

Development of a Deep Learning Model for the Prognosis of the Occurrence of Death from Stomach Cancer in Senegal

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Abstract

Context and Objectives: Stomach cancer ranks fifth in incidence and fourth in mortality worldwide. In Senegal, there were 597 new cases in 2020, with a mortality rate of almost 70%. The aim of this study was to develop a machine-learning model for the prognosis of death from stomach cancer 5 years after treatment. **Methods:** Our study sample consisted of 262 patients treated for gastric cancer at Aristide le Dantec Hospital and followed postoperatively between 2007 and 2020. We developed a multilayer perceptron with optimal hyperparameters and compared its performance with standard classification algorithms. We also augmented our data with a set of synthetic data generators to evaluate the behaviour of the model when faced with a larger amount of data. **Results:** Our model obtained an accuracy of 97.5%, outperforming the SVM (93%), RF (93.8%) and KNN (92.7%) models. An improvement of 1.5% in accuracy was achieved with synthetic data. Our study showed that the most pejorative factors in the evolution of the cancer were the appearance of hepatic metastases or adenopathy, smoking, and the infiltrative and stenosing aspects of the tumour on endoscopy. **Conclusion:** Our model predicted the occurrence of death from gastric cancer with very high accuracy, outperforming standard classification algorithms. The increase in training data produced an improvement in accuracy. Our study will help doctors to personalize the

management of gastric cancer patients.

Keywords

Artificial Intelligence, Multilayer Perceptron, Prognosis, Gastric Cancer, Synthetic Data

1. Introduction

According to the World Health Organisation (WHO), cancer is one of the leading causes of death worldwide [1]. Stomach cancer is responsible for more than one million new cases in 2020 and around 769,000 deaths, ranking fifth in terms of incidence and fourth in terms of mortality worldwide, according to GLOBOCAN 2020 data [2]. In Senegal, its incidence is estimated at 597 cases in 2020, with a mortality rate of 70%, again according to GLOBOCAN 2020. The poor prognosis of gastric cancer is largely attributable to late diagnosis, but also and above all to a lack of understanding of the impact of clinical, pathological and therapeutic factors on patient survival [3].

Artificial intelligence (AI) is a discipline that brings together three scientific fields that are, on the face of it, quite distinct: mathematics, cognitive science and computer science [4]. It opens up an infinite number of possibilities and development methods. In recent years, the advent of AI models has made a significant contribution to predictive, preventive and personalised medicine by taking advantage of unprecedented quantities of data [5]. The multilayer perceptron (MLP) [6] is a deep neural network with a self-learning capability. It is constantly being updated and provides increasingly accurate results. The application of MLP in the fight against cancer has made it possible to predict long-term survival for patients with gastric cancer [7] [8], and to specify the diagnosis and prognosis of death due to gastric cancer [9]-[11]. MLP achieves very high accuracies, sometimes even surpassing those of human specialists in the detection of gastric cancer [12] and in the risk stratification of gastric cancer [13].

The main objective of our study was to develop a machine learning model to predict the occurrence of death from gastric cancer at 5 years post-treatment.

Our study sample consisted of 262 patients treated for gastric cancer and followed up postoperatively.

To achieve this objective, we opted for the multilayer perceptron. The medical data we process are characterised by intermediate and interdependent causal relationships. This means that the data is not linearly separable. Numerous studies have shown that deep neural networks (ANNs) handle non-linear statistical relationships better than traditional analysis methods, including studies on various cancer prognoses [14]. In addition, to our knowledge, no study has yet been conducted in Senegal on the application of ANN models to the occurrence of death from stomach cancer.

We explored different MLP hyperparameters to select the most optimal ones. We compared the performance of our model with standard classification algorithms such as Random Forest (RF), Support Vector Machine (SVM) and k-nearest neighbors (KNN).

We also augmented our real data using a set of synthetic data generators and statistical tests to evaluate the behaviour of our model in the presence of a large amount of data.

In a context of data rarity or unavailability, synthetic data generation makes it possible to produce new data based on the structure and statistical properties of the real data available [15] [16]. Synthetic data have been used to improve the performance of AI models for the prognosis [17] and diagnosis [18] of gastric cancer.

Two main approaches are used to generate synthetic data. These are generative adversarial networks (GANs) [19] and variational autoencoders (VAEs) [20]. The role of a GAN is to generate synthetic data by estimating the potential distribution of existing real data. The use of data from GANs has shown a substantial increase in accuracy for standard Vanilla classifiers, which are considered to be an extension of the supervised linear regression algorithm [21]. As for VAEs, they can be used to deduce responses for a new variable based on the distribution of existing real data. Q. Wei *et al.* [22] used a VAE in a semi-supervised context to generate significant latent features on the response to chemotherapy drugs for several types of cancer. The data were used to train the decision tree algorithm in a supervised approach to predict this response. The results show that VAE coding preserves the identity of the cancer type.

Our approach to generating synthetic data was to use packages already available such as Ydata, Gretel, or MostlyIA, reinforcing the validation conditions with a series of statistical tests to ensure that the data generated follows the same distribution and retains the same statistical characteristics as the real data.

