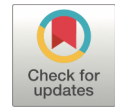


ORIGINAL ARTICLE



Artificial neural network to predict risk factors associated with postoperative complications secondary to pneumothorax treatment

Red neural artificial para predecir factores de riesgo asociados a complicaciones postoperatorias secundarias al tratamiento del neumotórax

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Abstract

Introduction. Due to the absence of statistically significant predictive models focused on postoperative complications in the surgical management of pneumothorax, we developed a model using neural networks that identify the independent variables and their importance in reducing the incidence of postoperative complications.

Methods. A retrospective single-center study was carried out, where 106 patients who required surgical management of pneumothorax were included. All patients were operated by the same surgeon. An artificial neural network was developed to manage data with limited samples. The data is optimized and each algorithm is evaluated independently and through cross-validation, to obtain the lowest possible error and the highest precision with the shortest response time.

Results. The most important variables according to their weight in the decision system of the neural network (AUC 0.991) were the approach via video-assisted thoracoscopy (OR 1.131), use of pleurodesis with talc (OR 0.994) and use of autosutures (OR 0.792, $p < 0.05$).

Discussion. In our study, the main independent predictors associated with a higher risk of complications are pneumothorax of secondary etiology and recurrent pneumothorax. Additionally, we confirm that the variables associated with a reduction in the risk of postoperative complications have statistical significance.

Conclusion. We identify video-assisted thoracoscopy, use of autosuture and talc pleurodesis as possible variables associated with a lower risk of complications and raise the possibility of developing a tool that facilitates and supports decision-making, for which external validation in prospective studies is necessary.

Keywords: artificial intelligence; computer neural networks; pneumothorax; thoracoscopy; talc; postoperative complications.

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Resumen

Introducción. Debido a la ausencia de modelos predictivos estadísticamente significativos enfocados a las complicaciones postoperatorias en el manejo quirúrgico del neumotórax, desarrollamos un modelo, utilizando redes neurales, que identifica las variables independientes y su importancia para reducir la incidencia de complicaciones.

Métodos. Se realizó un estudio retrospectivo en un centro asistencial, donde se incluyeron 106 pacientes que requirieron manejo quirúrgico de neumotórax. Todos fueron operados por el mismo cirujano. Se desarrolló una red neural artificial para manejo de datos con muestras limitadas; se optimizaron los datos y cada algoritmo fue evaluado de forma independiente y mediante validación cruzada, para obtener el menor error posible y la mayor precisión con el menor tiempo de respuesta.

Resultados. Las variables de mayor importancia según su peso en el sistema de decisión de la red neural (área bajo la curva 0,991) fueron el abordaje por toracoscopia video asistida (OR 1,131), el uso de pleurodesis con talco (OR 0,994) y el uso de autosuturas (OR 0,792; $p < 0,05$).

Discusión. En nuestro estudio, los principales predictores independientes asociados a mayor riesgo de complicaciones fueron el neumotórax de etiología secundaria y el neumotórax recurrente. Adicionalmente, confirmamos que las variables asociadas a reducción de riesgo de complicaciones postoperatorias tuvieron significancia estadística.

Conclusión. Identificamos la toracoscopia video asistida, el uso de autosuturas y la pleurodesis con talco como posibles variables asociadas a menor riesgo de complicaciones. Se plantea la posibilidad de desarrollar una herramienta que facilite y apoye la toma de decisiones, por lo cual es necesaria la validación externa en estudios prospectivos.

Palabras clave: inteligencia artificial; redes neurales de la computación; neumotórax; toracoscopia; talco; complicaciones posoperatorias.

Introduction

Algorithms based on artificial intelligence provide a point of support for doctors who, together with the patient and the rest of the multidisciplinary team, are looking for tools that allow them to make the best possible decisions.

A specific area of research that continues to develop for thoracic surgery is the development of individualized pre-surgical risk classification systems. Due to the constant search for means to reduce the morbidity associated with the surgical procedures used in thoracic surgery, in this study we address the complications associated with the surgical management of pneumothorax from a preventive approach.

