Article

Predicting lung cancer survivability: A machine learning regression model

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Abstract
Lung cancer is one of the main leading causes of cancer death in all over the world. Accurate prediction of lung cancer survivability can enable physicians to make more reliable decisions about a patient's treatment. The objective of this research is to design robust machine learning model with supervised regression model to predict survivability of the lung cancer patients. This work includes Multiple Linear Regression, Support Vector Regression with Radial Function, Random Forest, Extreme Gradient Boosting Tree regression algorithms to build an ensemble model using stacking technology with meta-learner Gradient Boosting Machine. This experiment is performed on large SEER 2011-2017 dataset. The novel model achieved a high root mean squared error (RMSE) value of 8.58459 on the test dataset which outperforms the base models. The experimentation results show that the proposed system attains better result compared to the existing models.

Keywords lung cancer; regression; stacking technology; ensemble; Extreme Gradient Boosting Tree.

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1 Introduction

Lung cancer happens when cells in the lung grow without order and cluster together to form tumor. Lung cancer is the second most common cancer, accounting for about one out of five malignancies in men and one out of nine in women (SEER Training, 2020). It is also the dominant cause of cancer death among men and second primary cause of cancer death among women worldwide (Zhang, 2018). According to the World Health Organization (WHO), it is responsible for approximately 2.09 million new diagnoses each year and about 1.76 million death cases (Cure Today, 2019). It is estimated that the number of incident cases in 2020 for lung cancer will be 2.21 million (Cancer Tomorrow, 2020). Estimating the survivability of lung cancer patients can help to develop better treatments and quality of life for patients. Lung cancer survivability prediction is a challenging research task. Researchers apply machine learning techniques for predicting the

survivability so that doctors can work better in diagnosing.

Machine learning allows the system to learn and make predictions based on some experience which is data in terms of the system. Machine learning techniques are used in constructing an accurate predictive model for survival of patients diagnosed with lung cancer. In most cases, cancer patient survival models are classification models. But regression models can be more useful for this application as the output time continues.

Ensemble method is one of the most important approaches for improving the performance of single methods. An ensemble of regression algorithms is a combination of various regression models, where the decisions of every single regressor are combined. In stacking ensemble, the outputs of different unrelated models are collected as input for the meta-level learner.

This study employs a stacking ensemble model of different regression algorithms for analyzing the lung cancer data obtained from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (NCI) (NCI_SEER_Training, 2020; NCI_SEER_Overview, 2020) and predict the survival time in months.

Machine learning is not a new thing in the survivability predictions. Several methods were proposed to predict the survivability of a patient. SVM and logistic regression were used to analyze a lung cancer dataset from the SEER database for prediction (Fradkin, 2006). SVM as a classification algorithm and fuzzy clustering as a segmentation technique is used in Sivakumar et al. (2013). Ensemble clustering-based approach was also used on SEER data (Chen et al., 2009). Pradeep et al. (2018) had used SVM with linear kernel, C4.5, Naïve Bayes for classification of lung cancer dataset between two class “Less Survivability” and “more Survivability”. In Fenwa et al. (2015), SVM and ANN were used for classification of lung cancer.

Lynch et al. (2017) used supervised machine learning classification techniques such as linear regression, Decision Trees, Random Forest, GBM, SVM using polynomial kernel function and a custom ensemble method for the lung cancer survival prediction (Lynch et al., 2017).

Lung cancer patient survivability was predicted using SVM and logistic regression in Hazra et al. (2017). A Random Forest-Based Decision tree was proposed to give the best prediction result between Random Forest and Decision Tree for the survivability of lung cancer patients by Zakaria and Rabia (2018). Lynch et al. (2017) used unsupervised analysis techniques to lung cancer data for prediction of survivability where Self-Ordering Maps shows the best performance and revealed comparable result to supervised techniques.

A model was developed in Chen (2014) to predict the survivability of non-small cell lung cancer patients by using artificial neural network with gene expression. An ensemble of five Decision Trees classification models was developed in Agrawal et al. (2011, 2012). The analyses of lung cancer dataset from SEER database using classification techniques (Ramalingam et al., 1998; Owonikoko et al., 2007; Bhaskarla et al., 2010; Hayat et al., 2007; Thun et al., 2008; Fu et al., 2005; Wu et al., 2004; Wang et al., 2007) and statistical techniques (Skrypnyk, 2012; Agrawal and Choudhary, 2011; Kapadia et al., 2012) were made in past studies.