2. Methods

2.1. Type, Duration and Environment of the Study

We conducted a retrospective study. It was spread over a period of 13 years, from 2007 to 2020. The study site was the general surgery department and the oncology department of Aristide Le Dantec Hospital (HALD). HALD is one of the country's largest hospitals. It is located in of Dakar, the Senegalese capital.

2.2. Study Population

The patients included in our study had undergone treatment for gastric cancer, either by surgery alone or surgery combined with chemotherapy, and were monitored post-operatively. Patients who died within 30 days of treatment were excluded from the study as death was considered to be related to the surgical procedure. Our study sample comprised 262 patients.

For external validation of our model, we constructed a database of 75 patients followed up after treatment for gastric cancer at "Hôpital de la paix de Ziguinchor"

and the Belle-Vue clinic in Dakar. Ziguinchor is a region in the south of Senegal, 444 km from the capital Dakar. The “Belle Vue” Clinic is located in Dakar. It has a medical oncology unit and works in close collaboration with all the hospitals in Senegal to improve patient care conditions.

2.3. Real Data Collection

The parameters studied were: age, sex, history (epigastric pain, gastric ulcer, tobacco, salt and alcohol consumption, hypertension, diabetes, Cardiopathy), reasons for consultation (vomiting, abdominal mass, constipation), duration of symptoms, general signs (pale or colored mucous membranes, dehydration, malnutrition), biological data (haemoglobin, platelets, creatine), macroscopic appearance of the tumour on fibroscopy (stenosing, Burgeoning_ulcer, infiltrating), Hepatic_metastases, Adenopathy, treatment (exclusive surgery, surgery combined with chemotherapy), survival time, and occurrence of death with a 5-year follow-up.

Data collection, pre-processing and analysis were carried out in close collaboration with our multidisciplinary research team, comprising surgeons, oncologists, computer scientists and statisticians.

2.4. Selection of Pertinent Variables

To select the pertinent variables, we calculated the Relative Risk (RR) between the parameters studied and Death. The RR evaluates, at a significance level of 5%, the risk of death in the presence of a factor. We also used the Chi-square test of independence to identify statistically significant relationships.

2.5. The Multi-Layer Perceptron (MLP)

We have developed a multi-layer perceptron to learn data structures and establish a predictive model for the occurrence of death from stomach cancer.

The Multilayer Perceptron (MLP) is an artificial neural network architecture composed of several layers, including an input layer, one or more hidden layers and an output layer. Each layer is made up of neurons connected to those in the previous and next layers, forming an information processing network. The neurons in the last layer are the outputs of the overall system.

During network learning, the data undergoes two types of propagation. Forward Propagation and Backward Propagation.

In Forward Propagation, the input data is propagated from the input layer to the output layer. Each neuron in each layer performs a linear combination of the weighted inputs. This means that each neuron multiplies each input by a corresponding weight and sums the weighted results.

After the linear combination of the weighted inputs, an activation function is applied to each neuron. This function introduces non-linearity into the model, allowing the network to capture complex relationships between data.

Forward propagation continues through the hidden layers until the final predictions are obtained at the output layer. These predictions can be probabilities in

the case of classification, or continuous values in the case of regression.

Then, in the Backward Propagation phase, gradients are calculated retroactively from the output layer to the input layer.

The gradients represent the slope of the loss function with respect to the network weights. They are calculated using the chain rule backwards through the network from the output layer. This calculation is based on the derivative of the loss function with respect to the model predictions.

Once the gradients have been calculated, the network weights are updated using an optimisation method such as gradient descent. This method adjusts the weights in the direction that minimises the loss function, allowing the model to train itself to improve its predictions.

Back propagation and weight updating are repeated for each batch of data in the training set over several iterations, until the model converges to optimal weights that minimise the loss function.

Forward Propagation obtains the model predictions by propagating the data through the network, while Backward Propagation calculates the gradients and updates the network weights to improve these predictions. These two phases are essential for the efficient training of deep neural networks.

An MLP can use a multitude of functions known as hyperparameters. Hyperparameters are defined as values or weights that can determine the learning properties of the algorithm. The challenge is to find the right ones among these that guarantee the best training to provide accurate results based on the available data.

2.6. Determining Hyperparameters

We determined the hyperparameters using the 'GridSearchCV' method [23], available in Scikit-learn [24]. For each model, depending on the hyperparameters and their possible values, we supplied GridSearchCV with several. The algorithm performs all the possible combinations and provides the best hyperparameter values that have obtained the best scores when applied to the available data by cross-validation.

2.7. Comparison with Other Classification Algorithms

We compared the performance of our model with standard classification algorithms. These were SVM, Random Forest and KNN. We also used GridSearchCV to select the best hyperparameters for each of these algorithms. The accuracy score (accuracy) was used for comparison. The models were trained on a sub-sample of 70% ($n_1 = 183$) of our data and tested on the remaining 30% ($n_2 = 79$).