Starting from the experience in a healthcare center, based on preoperative, intraoperative and postoperative characteristics, we focus our algorithm to generate an artificial neural network model that leads to selecting the best approach technique for pneumothorax, allowing us to determine in

real time which are the variables that influence a lower incidence of postoperative complications, and thus generate a complementary tool to support clinical judgment in favor of a better result for the patient.

Methods

Study design

Retrospective observational study, carried out in the Thoracic Surgery Service of the Santo Tomás Hospital in Panama City, Panama. The universe corresponded to all the patients admitted with a diagnosis of primary or secondary pneumothorax that required surgical management, between January 1991 and December 2016. The decision on the type of surgery was made according to the experience of the surgeon and the type of surgery recommended in the international literature. All patients in the study cohort were operated on by the same surgeon, which minimized the hetero-

geneity of the procedure and avoided the effect of different learning curves on the results.

The patients were divided into two groups, with primary pneumothorax (PN) and secondary pneumothorax (SN). The clinical data collected for the statistical analysis included: sex, age, persistence of the pneumothorax, recurrence of the pneumothorax, year in which the surgery was performed, surgical procedure performed, intraoperative bleeding, complications, presence of prolonged leak, and hospital days. Additionally, data from the performance of pleurodesis, either with talcum powder, abrasion, pleurectomy or pleural tent, were collected for subgroup analysis. For the calculation of the adjusted hospital stay, patients with a stay of more than 14 days and patients for whom the information was not available were excluded.

Database

In this study, a database created by the doctors of the Thoracic Surgery Service was used as a source of information, by recording the retrospective information obtained from the medical records in a document in xlsx format of the Microsoft Excel® program (Microsoft Corporation, Redmond, USA). In order to use them as a database in the artificial intelligence model, the format was changed into a csv file or comma-separated values, for its acronym in English.

Using the Python programming language (Python Software Foundation, Delaware, USA) version 3.9.6, the data was sequentially transformed, first eliminating the special characters, then creating a dictionary that transformed the abbreviations into words, and subsequently reducing to lowercase letters all the letters contained in the information of each variable. Empty cells were eliminated creating columns with complete information without empty values, with the same text format and valid data to be processed. Once the data was cleaned, we proceeded to use the Python pandas library (Python Data Analysis Library) version 1.4.1, to transform the information into a data frame, which served as a database and starting point for storing information in test and

validation variables, which were finally used by our models.

Artificial intelligence model

Our model consists of an artificial neural network whose schematic representation can be seen in figure 1. It is a multilayer topology neural network, with an input layer or input variables that receives N variables in its first interaction. This number of input variables is modified to obtain different variants of the model and to assess the sensitivity, specificity, and area under the curve of each model.

The initial model consisted of a number of 32 neurons per layer and 8 hidden layers. The ReLU activation function was used in the intermediate layers, alternated with sigmoid functions in the different variants; likewise, the number of epochs on which the model would be trained was changed. These changes and the multiple variations are due to the low number of data available, in an attempt to obtain various models and be able to compare them, not only with each other but also with models that use other computational learning methods.

In the last layer or output layer, a sigmoid function was used to normalize the values in a range from 0 to 1. For the classification task, the binary cross entropy loss was used, with the Adam optimizer and a group or batch size of 512. This initial model was modified in multiple variations and contrasted with other models to report the data obtained from the statistical comparison of models and the clinical results suggested by the best model.

Model Training

The training process was carried out using data obtained from the initially created data frame, which was divided randomly using the `test_train_split` module of the scikit-learn library in its version 1.0.2. Four variables called `x_train`, `x_test`, `y_train` and `y_test` were created, to which 75% of the data available in the training variables were assigned; the test variables, which would be used to validate the model, were assigned 15% of the remaining data.