It could be seen that several studies had been conducted to analyze lung cancer survivability through machine learning. But the majority of studies considered whether the patients were alive or not after 5 years since the first diagnosis as having survived the cancer using the classification techniques. This proposed method focused on using various machine learning regression algorithms to predict lung cancer patient survivability using a two-phase stack ensemble model. The major contribution of the proposed work is defined below:

-Perform supervised regression algorithms to predict the survivability on SEER dataset and measure performance.

- Develop an ensemble model using stacking technology for the prediction.

The paper is organized as follows: Section 2 describes proposed ensemble model with dataset, system architecture, system algorithm. Section 3 shows the experimental results, achieved outcomes and discusses results with previous works. The work is finally concluded in Section 4.

2 Material and Methods

The machine learning technique to predict the survivability of lung cancer patients is represented in this section. Base models were used to train using the training dataset and combine them using stacking technology. 5- folds cross-validation was used for the training of each model. Each base model was fitted in 4-folds and predictions were made on the 5th fold of the training dataset. The base model was then fitted on the whole training dataset and then the performance was measured using RMSE value. The initial comparison was held and topmost base models were selected based on RMSE. The predicted result of the topmost base learners was used as the input and the test dataset was used as the output for the meta-level learner. The final output on test dataset was predicted using the stack ensemble technique.

In this method, there are two phases; in phase (1) six different base models were trained using the training dataset, and in phase (2) the topmost base models output on training dataset were used as the input for the high-level model. The workflow of the proposed work is given in Fig. 1 and the pseudo code of the proposed method is shown as follows.