2.8. Validation

We performed two types of validation (internal and external) for our model.

2.9. Internal Validation or Cross-Validation

To perform cross-validation, we partitioned our dataset into three subgroups. The

model is trained on the first two subgroups and its performance is evaluated on the last. The procedure is repeated 3 times, swapping the subgroups so that each plays the role of a validation set. Finally, performance is estimated on average according to the rate of correct classifications obtained. This resampling method is known as k-folds cross-validation [25].

Cross-validation makes it possible to limit underfitting and overfitting, which correspond to situations where the model does not learn the structure of the data sufficiently, or where it memorises particular points in the training dataset instead of learning the general law of the problem being studied. By providing the model with sub-groups in turn, it develops its performance and its ability to generalise.

2.10. External Validation

We also carried out an external validation. This consisted of evaluating the classification capabilities of our model on an independent dataset, on which it has not been trained. To do this, we used a database of patients followed up postoperatively after treatment for stomach cancer at “Hôpital de la paix de Ziguinchor” and the “Belle-Vue” clinic in Dakar.

2.11. Synthetic Data Generation

We used the following synthetic data generators: Ydata [26], Mostly_Ia [27], Synthesized.io [28], Gretel [29], Copulas [30], Twinify [31] and Benerator [32]. The amplification process was carried out in successive stages with the selected variables.

First, we generated 400 synthetic data from the 262 real data available to us. We applied a set of statistical tests [33], to verify the following Hypotheses:

Hypothesis 1: Synthetic data follow the same distribution as real data. The tests used are: Chi-square test of fit, Kolmogorov-Smirnov test of fit, Fisher test. The general principle here is to test whether the two samples can be drawn from the same population. We compare the real ($F_r(\mathbf{x})$) and synthetic ($F_s(\mathbf{x})$) distribution functions, then calculate the maximum deviation (D_{\max}), defined by:

$$D_{\max} = \left(|F_r(\mathbf{x}) - F_s(\mathbf{x})| \right)$$

The critical values of D_{\max} are tabulated for each probability distribution. For example, for the Chi-square distribution, at the 5% threshold, $D_{\max} = 1.36.n^{0.5}$, with

$$n = \frac{n_r n_s}{n_r + n_s}$$

Hypothesis 2: The dependency relationships between the explanatory variables and the occurrence of death in the real data are preserved in the synthetic data. The relationship between each variable and the occurrence of death is assessed using the Mann-Whitney U, Lévene, Krusal-Wallis tests, and the Chi-square test of independence.

A contingency table is constructed and the frequencies of observation of the different values of the two variables are noted. The idea is to calculate the difference (Q) between the real (O_{ij}) and synthetic values (E_{ij}).

$$Q = \sum_{i=1}^r \sum_{j=1}^s \frac{(O_{ij} - E_{ij})^2}{E_{ij}}$$

This deviation is then compared with the value read from the chi-square table. If Q is greater, or if the p. Value is greater than the significance level set at 5%, we reject the hypothesis of similarity between the variables.

This amplification process is repeated several times, and at each stage we increase the synthetic database by 200 new data. When the two hypotheses are no longer supported by any of the statistical tests, we stop the amplification. The best synthetic database is chosen by majority vote on the basis of the test results.

With this synthetic data, we trained our model to assess its behavior when faced with a larger quantity of data. Here again, we used cross validation to limit the effects of possible overfitting.

2.12. Validation Metrics

At each stage of evaluating the performance of our model, we construct a confusion matrix. The confusion matrix compares the observed values of the dependent variable with those predicted by the model, and then counts the good and bad predictions. The advantage of this matrix is that it provides an indication of both the error rate and the way in which the model can go wrong. **Table 1** shows the general form of a confusion matrix with a dependent variable Y, coded as Death/Living, which is commonly explained as Positive = Death and Negative = Living.

Table 1. Generic form of a confusion matrix.

$Y_{\text{Predicted}} \cdot Y_{\text{Observed}}$	Death	Living	Total
Death	a = VP	b = FP	a + b
Living	c = FN	d = VN	c + d
Total	a + c	b + d	na + b + c + d

a represents the true positives, *i.e.* the number of patients for whom the model predicted death and who are actually alive in the observations. **b** are the false positives, *i.e.* the number of patients for whom the model predicted death and who are actually alive. Similarly, **c** are the false negatives and **d** are the true negatives.

Using the data in this matrix, it is easy to calculate the metrics below.

Sensitivity (Se): This represents the rate of individuals whose death is correctly predicted by the model.

$$Se = \frac{VP}{VP + FN}$$

Specificity (Sp): This is the rate of individuals alive and correctly predicted by

the model.

$$Sp = \frac{VN}{VN + FP}$$

Accuracy: This measures the rate of correct predictions (Death and Alive) for all individuals. It determines the classification power of the model.

$$\text{Accuracy} = \frac{VP + VN}{VP + VN + FP + FN}$$

2.13. Interpretability of Results

To interpret the results from our model, we used two techniques. The first technique is the Shapley Additive Explanations (SHAP) framework [34]. SHAP provides a comprehensive approach to understanding the reasoning behind model predictions. The concept comes from cooperative game theory, to find out the contribution of each player in a coalition game. The central idea is to distribute the total payoff fairly among the participants according to their individual contributions.