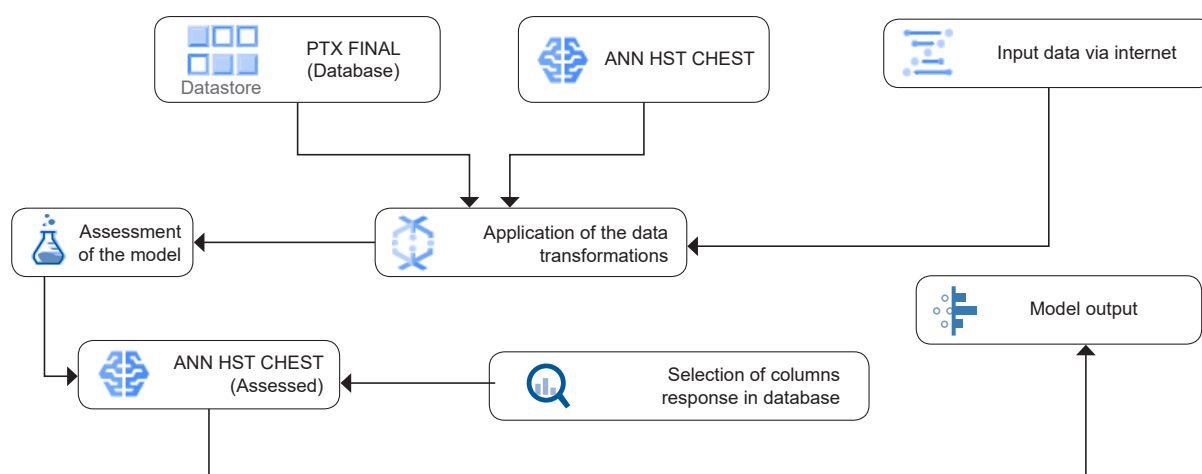


Figure 1. Visual representation of the final predictive model when deployed as an online service for real-time evaluation of results. Source: Database of the Thoracic Surgery Service of the Hospital Santo Tomás, Panama City, Panama. Built on Microsoft Corporation 2022 Azure digital cloud platform.

After obtaining the first model, which was already described and was assigned the name ptx pred 0.0.1, we proceeded to carry out the training and validation with the data obtained and adjust it to the lowest mean error with the highest precision and F1 score. Each variation of this model was given a similar name, increasing the numerical end of it by one, thus obtaining the models ptx pred .2, .3, ..., n. It should be noted that for each variation of the model, a new random distribution of data was carried out to ensure constant ignorance of the results by the model and to mask variables, which allowed that despite having a relatively small number of samples, they would work randomly to train multiple models, avoiding model overfeeding or the model learning the expected responses in advance, which would render it a stale model when faced with unknown data. To ensure that the models will deal with untested data in the training stage, the remaining 10% of the data was kept out from the first randomization and used as a means of validation to assess the final results of the different models and their multiples. variations.

Statistic analysis

Statistical analysis was performed using the SPSS program (IBM, SPSS Inc, Chicago, USA) version 17.0. Categorical data were presented as frequencies and percentages, comparison was made using the Chi-square test (N-1 test of two proportions) and Fisher's exact test. Continuous parametric and nonparametric data were presented as means and standard deviations (SD) and were assessed using Student's t and Mann-Whitney U tests, respectively. For subgroup analysis, they were divided into open thoracotomy (OT) and video-assisted thoracoscopy (VAT). Due to our sample size, in some subgroups confidence interval calculations were performed using the Wald interval fit. The value of p less than 0.05 was considered statistically significant.

Results

According to our inclusion criteria, in the period between January 1991 and December 2016, a total of 106 patients required surgical management for pneumothorax (primary or secondary). Table 1

presents the demographic data of this study population. It should be noted that 70 patients were managed by OT and 36 patients by VAT. This is an important aspect to highlight since, if we analyze the data as a time series, we can see how a change in the OT vs. VAT. In the last fifteen years, the use of VAT was much higher than OT, in a ratio of almost 4:1.

A model was obtained, which was called the final predictive model of artificial neural network. This was the best statistical model and, therefore, the model used for the subsequent analysis, since it reached a mean precision of 95.4%, with an area under the curve of 0.991, with a standard deviation of 0.064 and a p value of 0.003 (95% CI 0.877 - 0.992).

