESR level, the presence of leukocytosis (according to WBC differential), hyperemia of the palatine arches, the presence of caseous detritus in the lacunae PT, condition of submandibular lymph nodes, body temperature, smoking.

A stepwise multivariate regression analysis was performed in the Statistica 10.0 program to assess the significance of the factor characteristics influence. First, a correlation matrix was obtained, establishing the absence of pairwise correlation coefficients greater than 0.7. Thus, the presence of multicollinear factors of ChT progression gives reason to use all 13 above-mentioned factors to build a regression model. The next stage was the calculation of the regression coefficients “b” (Beta), which reflects the relationship regarding the influence on the development of the ChT progression in the examined patients for each selected

factor. The result of obtaining significant factors for predicting the risk of ChT progression when conducting a multivariate regression analysis in the Statistica 10.0 program is shown in Table 1.

Factors “Gender”, “Hyperemia of arches”, and “Condition of submandibular lymph nodes” with a significance level of $p \geq 0.05$ were excluded from the subsequent analysis. Since the significance levels of the ten risk factors were less than 0.05, they were included in the mathematical model to predict ChT progression.

After constructing a repeated correlation matrix and a multivariate regression model without considering “Gender”, “Hyperemia of arches”, and “Condition of submandibular lymph nodes”, the factor “Age” was also identified by the model as not liquid and was excluded from further analysis, since its significance level $p = 0.07$ (Table 2).

After constructing the correlation matrix without considering non-liquid factors, multicollinear factors were also absent since there were no pairwise correlation coefficients greater than 0.7. So, 9 factors were used to build a multivariate regression model. The result of obtaining significant factors for the prognosis

Table 1: The result of obtaining significant factors for the prediction of chronic tonsillitis progression (ChTP) during multivariate regression analysis in the Statistica 10.0 program.

N=100	Regression summary for dependent variable: RRCTP (1 in 1)					
	R= .91647711 R ² = .83993029 Adjusted R ² = .81573370 F(13.86)=34.713 p<0.0000 Std. Error of estimate: 2.1140					
	b*	Std.Err. of b*	b	Std. Err. of b	t (86)	P-value
Intercept			-63.4288	26.04476	-2.43538	0.016942
Sanitation of the oral cavity	0.473937	0.044315	4.6530	0.43507	10.69472	0.000000
ASL-O	0.249351	0.049736	0.0330	0.00658	5.01348	0.000003
CRP	0.352884	0.047271	1.5287	0.20478	7.46506	0.000000
RF	0.244936	0.044876	0.3648	0.06683	5.45809	0.000000
ESR	0.198981	0.047003	0.1708	0.04034	4.23333	0.000057
WBC level	0.107162	0.044342	0.2478	0.10253	2.41674	0.017774
Presence of caseous detritus in lacunae	0.488854	0.045008	4.7918	0.44117	10.86151	0.000000
Body temperature	0.104190	0.047114	1.5404	0.69656	2.21145	0.029657
Age	-0.102328	0.046504	-0.0369	0.01679	-2.20042	0.030458
Gender	-0.077889	0.047146	-0.7635	0.46213	-1.65207	0.102167
Smoking	0.138930	0.047126	1.3659	0.46332	2.94808	0.004116
Hyperemia of arches	0.072423	0.061771	0.7098	0.60536	1.17244	0.244257
Condition of submandibular lymph nodes	-0.055652	0.059758	-0.5494	0.58990	-0.93129	0.354311

Table 2: The result of obtaining significant factors for the prognosis of the chronic tonsillitis progression (ChTP) when performing a multivariate regression analysis in the Statistica 10.0 program without the factors “Sex”, “Hyperemia of arches”, “Condition of submandibular lymph nodes”.

