ORIGINAL ARTICLE

CONTENTS

# Using roc-analysis as a method of assessing the quality of prediction of the risk of progressing chronic tonsillitis

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## ABSTRACT

**Aim:** To propose a new and original approach to assessing the quality of a multivariate regression model for predicting the risk of progression of chronic tonsillitis based on ROC analysis with the construction of appropriate curves, the estimation of the area under them, and the calculation of operational characteristics

**Materials and Methods:** 183 patients were examined. To build a multifactorial regression model for predicting the risk of progression of chronic tonsillitis, 11 probable factors were selected.

**Results:** To determine the diagnostic value of the proposed model based on the obtained results, the sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NVP), the likelihood ratio of a positive result (LR+), the likelihood ratio of a negative result (LR-) and prediction accuracy % of the proposed mathematical model. To determine the prognostic value of the model, a ROC analysis was performed with obtaining of ROC curves.
Area under the curve AUC1 = 0.821; AUC2 = 0.789. Therefore, the prognosis of the risk of progression of chronic tonsillitis is high.

**Conclusions:** The use of multivariate regression analysis with the construction of a model that considers the most important risk factors for the progression of chronic tonsillitis allows predicting the possibility of the disease transitioning into a more severe form. The evaluation of the areas under the ROC-curves gives reason to assert the high quality for the classification of the prediction of the risk of chronic tonsillitis progression.

**KEY WORDS:** risk factors, prognosis, ROC analysis, chronic tonsillitis

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## INTRODUCTION

Today, from 12.5% to 22.1% of the population suffers from chronic tonsillitis (ChT), as evidenced by the data of various authors. This, in turn, makes up from 22% to 40% among all chronic pathology of the ENT organs [1-4].

Considering the significant progress in the study of the immune function of the tonsils, the tonsillar problem in its clinical aspect has shifted towards a gentle attitude to the lymphoepithelial structures of the pharynx [1,5,6]. Nevertheless, tonsillectomy continues to be one of the most common methods used by otolaryngologists [1,7].

According to the classification, specific and non-specific chronic tonsillitis are distinguished. Chronic specific tonsillitis is a lesion of the tonsils with infectious granulomas (tuberculosis, syphilis, scleroma). Chronic nonspecific tonsillitis is an infectious-allergic disease with local manifestations in the form of a persistent inflammatory reaction of the palatine tonsils (PT), which is morphologically manifested by alteration, exudation, and proliferation [8].

There are two forms of chronic non-specific tonsillitis: simple (compensated) and toxic-allergic (decompensated). At the same time, the toxic-allergic form (TAF) is divided into two subforms: TAF 1 and TAF 2.

With a simple form of ChT, local signs of inflammation prevail (swelling and thickening of the edges of the arches, liquid pus or purulent plugs in lacunae). An increase in regional lymph nodes may be observed.

With TAF 1, local signs of inflammation are joined by general toxic-allergic manifestations, without violations of the normal ECG pattern.

With TAF 2, the above-mentioned manifestations of ChT are joined by functional disturbances of the heart with a change in the ECG pattern and functional disorders in the joints, vascular system, kidneys and liver are revealed.

With a simple form and TAF 1, conservative therapy is carried out, and with TAF 2, surgical intervention - tonsillectomy - is the only method of choice.

Although a significant number of scientific studies have been published today, devoted to the study of

the process of transformation of the PT from an organ that performs useful functions into a focus of infection, the issue of further development of optimal sets of diagnostic tests for assessing the condition of the PT in order to dynamically monitor the effectiveness of conservative treatment and determining indications for surgical intervention remains open [1,9,10].

Today one of the most accurate methods of predicting the risk of progression of various diseases, including ChT, is the construction of a multivariate regression model, which includes several predictors that may be the cause of a repeated inflammatory process or disease progression [11]. However, determining the sensitivity, accuracy, and specificity of the proposed model requires an additional ROC analysis with the construction of a ROC curve.

## AIM

The purpose of the work is to propose a new and original approach to assessing the quality of a multivariate regression model for predicting the risk of progression in patients with various forms of chronic tonsillitis based on ROC analysis with the construction of appropriate curves, the estimation of the area under them, and the calculation of operational characteristics.