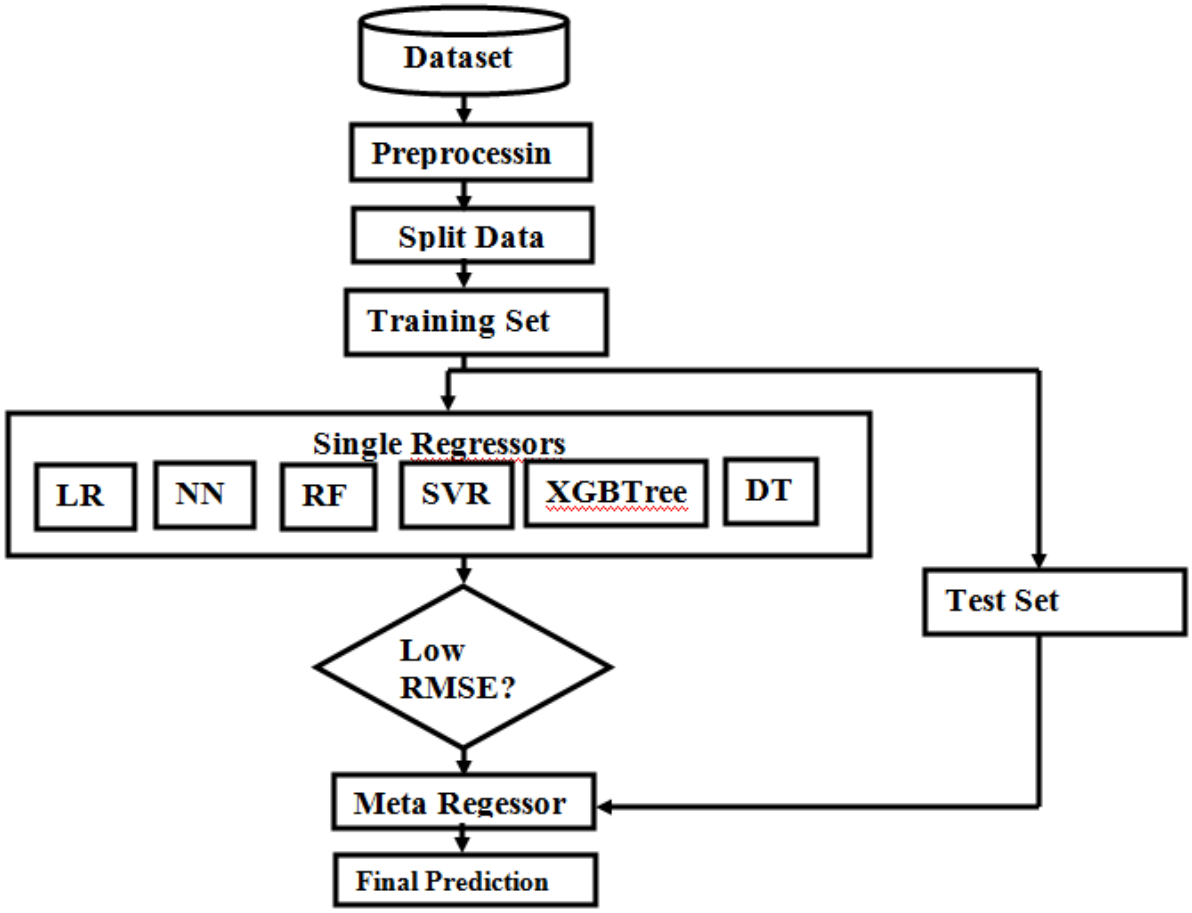


Fig. 1 Diagram of proposed method.

INPUT:
L = Dataset
S = {S_1, S_2, ..., S_l}, A set of learning algorithms
S_{meta} = Meta Algorithm
J = number of cross validation
Level 1 Regression (L, S_m)
L1 = the dataset for the Level 2 regression
Output: O_f = the final output
Step 1: Split the dataset into training set, x and test set, y.
Step 2: Randomly split the training set x into J almost equal size subsets {x_1, x_2,…….x_J}
Step 3: Train subsets with the base models
for j= 1 to J do
for k= 1 to l do
$M_k^{(-j)} = S_k (x^{(-j)})$
End for
End for
Step 4 : Predict on training set x and compare
for j=1 to J do
for each x_j
for k = 1 to l do
Z_{kn}= Prediction of the model $M_k^{(-j)}$ on x_j
If (Z_{kn}) meets the criteria
L1 = (Z_{kn}, y)
End for
End for
End for
End Level 1 Regression
Step 5: Train the selected base models output with meta-learner and create ensemble model
H(x) = S_{meta}(L1)
Step 6: Predict the ensemble model on the test set
O_f = prediction of the model H(x) on test dataset y
Return O_f

The whole experiment was performed on a Personal Computer (PC) of 64-bit Microsoft Windows 10 Professional. The PC configuration is 32 GB DDR4 RAM with 3900X (12 core Processor) of 4.6 GHZ. RStudio 3.6.0 has been used to conduct the full experiments. RX 580 8 GB GDDR5 GPU has been used for faster processing.

2.1 Dataset

The lung cancer dataset was collected from the Surveillance, Epidemiology and End Results (SEER). Data from years 2011 to 2017 was used in this paper. There are about 155497 records with a diagnosis of lung or bronchus.

We had first used a set of inclusions to select the data from SEER for further analysis. Only patients with age 30-79 were selected for further processing. Cases were included when the survival time is known. Attributes that are not directly related to that cancer are not considered. The attributes that vary too much or

too little were filtered.

We had also analyzed the data with ANOVA to select the relevant features for this method. There were 15,440 cases and major 12 attributes including the survival months were selected for further analysis. Fig. 2 depicts the tibble of the dataset. In the selected features, some of the features are categorical and some are numerical. Table 1 gives the details of categorical features and Table 2 gives the numeric features selected.

```
# A tibble: 6 x 12
    Age Tumor_size Primary_site Lymph_nodes malignant_tumors Grade      Laterality    Stage T     N     M     Survival_months
  <dbl>      <dbl>        <dbl>       <dbl>           <dbl> <chr>      <chr>         <chr> <chr> <chr> <chr>           <dbl>
1    72        100          341         200               2 Poorly dif~ Right - orig~ IV    T4    N2    M1NOS               7
2    61        120          340         200               2 Poorly dif~ Left - origi~ IV    T4    N2    M1b                10
3    78        999          341         600               2 Poorly dif~ Left - origi~ IIIB  T4    N3    M0                  0
4    71         90          343           0               2 Moderately~ Right - orig~ IIB   T3    N0    M0                 26
5    63         80          343         100               2 Poorly dif~ Right - orig~ IV    T4    N1    M1b                 1
6    76         24          341         200               4 Moderately~ Right - orig~ IV    T2a   N2    M1b                18
```

Fig. 2 Dataset.