Regression summary for dependent variable: RRCTP (1 in 1)						
R= .91204194 R ² = .83182051 Adjusted R ² = .81292393						
F(10.89)=44.020 p<0.0000 Std. Error of estimate: 2.1301						
N=100	b*	Std.Err. of b*	b	Std.Err. of b	t (89)	P-value
Intercept			-70.9379	25.28270	-2.80579	0.006165
Sanitation of the oral cavity	0.476126	0.044240	4.6745	0.43434	10.76223	0.000000
ASL-O	0.240260	0.047900	0.0318	0.00634	5.01587	0.000003
CRP	0.349160	0.046929	1.5125	0.20329	7.44014	0.000000
RF	0.242962	0.044687	0.3618	0.06655	5.43694	0.000000
ESR	0.178434	0.046169	0.1531	0.03962	3.86478	0.000211
WBC level	0.112410	0.044559	0.2599	0.10303	2.52274	0.013421
Presence of caseous detritus in lacunae	0.483190	0.044347	4.7362	0.43470	10.89556	0.000000
Body temperature	0.116193	0.046131	1.7179	0.68203	2.51874	0.013564
Age	-0.081543	0.045755	-0.0294	0.01652	-1.78218	0.078130
Smoking	0.141226	0.044730	1.3885	0.43977	3.15730	0.002174

of the ChT progression without considering non-liquid factors is shown in Table 3.

So, among the 13 analyzed factors in the Statistica 10.0 program (Table 1), 9 of the most significant risk factors were selected, which, according to the model, have

the greatest influence on the progression of this pathology: X1 – sanitation of the oral cavity; X2 – ASL-O; X3 – CRP; X4 – rheumatoid factor; X5 – erythrocyte sedimentation rate; X6 – level of WBC; X7 – presence of caseous detritus in lacunae; X8 – body temperature; X9 – smoking.

Table 3: The result of obtaining significant factors for the prognosis of the chronic tonsillitis progression (ChTP) when conducting a multivariate regression analysis in the Statistica 10.0 program without the “Age” factor.

Regression summary for dependent variable: RRCTP (1 in 1)						
R= .90874565 R ² = .82581865 Adjusted R ² = .80840051						
F(9.90)=47.411 p<0.0000 Std. Error of estimate: 2.1557						
N=100	b*	Std.Err. of b*	b	Std.Err. of b	t (90)	P-value
Intercept			-79.1533	25.15764	-3.14629	0.002242
Sanitation of the oral cavity	0.475436	0.044770	4.6677	0.43955	10.61944	0.000000
ASL-O	0.226602	0.047851	0.0300	0.00633	4.73555	0.000008
CRP	0.350908	0.047483	1.5201	0.20569	7.39021	0.000000
RF	0.235121	0.045005	0.3501	0.06702	5.22438	0.000001
ESR	0.171630	0.046564	0.1473	0.03996	3.68589	0.000389
WBC level	0.101779	0.044688	0.2353	0.10333	2.27752	0.025124
Presence of caseous detritus in lacunae	0.480955	0.044862	4.7143	0.43974	10.72067	0.000000
Body temperature	0.130467	0.045977	1.9289	0.67975	2.83769	0.005615
Smoking	0.134511	0.045107	1.3225	0.44347	2.98206	0.003683

Significant risk factors for the ChT progression are listed in Table 4.

Based on the results of the multivariate regression analysis of the prediction of the risk of ChT progression, which is shown in Table 3, we build a mathematical model for determining the risk ratio of the ChT progression (RRChTP):

$$RRChTP=4.6677*X1+0.03*X2+1.5201*X3+0.3501*X4+0.1473*X5+0.2353*X6+4.7143*X7+1.9298*X8+1.3225*X9-79.1533,$$

where RRChTP is the risk factor for the CT progression; X1–X9 – selected risk factors for the ChT progression with regression coefficients; 79.1533 is a constant.

To assess the quality of the regression model, it is advisable to analyze the residual deviations by obtain-

ing their histogram (Figure 1). As can be seen from the given histogram, the residual deviations are distributed symmetrically, approaching the curve of the normal distribution of the residuals, so we conclude that the statistical hypothesis that their distribution conforms to the normal distribution law is not rejected.

For additional confirmation of residual deviations from the normal law of distribution, a normal probability graph was constructed (Figure 2). Based on the graph data, we note the absence of systematic deviations from the normal-probability straight Line, confirming that the residual deviations are distributed according to the normal distribution law.

To check the dependence of the residual deviations on the predicted values, we construct a scatter diagram (Figure 3).

Table 4: Significant risk factors for the CT progression.