In the context of machine learning, SHAP aims to quantify the contribution of each feature (input variables) to the final prediction, thus providing insight into the model's behavior.

In fact:

- Let **X%** be the overall average accuracy. This is the average accuracy of the model over all predictions.
- Let **Y%** be the accuracy when the model predicts the death of a specific patient. This accuracy lies within a range of **X% ± K%**, where **K%** represents the deviation from the overall average accuracy.
- Each variable (**P_i**) in the model is associated with a coefficient (**C_i**) that indicates its impact on the accuracy deviation (**K%**). These coefficients indicate the extent to which each variable influences the evolution of accuracy.
- Shapley's framework of additive explanations (SHAP) quantifies the contribution of each variable to model accuracy. The sum of these individual contributions is equal to the overall accuracy deviation (**K%**).

$$Y\% = X\% \pm \sum_{i=1}^P (C_i)\%; \text{ where } \sum_{i=1}^P (C_i)\% = K\%$$

Having identified the influences of each factor on the occurrence of death, we set out to discover the causal structure that exists between them. Causal graph discovery is based on Bayes' principle of conditional probabilities, and aims to recover causal structures or relationships between variables. To achieve an unbiased result, it is necessary to eliminate the confounding factors produced by the relationships between the residuals. To this end, we applied the GIN (Generalized Independent Noise) algorithm [35]. GIN allows us to visualize existing relationships between residuals.

We applied the PC (Peter-Clark) algorithm [36]. This is one of the most general

causal discovery algorithms that can be used for tabular data. The PC algorithm makes four main hypotheses:

1. Markov causal condition, which implies that two separate variables in a causal graph are probably independent;
2. Fidelity, *i.e.* no conditional independence can be verified unless the Markov causal condition is fulfilled;
3. No hidden confounding factors, (check with GIN);
4. No cycles in the causal graph.

The PC graph highlights the direct and conditional causal links between the explanatory variables and the variable of interest.

3. Results

The patients in our series ranged in age from 26 to 82 years. The mean age was 52 with a standard deviation of 10. There were 135 men and 127 women, giving a sex ratio of 1.06. The overall mortality rates at 6 months, 1 year and 5 years after treatment were 26%, 43% and 62% respectively.

The relative risk of death was 8 times greater in patients with hepatic metastases. Smoking increased this risk by a factor of 3 (**Table 2**).

Table 2. Relative risk of factors on the occurrence of death.

Factors	Relative risk	P. value (Test Khi-2)
Hepatic metastases	8,322	0.0001
Adenopathy	3,555	0.007
Smoking	3,003	0.0089
Infiltrating	2,7	0.004
Stenosing	2,3	0.0012
Gastric ulcer	2,23	0.002
Epigastric pain	2,1	0.03
Cardiopathy	2,058	0.0047
Burgeoning ulcer	2,05	0.01
Mucinous	2,04	0.01
Denutrition	1,46	0.0075

Our MLP achieved 77 correct classifications in the test sub-sample and was wrong (false positives) in predicting death in two patients (**Table 3**).

The optimal hyperparameters of our MLP were:

Activation function = ReLU, Number of hidden layers = 2 : (10, 20), and Random_state = 3.

The accuracy of our model was 97.5%, higher than SVM (93%), RF (93.8%), and KNN (92.7%) (**Table 4**).

Table 3. Confusion matrix of MLP with test data.

$Y_{Observed}$ $Y_{Predicted}$	Death	Living	Total
Death	44	2	46
Living	0	33	33
Total	44	35	79

Table 4. Comparison between MLP, RF, SM, and KNN, with real data.

Model	Accuracy	Sensitivity	Specificity	Best params
KNN	0.927	95.60%	90%	'n_neighbors': 5 'p': 1 'weights': 'uniform'
SVM	0.933	96.50%	91.60%	'C': 1 'kernel': 'rbf'
Random_Forest	0.938	100%	80.90%	'n_estimators': 10 'activation': 'relu'
MLPClassifier	0.975	100%	94%	'hidden_layer_sizes': (10, 20) 'random_state': 3

Legend: **KNN:** 'n_neighbors': Number of neighbours to be used by default. **p:** Parameter used to calculate the distance between neighbours (p = 1: Manhattan distance, p = 2: Euclidean distance). **weights:** parameter used in prediction. 'uniform' means that all points in each neighbourhood are weighted in the same way. **SVM:** **C:** Regularisation parameter, used to adjust the balance between margin and classification errors. **rbf:** Kernel used to map data points in order to linearly separate decision classes. **RF:** n_estimators: number of decision trees in the forest. **MLPClassifier:** **activation:** activation function; **hidden_layer_sizes:** represents the number of neurons in the hidden layer; **random_state:** Determines the generation of random numbers for the initialization of weights and biases.