## MATERIALS AND METHODS

In the course of our work, we examined 183 patients aged 18 to 70, including 96 women and 87 men, with a diagnosis of chronic tonsillitis, who were receiving outpatient treatment in the surgical department of the polyclinic of the CNE "City Clinical Hospital No. 3" of Ternopil City Council (now CNE "Ternopil City Communal Emergency Hospital"). The average age of the patients was 37 years, and the duration of the disease varied within 5-8 years.

All patients signed an informed consent to participate in the study. After receiving the opinion of the bioethics commission at I. Horbachevsky Ternopil National Medical University (minutes no. 77 dated April 18, 2024), research was conducted in compliance with all moral and ethical principles, taking into account the World Medical Association Declaration of Helsinki.

Previously, each patient underwent a complex clinical and laboratory examination, which included anamnesis collection, examination of the oropharynx, general blood analysis with the formula, levels of Antistreptolysin-O (ASL-O), C-reactive protein (CRP), rheumatoid factor (RF).

According to a specially developed questionnaire for assessing the prognosis of the risk of chronic tonsillitis progression, all patients were surveyed, which included 13 risk factors for the progression of ChT: age, sex, sanitation of the oral cavity, level of ASL-O, CRP, RF, ESR level, presence of leucocytosis (according to the leukocyte formula), hyperaemia 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.

Multivariate regression analysis involves creating a mathematical model for predicting the explored disease, including the most important risk factors for which the significance level is $p < 0.05$. All risk factors for which $p > 0.05$ are excluded from the mathematical model for predicting the explored disease.

With the help of multivariate regression analysis, a prognostic model of the risk of ChT progression was built.

For the initial verification of the adequacy of the mathematical model, a histogram of residual deviations and a normal probability plot were constructed, and the Nigelkirk coefficient of determination ($R^2$) was analyzed, which shows what part of the factors is taken into account in the forecast and additionally confirms the effectiveness of the proposed mathematical model.

The statistical processing of the obtained research results was carried out using the statistical package Statistica 10.0 and the table editor Microsoft Excel 2019.

To obtain a numerical value of the clinical significance of the test, as well as to compare several tests, calculations of ROC analysis were carried out in the Matlab program using the integral indicator of the area under the ROC curve - AUC (Area Under Curve).

The ROC curve is a characteristic curve that shows the dependence of the number of correctly diagnosed positive cases on the number of incorrectly diagnosed negative cases when varying the threshold of the decisive rule [12].

## RESULTS

The creation of a mathematical model using the method of multivariate regression analysis for the prognosis of the risk of 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 progress of the disease and to choose the most optimal and effective methods for treatment and prevention of this pathology.

To build a multivariate regression model for predicting the risk of ChT progression, 13 probable factors were selected: age, sex, sanitation of the oral cavity, level of ASL-O, CRP, RF, ESR level, presence of leucocytosis

**Table 1.** Significant risk factors for the ChT 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 |
| ESR level | **X4** | Norm | 0 |
| | | Elevated | 1 |
| WBC level | **X5** | Normal | 0 |
| | | Elevated | 1 |
| Presence of caseous detritus in lacunae | **X6** | 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 | **X7** | Normal temperature | 0 |
| | | Subfebrile | 1 |
| | | About 38° C | 2 |
| | | > 38° C | 3 |
| Age | X8 | 18-25 | 0 |
| | | 25-44 | 1 |
| | | 44-60 | 2 |
| | | 60-75 | 3 |
| | | 75-90 | 4 |
| Smoking | **X9** | No | 0 |
| | | Yes | 1 |
| Hyperaemia of palatine arches | **X10** | No hyperemia | 0 |
| | | Slight hyperemia | 1 |
| | | Pronounced hyperemia of the arches and mucous membrane of the tonsils | 2 |
| | | Pronounced hyperemia of the arches, mucous membrane of the tonsils, lateral and posterior walls of the pharynx | 3 |
| Condition of submandibular lymph nodes | **X11** | Normal | 0 |
| | | Slightly enlarged | 1 |
| | | Periodically enlarged and painful | 2 |
| | | Permanently enlarged and periodically painful | 3 |