Name of factors	Conventional designations of factors in the mathematical prediction model	Factor ranges and names of their possible variants	Numerical values of factor ranges
Sanitation of the oral cavity	X1	Yes	0
		No	1
ASL-O	X2	Not elevated	0
		Elevated	1
CRP	X3	Not elevated	0
		Elevated	1
RF	X4	Not elevated	0
		Elevated	1
ESR level	X5	Normal	0
		Elevated	1
WBC level	X6	Normal	0
		Elevated	1
Presence of caseous detritus in lacunae	X7	Absence of pathological content in lacunae	0
		Only single-caseous plugs	1
		Moderate caseous and pus discharge from lacunae without pressing on the tissue	2
		Purulent content in lacunae	3
Body temperature	X8	Normal temperature	0
		Subfebrile	1
		About 38°C	2
Smoking	X9	>38°C	3
		No	0
		Yes	1

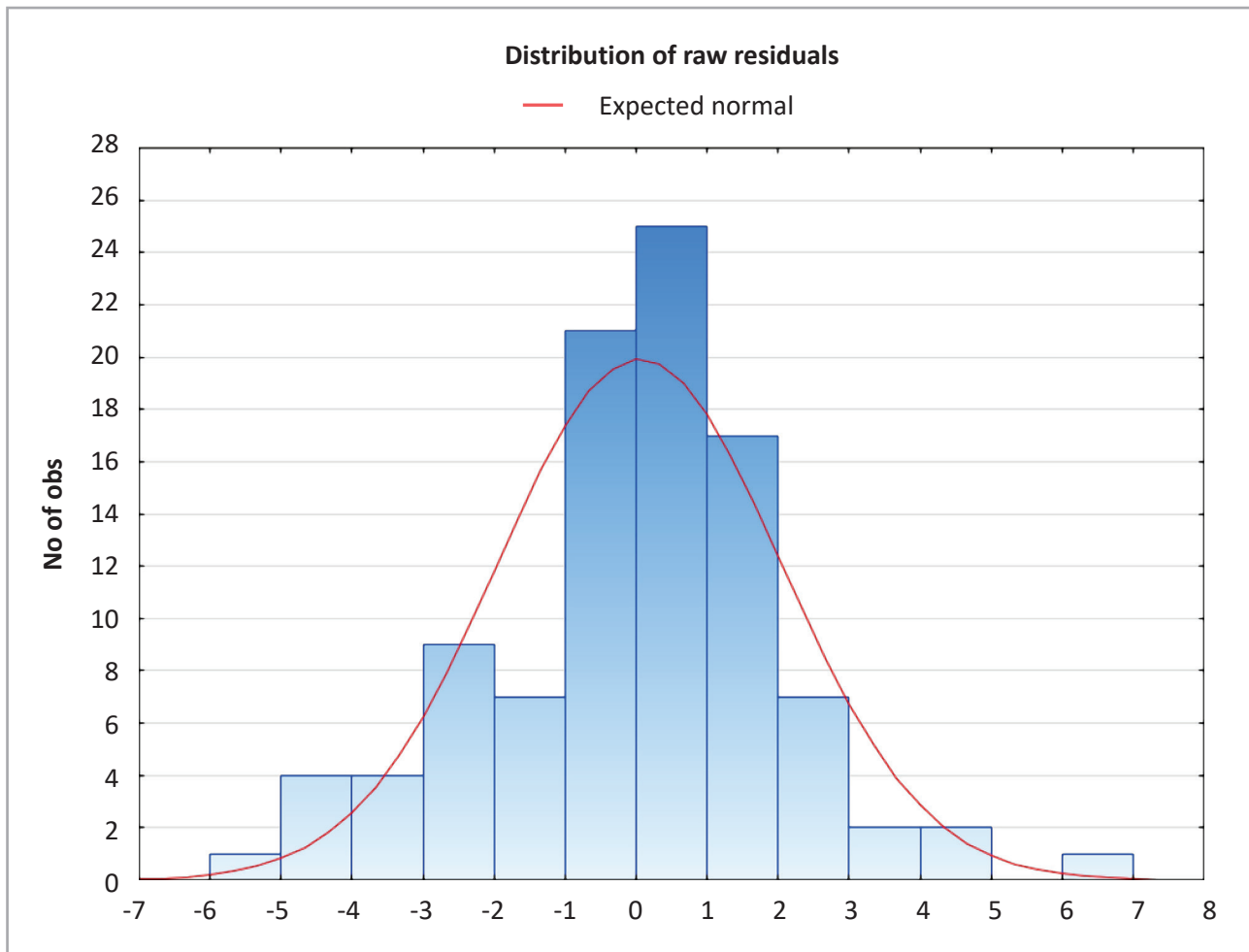


Figure 1: Histogram of the residual deviations of the multivariate regression model for the prediction of the chronic tonsillitis progression (ChTP).