Among the preoperative variables, it was observed that the greatest contribution to the development of postoperative complications in the surgical management of pneumothorax, based on the independent weight of the variables

in the model, was made by age (4.2%), secondary pneumothorax (3.8%) and right pneumothorax (3.5%) (Table 2). However, during the multivariate logistic regression analysis with the occurrence of complications, only secondary pneumothorax reached statistical significance individually (OR=0.524; p=0.05).

Regarding the trans and postoperative variables described in table 3, the greatest statistical significance was found in the type of surgery (14.1%), the use of autosutures (5.2%) and the use of talcum powder for the pleurodesis (11.9%). In the logistic regression, the independent predictors associated with a lower risk of complications were VAT (OR=1.131; p=0.003), using autosutures (OR=0.792; p=0.04), and using talcum powder for pleurodesis (OR=0.994; p<0.001) (Table 4).

Our definitive neural network model presents an area under the curve of 0.991 (p=0.003) with an accuracy of 95.4%.

Table 1. General characteristics of the patients included in the study.

Variable	Open thoracotomy n=70 (%)	Video assisted thoracoscopy n=36 (%)
Sex		
Male	61 (87.1)	30 (83.3)
Female	9 (12.9)	6 (16.7)
Age (years)		
<20	10 (14.3)	8 (22.2)
20-40	44 (62.8)	17 (47.2)
>40	16 (22.9)	11 (30.6)
Pneumothorax etiology		
Primary	27 (38.6)	16 (44.4)
Secondary	43 (61.4)	20 (55.6)
Hospital stay (days)		
1-6	50 (71.4)	27 (75.0)
>7	20 (28.6)	9 (25)

Discussion

In patients belonging to the normal risk group with thoracic pathologies whose management requires surgical interventions, we can expect up to 5% of postoperative complications¹. Because the area of personalized risk classification systems in thoracic surgery is a developing area and no studies have yet been published that generate the information necessary to establish individualized risk classification systems², to date there is no statistical reference point developed in a previous study to contrast its results with a model similar to ours.

Multiple studies cite the need to carry out prospective investigations to determine the best surgical approach and the best pleurodesis technique, if necessary, in order to have the lowest percentage of recurrence and postoperative complications³⁻⁵; however, studies are lacking to determine which are the independent variables associated with a better clinical evolution or that allow the use of an individualized risk measurement system, which can be applied to each patient as its own entity, and not categorized into a risk group whose heterogeneities can create biases against the benefit of the patient⁵.

Table 2. Preoperative variables and their relationship with the development of postoperative complications in patients with surgical management of pneumothorax.

Variable	Frequency (%)	Importance (%)*
Age (years), mean (SD)	32.2 (10.7)	4.2
Etiology		
Primary	43 (41)	2.5
Secondary	63 (59)	3.8
Type of pneumothorax		
Persistent	70 (67)	2.2
Recurrent	35 (33)	3.1
Anatomical site		
Right	71 (75)	3.5
Left	23 (25)	2.1

*Percentage of importance that the variable has (weight within the neural network) in relation to the other variables computed by the model.

Table 3. Description of trans and postoperative variables.

Variable	Frequency (%)	Importance (%)*
Type of Surgery		
Video-assisted thoracoscopy	36 (33)	10.5
Open thoracotomy	70 (66)	3.6
Bulla treatment		
Ligature	38 (36)	4.2
Autosuture	59 (56)	5.2
None	7 (6)	1.9
Release of adhesions		
Yes	28 (26)	3.2
No	78 (74)	2.8
Pleurodesis		
Talcum powder	31 (41)	11.9
Abrasion	39 (52)	5.1
Pleurectomy	5 (6)	3.1
Complications		
Bleeding	7 (29)	3.9
Prolonged air leak	10 (41)	3.7
Empyema	1 (4)	2.9
Pneumonia	3 (12)	2.6
reoperation	3 (12)	3.4

*Percentage of importance that the variable has (weight within the neural network) in relation to the other variables computed by the model.

Table 4. Significant independent variables after multivariate logistic regression.