Table 1 Discrete variables.

Variable Name	Number of distinct value
Grade	4
Laterality	6
Stage	9
T	9
N	4
M	4

Table 2 Numerical variables.

Variable Name	Range
Age	30-79
Tumor_size	0-200
Primary_site	340-349
Lymph_nodes	0-800
No. of malignant tumors	1-8
Survival_months	0-36

2.2 Data analysis and preprocessing

Exploratory data analysis was performed like checking the dataset, data types, row names, column names, summary of the attributes, correlation between the attributes, checking the target variable(survival months) etc.

The categorical data were converted into factor for better performance. The noisy, uninformative, duplicated data were removed from the data. The unknown data are also removed from the dataset. The outliers were also removed. The range of survival months is 0 to 36 months, which is 3 years. Fig. 3 presents the frequency of the survival months of the dataset.

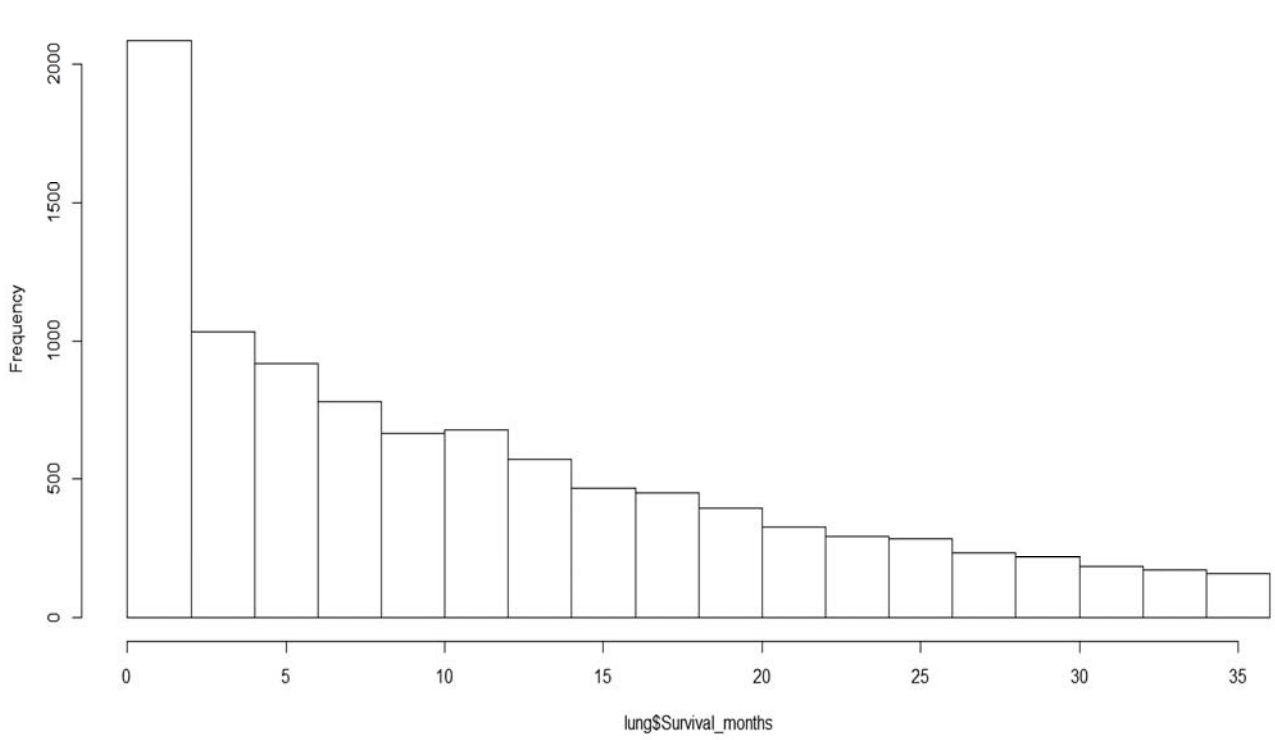


Fig. 3 Frequency of survival months.