The results obtained from the constructed diagram show that the residuals relative to the predicted values are scattered chaotically, which indicates the absence of dependence on the predicted values for the risk of chronic tonsillitis progression. The histogram and the normal probability graph confirm compliance with the normal law of the distribution of residual deviations, and therefore, the obtained model for predicting the risk of chronic tonsillitis progression is qualitative and adequate.

To assess the acceptability of the whole model, the next step was ANOVA analysis of variance (Table 5). Based on the obtained data, it can be concluded about the high acceptance level of the prediction model for the risk of chronic tonsillitis progression, in general, using this analysis since the level of significance is $p < 0.001$, and the model itself will work better than a simple prediction using average values.

To additionally evaluate the quality of the mathematical model for predicting the risk of chronic tonsillitis progression, the coefficient of determination (R^2)

was analyzed, which shows what part of the factors is considered in the prediction. It is considered a universal measure of the relationship of one random variable with others. The coefficient of determination varies from 0 to 1. The closer its value is to "1", the higher the quality of the multivariate regression model. In the proposed mathematical model for predicting the risk of chronic tonsillitis progression, the coefficient of determination is $R^2 = 0.8258$ [in the Statistica 10.0 program $R^2 = .82581865$ (Figure 3)].

So, in our case, 82.58% of the factors are considered in the prediction model of the risk of chronic tonsillitis progression. The coefficient of determination indicates how well the obtained observations confirm the mathematical model.

Discussion

In the point assessment of the condition of patients with chronic tonsillitis and the effectiveness of