Schematically, the neural network we have developed is shown below, with the eleven input nodes corresponding to the relevant factors, the two intermediate layers of 10 and 20 neurons and the output node indicating the prediction of the patient’s living or dead status (**Figure 1**).

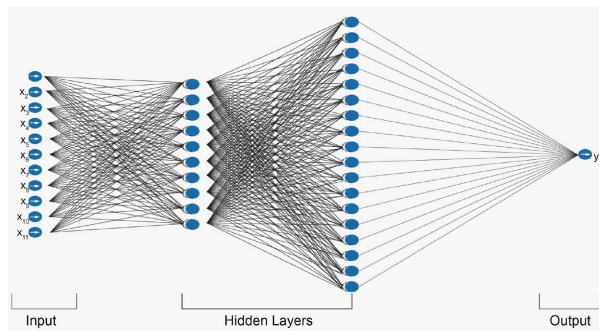


Figure 1. Multilayer perceptron (10, 20).

3.1. Validation of Our Model

Internal validation using the 3-subgroup cross-validation technique yielded accuracies of 98.9, 97.41 and 96.13, giving an average of 97.48.

In external validation, using data from the “Hôpital de la paix de Ziguinchor” and the “Belle Vue” clinic in Dakar, the model achieved 64 correct classifications out of 75 patients. It was wrong for 11 patients, *i.e.*, 8 false positives and 3 false negatives. This gives an accuracy of 85%, a sensitivity of 93% and a specificity of 75%.

3.2. Synthetic Data

Each of the generators we used produced a synthetic database of 1000 records. Statistical tests were used to check, at the 5% threshold, the similarities between the real data and the synthetic data in terms of distribution and dependency relationships. The data produced by the Ydata generator were the most faithful to the real data. The p-values for all the statistical tests were below 5% (Table 5).

By applying our model and the above-mentioned standard classification algorithms to the synthetic data produced by Ydata, with the optimal hyperparameters selected earlier, we observed slight increases in accuracy. The highest accuracy was always obtained with our MLP of the order of 99%, *i.e.* an improvement of 1.5% compared with the real data (Table 6).

Table 5. Generation of synthetic data (n = 1000).

Generators/ Statistical tests	Fisher test	Kolmogorov- Smirnov adjustment test	Chi-square adjustment test	Levene test	Mann- Whitney test	Krusal-Wallis test	Chi-square independence test
Ydata	P.v. = 0.0003	P.v. < 5%	P.v. < 5%	P.v. < 5%	P.v. < 5%	P.v. < 5%	P.v. < 5%
Mostly_Ia	P.v. = 0.004	P.v. > 5%	P.v. > 5%	P.v. > 5%	P.v. > 5%	P.v. > 5%	P.v. < 5%
Synthesized.io	P.v. = 9E-89	P.v. > 5%	P.v. < 5%	P.v. < 5%	P.v. > 5%	P.v. > 5%	P.v. < 5%
Gretel	P.v. = 2.26E-158	P.v. < 5%	P.v. < 5%	P.v. < 5%	P.v. < 5%	P.v. < 5%	P.v. < 5%
Copulas	P.v. = 3.21E-23	P.v. < 5%	P.v. > 5%	P.v. < 5%	P.v. > 5%	P.v. > 5%	P.v. < 5%
Twinify	P.v. = 1.03E-61	P.v. < 5%	P.v. < 5%	P.v. > 5%	P.v. < 5%	P.v. < 5%	P.v. < 5%
Benerator	P.v. = 5.44E-07	P.v. < 5%	P.v. > 5%	P.v. < 5%	P.v. < 5%	P.v. < 5%	P.v. > 5%

Table 6. Comparison of MLP, RF, SM and KNN with synthetic data.

Model	Accuracy		Improved Accuracy (Real vs Synthetic)
	Real	Synthetic	
MLPClassifier	97.50%	99.00%	+1.50%
Random Forest	93.80%	94.00%	+0.20%
Svm	93.30%	93.50%	+0.20%
KNN	92.20%	92.35%	+0.15%

3.3. Interpretation

Our model achieved an overall average accuracy of 97.5% with real data. To better understand the reasoning behind this prediction, we randomly selected two patients from the test dataset (we call them Patient 1 and Patient 2). We produced Shapley values for each of them.

Patient 1

The model predicted his death with 100% accuracy. This +2.5% variation in accuracy corresponds to the sum of the contributions of the explanatory factors. The SHAP values indicate that Patient1 is at risk of death primarily because of the presence of hepatic metastases (0.77%) and adenopathy (0.52%), smoking (0.41%) and the infiltrative (0.28%) and stenosing (0.23%) aspects of the tumour on endoscopy. The mucinous type of adenocarcinoma and denutrition had little impact on the occurrence of death (Figure 2).