Random sampling was used to split the dataset of 11841 data into 75% for training set and 25% for test set. To make the regression model to learn, training set is used and the test set is used to predict the output using the trained model.

2.3 Models used

In phase (1), Multiple Linear Regression, Support Vector Regression with Radial Function, Random Forest Regression, Extreme Gradient Boosting Tree, Decision, Neural Network model were used as base learner and according to the RMSE value finally multiple linear regression, SVR, RF, XGBTree were selected for phase (2). This section gives the brief descriptions of the machine learning models used for the survivability prediction of lung cancer patients.

2.3.1 Multiple Linear Regression

Multiple Linear Regression is used to create a best fit line, which will be able to predict the dependent value. The best fit line will be selected where the residual errors are minimal by using the cost function. In Multiple Linear Regression, there is many to one relationship. One dependent variable and two or more independent variables are used to explain the variation or predict the value of the dependent variable. The equation of Multiple Linear Regression is

$$y = a_0 + x_1 a_1 + x_2 a_2 + \ldots\ldots$$

here, y is the dependent variable,

a_0 is the intercept,

$x_1, x_2 \ldots$ are the independent variable,

$a_1, a_2 \ldots\ldots$ are the coefficients.

2.3.2 Support Vector Regression (SVR)

SVR is a machine learning model which is used to apply in regression problems that is continues output. To tackle non-linear regression support vector machine is effective. The SVR maps, nonlinearly, the original information into a higher dimensional component space (Georey et al., 2015). It tries to fit the best line within predefined error boundary. It classifies all the prediction line in two categories, whether the lines pass the error boundary or not. It uses a mathematical function to expand the dimensions of the sample, which is known as kernel function.

2.3.3 Random Forest Regression

Random Forest Regression is a bagging technique, which uses decision tree as the base model with different parts of a dataset. It trains every tree with random samples from the main dataset using row sampling and feature sampling with replacement. All the decision trees give continuous value and then aggregates these results using either the mean of all the outputs or the median of the outputs is used. Basically multiple decision trees are used in random forest and each of them has high variance. But when these decision trees are combined the high variance converts into low variance.

2.3.4 Extreme Gradient Boosting Tree

Extreme Gradient Boosting Tree has high predictive power and highly effective for large complicated datasets. It uses variety of regularization techniques to reduce overfitting. It starts out as a single leaf and builds trees using the average of two observations as threshold. Every time it calculates the similarity score using regularization parameter and gain to check which threshold is better in splitting. The tree complexity parameter gamma is used to prune and then calculate the output value using the learning rate parameter for the remaining trees. XGBoost tree optimizes different models through parallel processing and handles missing values.

2.3.5 Decision Tree

Decision Tree algorithm is suited very well in regression problems. It builds a tree in which root node and the sub node are attributes of the dataset and the leaf nodes contains the target results. It splits the dataset into subsets such that each contains homogeneous data until the leaf nodes are find. The tree predicts the target value according to the answers of the question it ask to move from one node to another.

2.3.6 Neural Network

Neural Network is the supervised machine learning algorithm which assign every input values to an output based on the prediction. The processing in a neural network occurs when an input value passes through a series of batches of activation units which are known as layers (Zhang, 2010; Georey et al., 2015; Hatem et al., 2018). The one layer of activation units use the previous unit as input and it also performs as the output for the next unit until the final prediction is achieved.

2.3.7 Ensemble Model

Ensemble Model is the technique of combining the predictions from multiple different machine learning algorithms to improve overall performance. Ensemble with stacking technology used to train the particular dataset with multiple models and the output of these models are used as the input of a meta-learner to predict the dependent variable. Gradient Boosting Machine is used as the meta-learner as it is a powerful model for prediction.

3 Results and Discussion

In this section, we discuss the result obtained from the proposed model and analyze the accuracy level and performance of the proposed model.