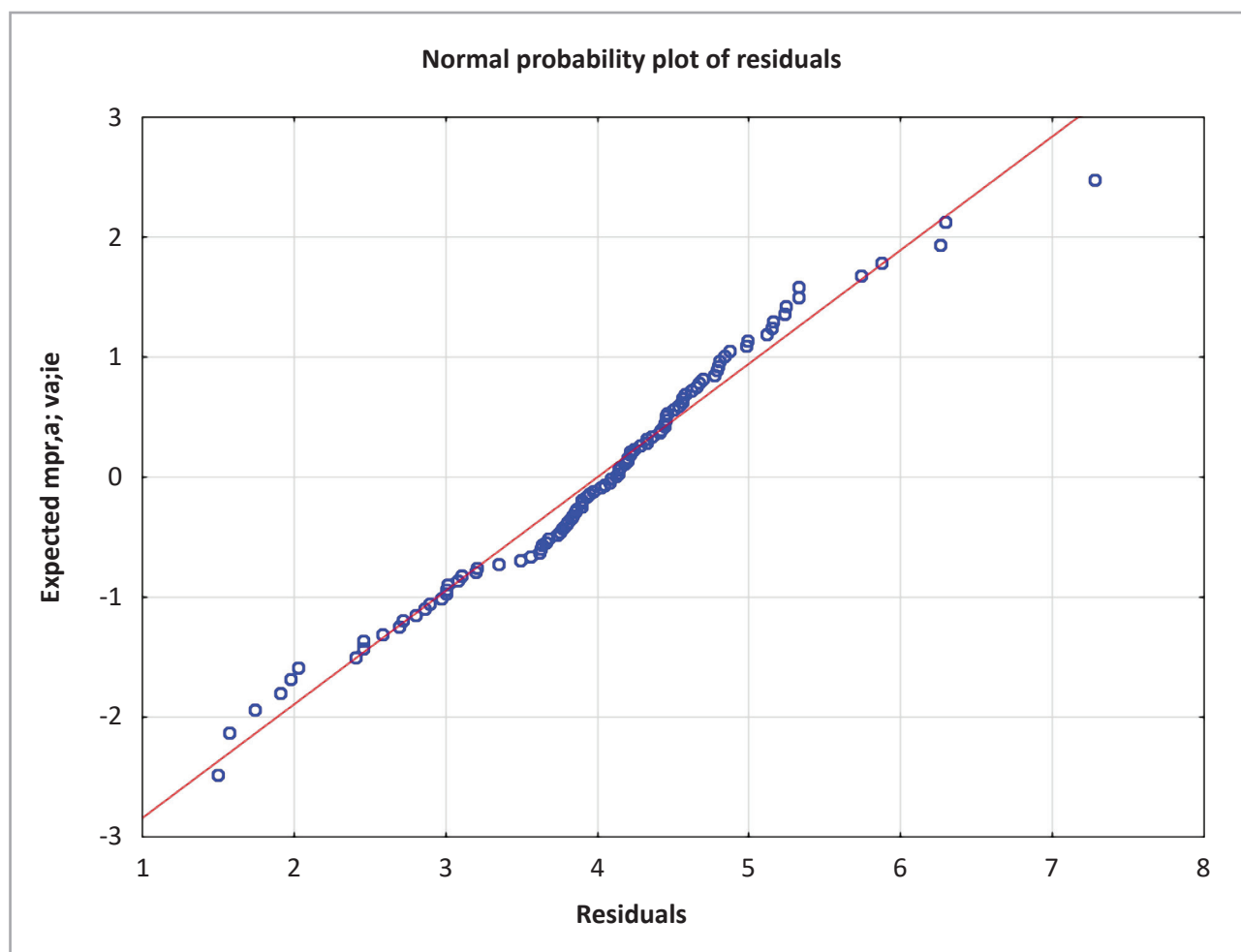


Figure 2: The normal-probability plot of the residual deviations of the multivariate regression model for the prediction of chronic tonsillitis progression (ChTP).

its treatment, we used the proposed by D.I. Zabolotnyi and coauthors [11] of clinical indicators, which include the degree of hyperemia of the arches; the presence of caseous-purulent detritus in lacunae; condition of submandibular lymph nodes; body temperature during exacerbation of chronic tonsillitis. However, some of these indicators, in particular, “Hyperemia of arches” and “Condition of submandibular lymph nodes,” were rejected by the model. These diagnosis factors and risk prognosis are more subjective than objective and do not give a clear diagnostic picture of the pathological process.

The results of our previous studies show that women suffer from CHT 1.43 times more often than men. Most often, the disease is registered in the age period from 18 to 44 years, that is, in people of working age, which is 94.5% of all hospitalized patients. In people older than 75 years, ChT was rarely registered [16]. However, based on the results of the multivariate regression analysis, the sex-age characteristic is also not an objective indicator of the reflection of the real state

of the palatine tonsils and was not considered by the model as a significant factor in predicting chronic tonsillitis progression.

On the contrary, the mathematical model of the multivariate regression analysis was more inclined to objective indicators, in particular, the condition of the oral cavity; levels of Antistreptolysin-O, C-reactive protein, rheumatoid factor, erythrocyte sedimentation rate; WBC level; the presence of caseous content in the lacunae of the palatine tonsils; body temperature indicators; smoking, which confirms the importance of objective indicators.

The use of the mathematical model proposed by us, which considers possible risk factors for the prediction of the ChT progression and rejects non-liquid factors, provides the possibility of early prediction of potential complications and the probability of disease progression. This, in turn, contributes to early diagnosis and selection of more effective and less harmful methods of CT treatment and prevents the possible development of metatonsillar complications.