(according to the leukocytes formula), hyperaemia of palatine arches, presence of caseous detritus in PT lacunae, the condition of submandibular lymph nodes, body temperature, smoking with the calculation of the regression coefficient "b" (Beta), which reflects for each selected factor the relationship, regarding the impact on the risk of ChT progression in the examined patients. Risk factors with a significance level of $p > 0.05$ were excluded from further analysis (Table 1). Since the significance levels of eleven risk factors were less than

| N=183 | Regression Summary for Dependent Variable: Risk factor for prog<br>R= ,89521216 R?= ,80140481 Adjusted R?= ,78862968<br>F(11,171)=62,732 p<0,0000 Std.Error of estimate: ,99115 | | | | | |
|---|---|---|---|---|---|---|
| | b* | Std.Err. of b* | b | Std.Err. of b | t(171) | p-value |
| **Intercept** | | | -66,7083 | 8,958831 | -7,44610 | 0,000000 |
| sanitation of the oral cavity | 0,163761 | 0,035414 | 0,7108 | 0,153717 | 4,62421 | 0,000007 |
| ASL-O | 0,152897 | 0,038388 | 0,0091 | 0,002286 | 3,98296 | 0,000101 |
| CRP | 0,106450 | 0,036958 | 0,2123 | 0,073722 | 2,88026 | 0,004482 |
| ESR | 0,371212 | 0,036527 | 0,1396 | 0,013737 | 10,16265 | 0,000000 |
| WBC level | 0,081100 | 0,036291 | 0,0814 | 0,036440 | 2,23470 | 0,026732 |
| Presence of caseous detritus in lacunae | 0,431332 | 0,035634 | 1,8627 | 0,153887 | 12,10462 | 0,000000 |
| Body temperature | 0,288037 | 0,036777 | 1,8865 | 0,240873 | 7,83198 | 0,000000 |
| Age | -0,129254 | 0,036492 | -0,0216 | 0,006088 | -3,54196 | 0,000512 |
| Smoking | 0,243674 | 0,035276 | 1,0485 | 0,151793 | 6,90771 | 0,000000 |
| Hyperemia of the palatal arches | 0,270694 | 0,043323 | 1,2008 | 0,192186 | 6,24825 | 0,000000 |
| Condition of submandibular lymph nodes | 0,404110 | 0,040827 | 1,7389 | 0,175679 | 9,89822 | 0,000000 |

**Fig. 1.** The result of obtaining significant factors for the prognosis of the risk pf chronic tonsillitis progression (ChTP) when conducting a multivariate regression analysis in the Statistica 10.0 program without non-liquid factors

**Table 2.** Initial data for the calculation of operational characteristics in the classification of the average (R-2) degree of risk of chronic tonsillitis progression, relatively low (R-1) and high (R-3) degrees

| **Degree of risk of ChT progression** | **The number of patients for the verification of the RChTP model with classification R 2, relative to R 1, R 3 among patients with chronic tonsillitis** | | | | |
|---|---|---|---|---|---|
| | True positive R 1, R 3 (a) | Amount R 1, R 3 | False positive R 2 (b) | Amount R 2 | Total (a+b) |
| R 1 | 80 | 80 | 7 | 7 | 87 |
| R 3 | 0 | | - | | |
| R 2 | False negative (c) | 4 | True negative (d) | 92 | Total (c+d) 96 |
| Total | a+c 84 | | b+d 99 | | a+b+c+d 183 |

**Table 3.** Generalized operational characteristics of the mathematical model for predicting the risk of chronic tonsillitis progression

| **Designation of operational characteristics** | **Levels of risk of chronic tonsillitis progression** | | **Average values of operational characteristics** |
|---|---|---|---|
| | **R-1** | **R-2** | |
| Se, % | 91,43 | 95,2 | 93,3 |
| Sp, % | 91,02 | 92,92 | 91,9 |
| PPV, % | 93,2 | 91,95 | 92,5 |
| NPV, % | 88,75 | 95,8 | 92,2 |
| LR+ | 10,18 | 13,44 | 11,8 |
| LR- | 0,09 | 0,05 | 0,07 |
| Prediction accuracy, % | 91,2 | 93,9 | 92,5 |

Note. Se – sensitivity; Sp – specificity; PPV - positive prognostic value; NPV - negative prognostic value; LR+ – the likelihood ratio of a positive result; LR- the likelihood ratio of a negative result.