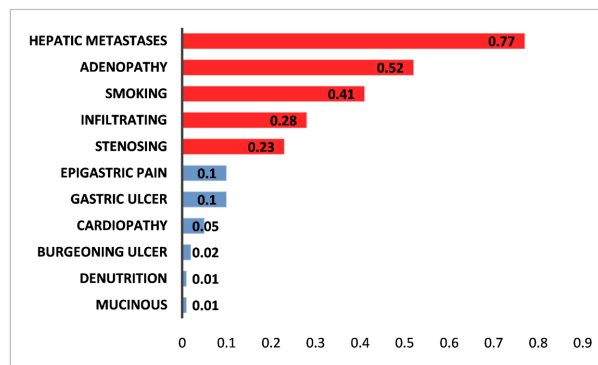


Figure 2. SHAP values obtained for Patient 1.

Patient 2

For patient 2, the accuracy of the model was 97.778%, i.e., a variation of +0.278%. The SHAP values show that patient2 is at risk of death primarily because of the stenosing aspects (0.116%) and infiltration (0.085%) of the tumor on fibroscopy (Figure 3).

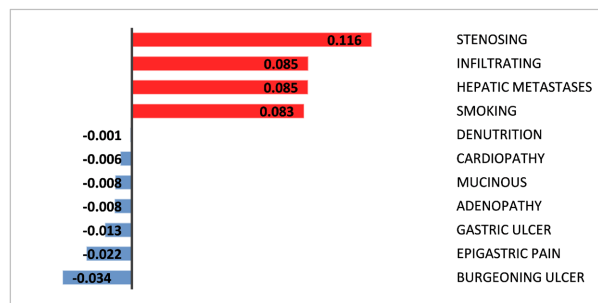


Figure 3. SHAP values obtained for Patient2.

After identifying the variables with a strong influence, we sought to determine the causal structure between these factors. Firstly, the application of the GIN (Generalized Independent Noise) method revealed the absence of confounding

factors. There was no link between the residuals of the factors (Figure 4).

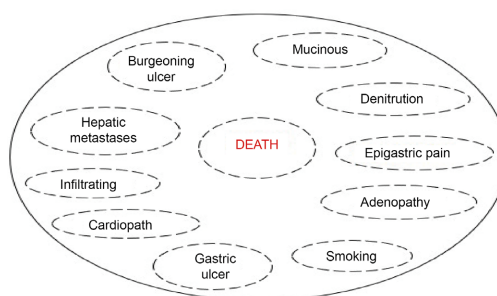


Figure 4. GIN plot, link between factor residuals.

The pipeline resulting from the application of the PC (Peter-Clark) algorithm clearly identifies the structure of the causal relationships between the various perorative factors and death. As a result, hepatic metastases, adenopathy, smoking, infiltrate type of tumour and cardiopathy represent the factors whose presence is fatal for the patient. For the other factors, their impact on death is conditional on their relationship with the factors whose presence is fatal.

This structure shows the complexity of separating the data linearly.

HEPATIC METASTASES - > DEATH;

ADENOPATHY - > DEATH;

SMOKING - > DEATH;

INFILTRATING - > DEATH;

CARDIOPATHY - > DEATH;

DENUTRITION - > INFILTRATING - > DEATH;

MUCINOUS - > ADENOPATHY - > DEATH;

GASTRIC ULCER - > MUCINOUS - > ADENOPATHY - > DEATH;

EPIGASTRIC PAIN - > ADENOPATHY - > DEATH;

BURGEONING ULCER - > EPIGASTRIC PAIN - > ADENOPATHY - > DEATH;

STENOSING - > BURGEONING ULCER - > EPIGASTRIC PAIN - > ADENOPATHY - > DEATH.

The relationships indicated in the pipeline are shown below (Figure 5).

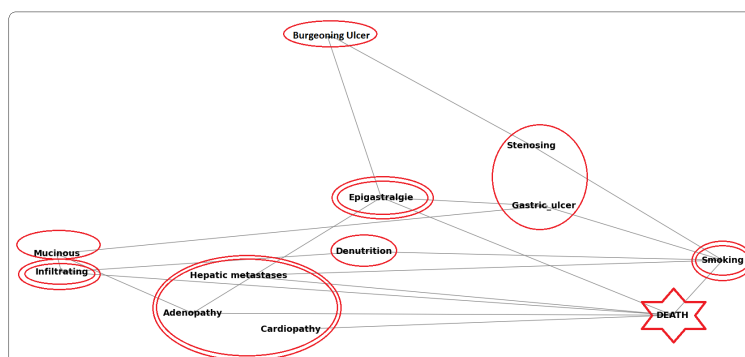


Figure 5. PC (Peter-Clark) graph, Structure of causal relationships. **Legend:** The target variable: **Death**. Double circled: variables with a direct causal relationship with death. Single circled: variables with a conditional causal relationship with death.

4. Discussion

The aim of this study was to develop a machine learning model to predict the occurrence of death from gastric cancer 5 years after treatment. Treatment consisted of either surgery alone or surgery combined with chemotherapy. After treatment, two types of death can occur. One occurs within 30 days of surgery and the other afterwards. The first is attributed to the surgical procedure, while the second, which is the subject of our study, is due to the evolution of the cancer.