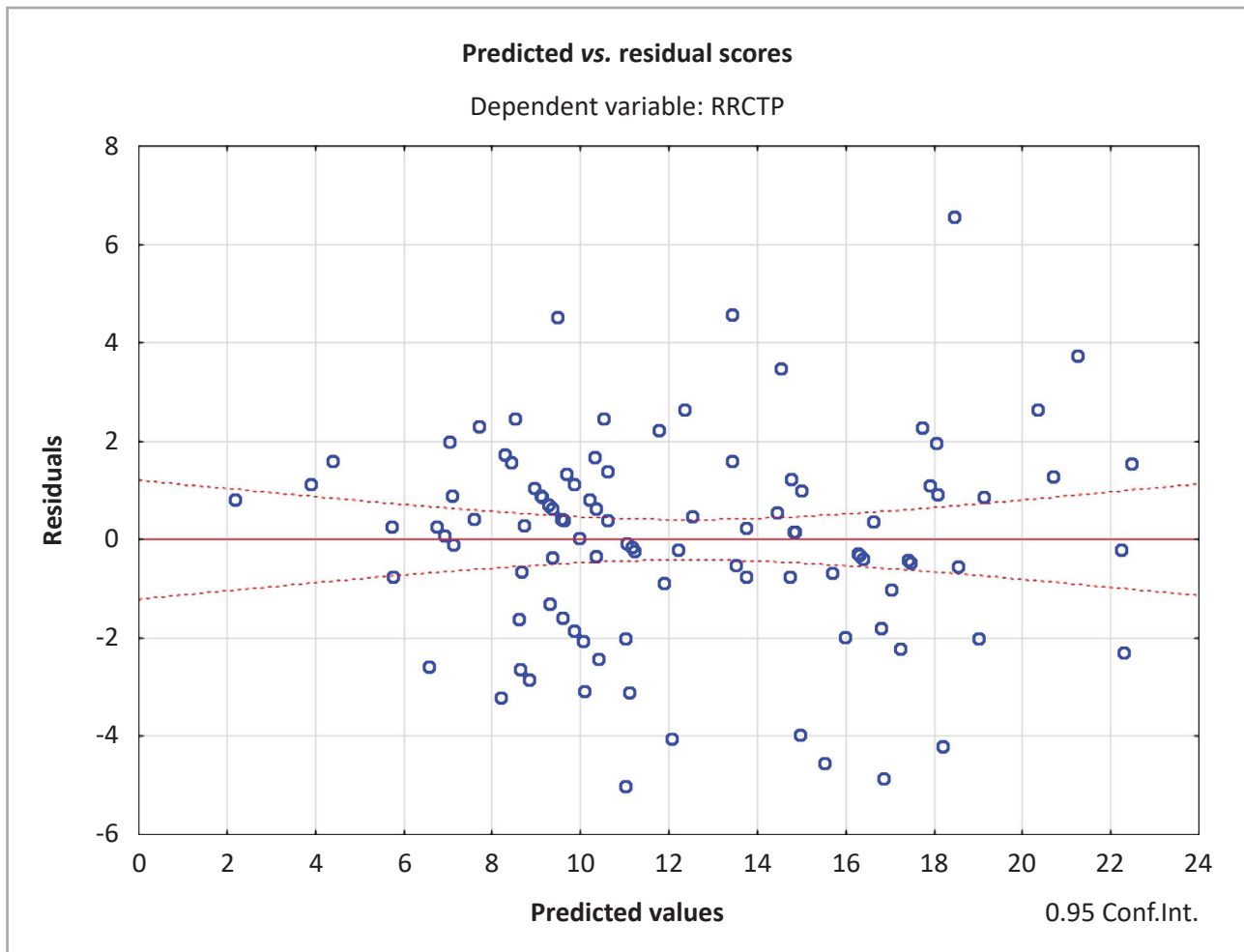


Figure 3: Scatter diagram of the residual deviations of the multivariate regression model for predicting the risk of progression of chronic tonsillitis.

Table 5: ANOVA analysis of variance.

Effect	Analysis of variance; DV: RRCTP (1 in 1)				
	Sums of squares	df	Mean squares	F	P-value
Regress.	1982.824	9	220.3137	47.41143	0.000000
Residual	418.216	90	4.6468		
Total	2401.040				

In the following studies, it is necessary to conduct an ROC analysis to determine the sensitivity, specificity, and accuracy of the proposed mathematical model for predicting chronic tonsillitis progression.

Conclusion

The proposed mathematical model considers significant factors and screens out insignificant non-liquid risk factors for the progression of chronic tonsillitis. A

multivariate regression model that considers the risk factors for the ChT progression makes it possible to predict potential meta tonsillar complications and the possibility of timely disease prevention. Using this model will make it possible to perform tonsillectomy on time and, in turn, reduce possible postoperative complications. In the future, the obtained results can be used to design an information-diagnostic system for assessing and predicting the ChT progression, which develops because of the joint influence of a few socioeconomic and medical-biological factors in patients with ENT diseases.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Ethics Committee of the Ternopil National Medical University, Ternopil, Ukraine (minutes no. 74 dated September 1, 2023). Research was conducted in compliance with all moral and ethical principles, taking into account the World Medical Association Declaration of Helsinki.

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