Variable	Odds Ratio	p-value
Secondary pneumothorax	0.524	0.05
Recurrent pneumothorax	0.377	0.04
Video-assisted thoracoscopy	1.131	0.003
Autosuture	0.792	0.04
Talcum powder	0.994	<0.001

Currently, in all fields of science there are multiple predictive models based on artificial intelligence systems⁶⁻⁸, since the analysis of databases through neural networks allows non-linear relationships to be found, which are not perceptible through of traditional statistical methods, in addition to create systems that can be applied individually through knowledge transfer, providing a risk-benefit calculation for our patient based on their unique characteristics, which allows for more precise medicine. and, theoretically, a better probability of reducing the morbidity associated with the type of surgical procedure selected for the management of pneumothorax.

Our findings regarding the independent predictive variables coincide with those reported by Cardillo et al.⁸, where the most frequent indications for video-assisted thoracoscopy and talcum powder pleurodesis were recurrent pneumothorax (92.2%) and persistent air leak (6.5%), with 2% complications. As described by Hallifax et al.⁹, there are no prospective randomized studies that evaluate the efficacy of talcum powder pleurodesis via VAT, but there are retrospective studies that demonstrate a shorter hospital stay and a fewer number of complications in the group who underwent talcum powder pleurodesis compared with abrasion (p=0.116).

In our study, the final model of the neural network satisfies the statistical criteria of the proposed objectives. It is relevant to describe that statistical significance was reached despite having been generated from a small database, which is consistent with previous studies¹⁰⁻¹¹ in

which algorithms are proposed to obtain data and significantly improve the predictive characteristics of neural networks, using optimized algorithms to find causal relationships between variables despite having small databases.

Limitations of the study

There are several expected limitations in our study. Since depending on a system of data extracted manually from non-digitized clinical records, there is the possibility of human error and loss of information, which translates into empty cells, which ended up being eliminated in the data processing, thus losing possible valuable information, which may or may not have modified the model result towards one recommendation or another.

Another limitation of our study is the size of the sample, since we are in the era of “big data” in which many consider that to train a model millions of data must be available¹⁰. In our case we are facing the opposite problem, the risk of data underfeeding or “underfitting”¹⁰⁻¹². However, with data mining techniques, changes in the groups of variables that we used as entry points, and changes in the hyper parameters, we were able to obtain a model with a statistically significant response from a small number of data^{10,11}.

Conclusion

In our series of patients, video-assisted thoracoscopy, the use of autosutures, and talcum powder pleurodesis were the variables associated with a lower risk of complications. These findings, seen from the perspective of the introduction of new methods of analysis and synthesis of information, with the corresponding limitations of the study, show the benefits that could had on a population of patients, allowing the evaluation as individuals with risks adjusted to their comorbidities, thus generating better post-surgical results.

It is clear that this study was carried out with a limited sample and that external validation is required, for which we consider it vitally important to carry out a multicenter prospective study, to evaluate the changes required to obtain the best possible model and thus, that it becomes an un-

supervised learning tool with specific parameters, which serves as support in decision-making and positively influences the postoperative outcome of our patients, reducing the morbidity associated with the procedures.

Compliance with ethical standards

Informed consent: This is a retrospective study of medical records review that does not imply risk for patients, so informed consent was not required. The guidelines established in Resolution 008430 of 1993 of the Colombian Ministry of Health and the Declaration of Helsinki established in 1964, last amended in 2008, were followed. The security and confidentiality of the data of the patients included in this study was guaranteed, during the process of collection, analysis and after the publication of the results.

Conflict of interest: none declared by the authors.

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Author's contributions

- Conception and design of the study: Saturnino Domínguez, Rafael Andrade-Alegre.
- Acquisition of data: Rafael Andrade-Alegre.
- Data analysis and interpretation: Saturnino Domínguez, Rafael Andrade-Alegre.
- Drafting the manuscript: Saturnino Domínguez, Rafael Andrade-Alegre.
- Critical review and final approval: Saturnino Domínguez, Rafael Andrade-Alegre.

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