0.05, they were included in the mathematical model for predicting the risk of ChT progression (Fig. 1).

Based on the results of the multivariate regression analysis of the prediction of the risk of ChT progression, which are shown in fig. 1, we build a mathematical model for determining the coefficient of risk factor for the ChT progression (CRFChTP):

CRFChTP=0,7108*X1+0,0091*X2+0,2123*X3+0,1396*X4+0,0814* *X5+1,8627*X6+1,8865*X7-0,0216*X8+1,0485*X9+1,2008*X10+1,7389*X11-66,7083,

where CRFChTP is the coefficient of risk factor for the ChT progression;

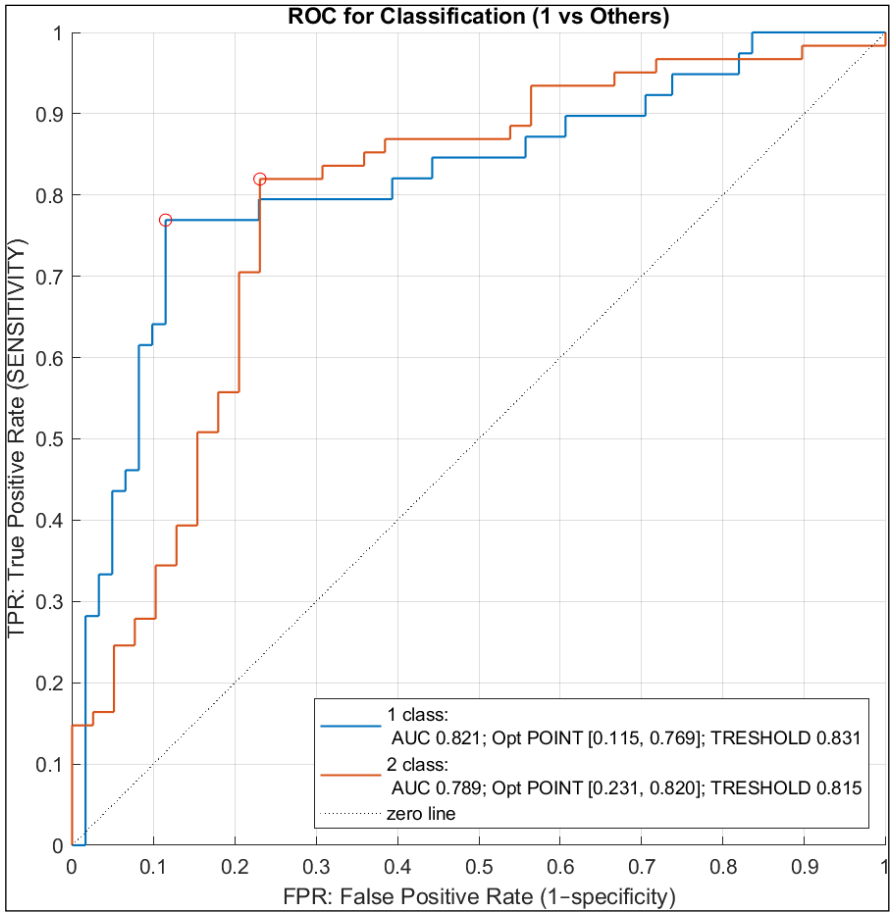


**Fig. 2.** ROC curves for predicting the risk factor of the chronic tonsillitis progression R-1 and R-2

X1-X11 – selected risk factors for the ChT progression with regression coefficients;

-66,7083 is a constant.