Our study population comprised 262 patients. It should be noted that not all Senegalese patients have access to healthcare. Cancer treatment is very expensive. Added to this is the absence of a system for collecting and centralizing medical data.

The pipeline derived from the causal structure of the PC graph indicates that hepatic metastases, adenopathy, smoking, infiltrating type of tumour and cardiopathy represent the factors whose presence is fatal for the patient.

For the other factors, their impact on death is conditional on their relationship with the factors whose presence is fatal.

This structure shows the complexity of separating the data linearly.

GLOBOCAN estimated that there would be 597 cases of gastric cancer in Senegal by 2020. This only represents an estimate of diagnoses. However, for our study, the inclusion criterion was not the number of cases, but rather patients who had received full treatment and were placed on post-operative surveillance. It was on these patients that we could collect the maximum amount of information.

The collection of medical data has always been an obstacle to research. In a study of the surgical treatment of gastric adenocarcinoma at the Dakar University Hospital, Dieng, M. *et al.* [37], collected only 136 patients over a 10-year period from 1995 to 2005. The situation is also similar in African series. Bang, GA *et al.* [38] collected 120 cases of gastric cancer over 6 years in Cameroon, D. Tamegnon *et al.* [39] collected 32 cases of gastric cancer over 4 years in Togo.

However, we have found studies in the literature that apply artificial intelligence methods to smaller quantities of data than ours, such as that carried out by C. Neto *et al.* [40].

The data we have collected included clinical, pathological, therapeutic and follow-up factors. The mean age of the patients was 52, with extremes of 26 and 82, and a standard deviation of 10. There were 135 men and 127 women, giving a sex ratio of 1.06.

Sixty-two per cent (62%) of patients had been treated exclusively by surgery, and in 38% of patients, surgery was combined with preoperative chemotherapy.

The overall mortality rate at 6 months, 1 year and 5 years after treatment was 26%, 43% and 62% respectively.

This trend has been observed in African series, with very low 5-year survival rates of around 20% - 30% [41]-[43].

The existence of hepatic metastases, smoking, infiltrative aspects, budding and stenosing ulcers on fibroscopy, a history of gastric ulcers, epigastric pain and heart

disease, the existence of adenopathy, the mucinous type of adenocarcinoma and malnutrition were the factors with a significant impact on the occurrence of death.

The performance of our model outperformed that of the KNN, RF and SVM algorithms. These standard models have many advantages in simple classification tasks. In other words, when the data are linearly separable and the causal relationships between factors are not very complex. However, they do have some limitations.

The KNN algorithm [44], assuming that nearby or neighboring data points belong to the same class. KNN works by looking for a distance between the points or classes of the variable of interest and the set of variables in the study, then selects an optimal number ($K = 5$, for our study) to decide the classification of a new individual by comparing the distances.

The disadvantage of this method is that KNN requires a lot of memory and is costly in terms of training. Indeed, it has to keep track of all the training data to find the optimal neighboring nodes. As a result, the response becomes slow depending on the variables and their characteristics.

Support vector machines (SVM) [45] can be considered as an extension of the KNN algorithm. Instead of being limited to the distance between data points, SVM draw lines according to the classes to be predicted and look for the points closest to these lines. These points are called support vectors. And the distance represents the margin, the aim being to maximize it. SVM take a long time to train, and are less effective when faced with noisy data or data containing confounding factors, as is generally the case with medical information.

The Random Forest model [46] constructs several decision trees. Each tree is trained on a sub-sample of the study population. The prediction is obtained by a majority vote for the classification or the average of the predictions in the case of regression.

Although the accuracy of a group of trees is better than that of a single tree, the result is subject to fluctuations in the mean, which is sensitive to extreme values. In addition, the training time is long because it depends on the optimal number of trees in the forest (10 optimal trees for our study).

These limitations of standard algorithms are corrected with neural networks, in particular the multilayer perceptron. The depth of the hidden layers and the activation function give this model many benefits.

MLPs are self-learning. Once the network has been designed and trained, the model is constantly updated to improve its results.

Effective filtering of noise in the data is also one of the properties of artificial neural networks. The algorithm is able to isolate the noise that constitutes the confounding factors, to focus only on the relevant factors.

The major advantage of neural networks is undoubtedly the speed with which they can be trained compared with standard algorithms. They have enormous computing power, enabling them to provide an almost instantaneous response.

Our model achieved an accuracy of 97.5%, an average increase of 4% compared

with the Support Vector Machine, K-nearest neighbor and Random Forest algorithms. The classification performance of our model also exceeded that of a logistic regression that we had previously developed using our data [47], whose accuracy was 93%.

Our network is more accurate than the one designed by Z. Fan *et al.* [48]. In their study, they developed a multilayer perceptron with 3 hidden layers of 64, 32 and 32 neurons respectively. Their MLP predicted the development of gastric cancer with an accuracy of 86.8% and an AUC of 92%, also outperforming logistic regression, random forest, k-nearest-neighbor decision tree models.

Z. Xue *et al.* [49] used a hybrid model strategy with a multilayer perceptron and logistic regression to predict the occurrence of lymph node metastases in patients with stage 1 and 2 gastric cancer. Logistic regression was first used to detect clinical and pathological factors that have a significant impact on the occurrence of metastases. These were then given as input to the MLP to establish the prognostic model. The results were compared with the actual postoperative state. The model achieved an AUC of 75% compared with 54% for anatomopathological staging and 30% for clinical staging.

In external validation, using data from the “Hôpital de la paix de Ziguinchor” and the Belle-Vue clinic in Dakar, our model achieved an accuracy of 85%, a sensitivity of 93% and a specificity of 75%. This explains why our MLP is generally more sensitive than it is specific. In other words, it predicts patient death better than survival. The fact that our model is wrong on more false negatives than false positives is to the patient’s advantage. Because it would be better to improve treatment when the patient is not actually in mortal danger, than to believe that the danger has been averted when in fact it is fatal.

The Ydata synthetic data generator was used to amplify our data while respecting its distribution and the statistical properties of central tendencies and dispersions. An improvement of 1.5% in the accuracy of our model was obtained with these data.

M. Nabati *et al.* [50] found that a combination of 10% real data and 90% synthetic data generated by a GAN enabled their deep neural network model to achieve similar accuracy to that obtained using the full set of real data.

Our model predicted the occurrence of death from stomach cancer with an accuracy of 97.5%. This accuracy represents the average over all predictions. This result does not allow us to make a decision a priori. This is the case for most artificial intelligence solutions. The output of models does not provide any explanation of how they work or how they can be put into practice [51].

Several techniques have been developed to contribute to the interpretability of AI results. For example, R. Selvaraju *et al.* [52] proposed to produce ‘visual explanations’ from a large class of models based on deep neural networks, making them more transparent.

For the present study, the Shapley Additive Explanations (SHAP) framework and the discovery of the causal structure made it possible to determine the

relationships of dependence between the factors, and to identify the impact of each on variations in the accuracy of the model. This facilitated the classification of pejorative factors in the following decreasing order: appearance of liver metastases, adenopathy, smoking, infiltrating and stenosing aspects of the tumor on endoscopy, gastric ulcers and epigastric pain, ulcer-bourgeoning aspect of the tumor, mucinous type of adenocarcinoma and, finally, undernutrition.

In studies carried out by: C. Martel [53] and B. Eom [54], hepatic metastases and adenopathy were the factors most associated with mortality in patients with gastric cancer. Smoking favours an environment of vulnerability to cancer. The results of a study conducted by M. Koura *et al.* [55] in Burkina Faso on the epidemiological, anatomical and endoscopic aspects of gastric cancer showed that epigastric pain was the symptom most associated with mortality.

The treatment offered to patients included in our study was either exclusive surgery or surgery combined with chemotherapy. Chemotherapy was more appropriate in situations where the tumor was no longer confined to the stomach, but had spread via the lymphatic system. This is manifested by the appearance of liver metastases, adenopathy, which are lymph node metastases, or infiltrating adenocarcinoma. Recent studies [56] [57] recommend perioperative chemotherapy (before and after surgery) as the standard systematic treatment for gastric cancer, even in the absence of metastases, to improve prognosis and recurrence-free survival.

Our study will have a decisive impact on the management of Senegalese patients with gastric cancer. Classification according to risk of death and quantification of the impact of pejorative factors for each patient will make it possible to identify intervention priorities for personalized and optimized follow-up.

Deployment of our model will help to save time for healthcare staff and resources for patients, given the unavoidable role of artificial intelligence applications in the fight against cancer [58].

Limitations of Our Study and Recommendations

The main limitation of our study is the size of the sample. This justifies a generalization capacity of 85%. AI algorithms require thousands, hundreds of thousands, or even millions of data sets to ensure good training. This situation is mainly due to the lack of an effective system for collecting medical data in Senegal. And this situation suggests a low incidence of gastric cancer.

We recommend that Senegal and other African countries develop systems for collecting and centralizing data, so that they can benefit more fully from artificial intelligence solutions. And this requires the controlled and secure digitization of the healthcare system.

As far as Ydata is concerned, we found during our experiments that several synthetic samples with good fidelity scores were unable to satisfy the statistical tests we used for external validation in terms of distribution and structure. Without calling into question the quality of the data generated, we suggest

strengthening the validation metrics by involving several statistical tests and offering the user the choice according to their study objectives.

5. Conclusions

Our multilayer perceptron model predicted the occurrence of death from stomach cancer with very high accuracy, outperforming the logistic regression, wide margin separator, decision tree, K-nearest neighbour and Random Forest algorithms. MLP performance improves as a function of the size of the training data. An improvement in accuracy is obtained by increasing the training data.

Our study shows that patients with hepatic or lymph node metastases, smokers, and endoscopic tumour infiltration and stenosis deserve priority for intervention in the course of the cancer.

This study opens up good prospects for exploiting medical data using artificial intelligence methods to improve the quality of health care in general and cancer care in particular.

The next challenge is to make more real data available, which will require controlled and secure digitisation of the healthcare system.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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