For additional assessment of the quality of the mathematical model of CRFChTP, the Nigelkirk coefficient of determination ($R^2$) was analysed, which shows what part of the factors is considered during prediction. In the proposed mathematical model of CRFChTP, the coefficient of determination is $R^2 = 0.8014$ (in the Statistica 10.0 program R?= .80140481 (Fig. 1)). So, in our case, 80.14% of the factors are considered in the risk prediction model of ChT progression, which indicates how well the obtained observations confirm the mathematical model [10].

To determine the diagnostic value of the proposed model, based on the obtained results, we calculate the sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), the likelihood ratio of a positive result (LR+), the likelihood ratio of a negative result (LR-) and prediction accuracy % of the proposed mathematical model.

Based on the classification of the chronic nonspecific tonsillitis, we distinguish three degrees of risk of ChT progression: low (R-1), medium (R-2) and high (R-3). Since all patients were receiving outpatient treatment, there were no cases of decompensated form (TAF 2) requiring operative treatment.

Let's consider an example of calculating the operational characteristics (Se, Sp, PPV, NPV, LR+, LR- and prediction accuracy) of the proposed mathematical model on the example of the average (R-2) degree of risk of chronic tonsillitis progression (RChTP) (Table 2).

The sensitivity of detection of RChTP R-2 relative to R-1, R-3 is calculated according to the formula:

$$Se = (a / (a+ c))*100\%. \quad (1)$$

Considering the numerical values (Table 2), we get:

$Se = (80 /(80+4))*100\% = (80/84)*100\% = 95,2\%.$

To identify the specificity of RChTP R-2 relative to R-1, R-3, we calculate the result according to the following formula:

$$Sp = (d/(b+ d))*100\ \% \quad (2)$$

Considering the data in Table 2, we get:

$Sp = (92/(7+92))*100\% = (92/99)*100\% = 92,92\%.$

The prognostic value of a positive result in the classification of patients with RChTP R-2 relative to R-1, R-3 was determined by the formula:

$$PPV_{1234} = (a_{1234} /(a_{1234}+b_{1234}))*100\ \% \quad (3)$$

Based on the numerical values of table 2, we get

$PPV_{1234} = (80/(80+7))*100\% = (80/87)*100\% = 91,95\%.$

Therefore, the probability of identifying patients with R-2 RChTP with a positive classification result, relative to R-1, R-3, is 91.95%.

Regarding the prognostic value of the negative result of the classification of patients with R-2 relative to R-1, R-3, it is calculated according to the following formula:

$NPV_{1234} = (d_{1234}/(c_{1234}+ d_{1234}))*100\ \%$ (4)

By substituting the data in Table 2, we get the following result:

$NPV_{1234} = (92/(4+92))*100\% = (92/96)*100\% = 95,8\%.$

Accordingly, the probability of identifying patients with R-2 RChTP with a negative classification result, relative to R-1, R-3, is 95.8%.

We calculate the probability ratio of a positive result of detecting patients with RChTP R-2 relative to R-1, R-3 as follows:

$LR+_{1234} = (Se_{1234}/(100-Sp_{1234}))$ (5)

Considering the numerical values (Table 2), we get:

$LR+_{1234} = (95,2/(100- 92,92)) = 95,2/7,08 = 13,44.$

Therefore, the probability of receiving a positive result of RCTP in patients with R-1, R-3 is 13.44 times greater, compared to the probability of a positive result in patients with R-2.

The ratio of the probability of a negative result of detecting patients with R-2 relative to R-1, R-3 is as follows:

$LR-_{1234} = ((100-Se_{1234})/Sp_{1234})$ (6)

Considering the numerical values (Table 2), we get:

$LR-_{1234} = ((100-95,2)/92,92) = 0,05.$

Therefore, the probability of receiving a negative result of RChTP in patients with R-2 is 20 times greater (1/0.05), compared to the probability of a positive result in patients with R-1, R-3.

The accuracy of RChTP R-2 based on the obtained results is calculated as follows:

Accuracy of $RChTP_{1234} = ((a_{1234}+ d_{1234})/(a_{1234}+ b_{1234} +c_{1234}+ d_{1234}))*100\%$ (7)

Accuracy of $RChTP_{1234}= ((80+92)/(80+7+4+ 92))*100\% = (172/183)*100\% = =93,9\%$

Therefore, the share of correct prediction results of R-2 ChT is 93.9%.

Similarly, the calculation of operational characteristics was carried out for a low degree of risk of progression of chronic tonsillitis (R-1). The obtained operating characteristics of the mathematical model for predicting the risk of progression of chronic tonsillitis (R-1, R-2) and their average values are shown in the Table 3.

To determine the prognostic value of the CRChTP model, ROC-analysis was performed to obtain ROC-curves for low (R-1) and medium (R-2) degrees of risk of ChT progression, and the corresponding areas under them (AUC) were determined to evaluate the quality of the proposed mathematical model.

It is recommended that the diagnostic test be both highly sensitive and highly specific. To achieve a compromise between sensitivity and specificity, to adequately choose a diagnostic criterion and distinguish patients (sick persons) from healthy, it is recommended to construct a ROC curve.

After constructing the ROC curve, the corresponding data of the integral indicator of the area were obtained.

As can be seen from fig. 2, area under the curve AUC1 = 0.821 (classification quality R-1 CRChTP); AUC2 = 0.789 (quality of classification R-2 CRChTP). Therefore, according to the ROC analysis, the prediction of R-1, R-2 degrees of risk of ChT progression is high.

## DISCUSSION

The use of the mathematical model proposed by us, which considers possible risk factors for the ChT progression, provides the possibility of early prediction of potential complications and the probability of the disease transitioning into a more severe form. This, in turn, contributes to early diagnosis and selection of optimal treatment methods for ChT, which will reduce the risk of disease progression.

Approaches to building multivariate regression prediction models in medicine are considered in the works of Musiienko V. et al. (2021); Musiienko V. et al. (2022) [13,14], which closely echo the conducted research.

The concept of reliability in medicine is multifaceted and includes a complex of operational characteristics, each of which is a specific statistical indicator. This complex includes such components as sensitivity, specificity, positive and negative prognostic value, accuracy indicators and the likelihood ratio of positive and negative results.

Sensitivity (Se) - shows the proportion of individuals with a positive test result among individuals with the disease under investigation, and specificity (Sp) indicates the proportion of individuals with a negative test result among individuals without the disease under investigation.

In our case, the mathematical model shows a sensitivity and specificity index approaching 90% (Se – 93.3 %, Sp – 91.9 %), which indicates that more than 90% of cases were diagnosed correctly.

Based on the obtained results, we believe that the accuracy of the prediction of the risk of chronic tonsillitis progression is 92.5%, and the constructed ROC curves approach the upper left corner (AUC1 = 0.821 (quality of classification R-1 CRChTP); AUC2 = 0.789 (quality of classification R- 2 CRChTP). All this points to the strong diagnostic validity of this model and suggests that the model is of high quality and can be a useful application for doctors in identifying patients with different degrees of risk of chronic tonsillitis progression and making decisions about its treatment.

The results of ROC analysis for 3 degrees of climacteric syndrome are considered in the work of Chukur O. et

all. (2022); ROC analysis was also performed for the 3rd degree of risk of chronic rhinosinusitis recurrence in the work of Herasymiuk M. et al. [15,16]. In all cases, the performed ROC analysis showed a high and excellent result of the application of multivariate regression analysis.

## CONCLUSIONS

1. The use of multivariate regression analysis with the construction of a model that considers the most important risk factors for the ChT progression allows predicting the possibility of the disease transitioning into a more severe form with high values of sensitivity (93.3%), specificity (91.9%) and accuracy (92.5 %).
2. The evaluation of the areas under the ROC-curves gives reason to assert the high quality of the classification of low and medium degrees of risk of chronic tonsillitis progression, which allows timely and correct diagnosis of the severity of the disease, choose more effective treatment methods and avoid possible complications.
3. The use of this technique can be used for the development of medical calculators for assessing the severity of the risk degree of chronic tonsillitis progression, as well as for the design of relevant information and diagnostic systems in otolaryngology.

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## CONFLICT OF INTEREST

The Authors declare no conflict of interest

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