3.1 Performance evaluation parameters

The proposed method is compared with other models with different metrics. Table 3 describes the metrics

which are used to evaluate the performance.

Table 3 Performance metrics.

Evaluation Parameter	Description	Formula
RMSE	It measures the error between the actual dataset and predicted dataset.	$\text{RMSE} = \sqrt{\frac{\sum_{i=1}^{N}(Predicted_i - Actual_i)^2}{N}}$
R-squared	Represents the proportion of the variance for a dependent variable that's explained by independent variables	$R^2 = 1 - \frac{SSres}{SStot}$ $= 1 - \frac{\sum_{i=1}^{N}(Predicted_i - Actual_i)^2}{\sum_{i=1}^{N}(Predicted_i - Actual_{avg})^2}$

Cross Validation (CV) is used to measure the effectiveness of a model (Zhang, 2010). In this 5-fold cross validation technique is used, that is the dataset is randomly split into 5-folds. One-fold acts as the test set and other 4-folds act as the training set.

3.2 Proposed model implementation and evaluation

Six models were trained with the training dataset in phase-1 and their RMSE value was calculated. Table 4 depicts the RMSE values of the six models after training. The top models were selected according to their RMSE values as RMSE helps to indicate the quality of prediction. XGBTree has the lowest RMSE which is 8.68101 and linear regression is the second-best model. The smaller the RMSE, the better the model is. Fig. 4 shows the comparison of various algorithms according to their RMSE. So, the models which have lower RMSE are selected for the second phase.

Table 4 RMSE values of the algorithms with training dataset.

Models	RMSE
SVR	8.85738
Random Forest	8.83749
XGBTree	8.68101
Linear Regression	8.68873
Decision Tree	8.91342
Neural Network	14.0819

From the Table 4, Support Vector Regression, Random Forest Regression, Linear Regression and Extreme Gradient Boosting Tree have been selected and combined using the stacking technology to generate ensemble model for better prediction.

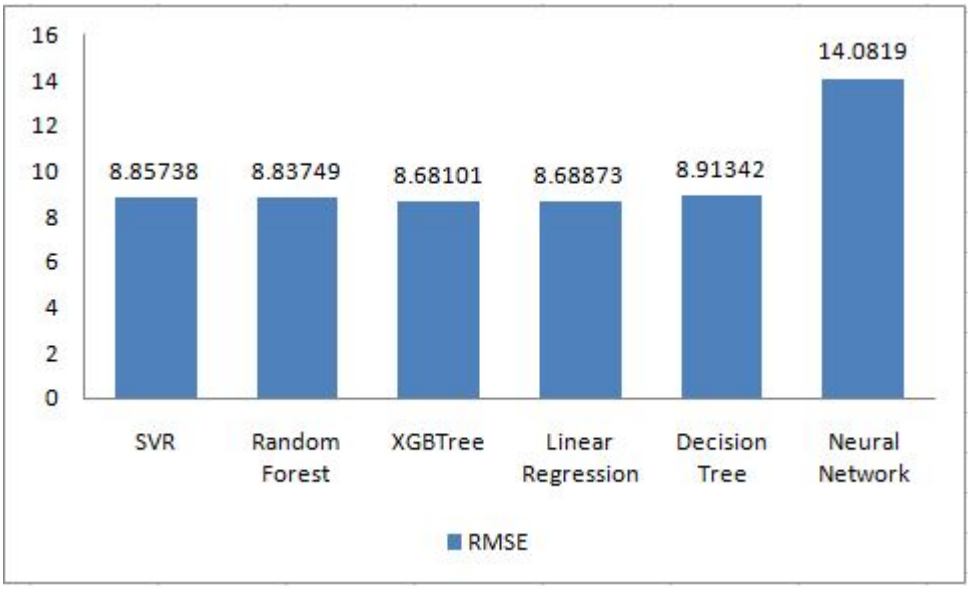


Fig. 4 Comparison of various regression algorithms on basis of RMSE.

The output of the base models i.e. linear regression, support vector machine with radial function, random forest regression and extreme gradient boosting tree were used as the input for the meta-learner to create the ensemble model. For stacking the models gradient boosting machine was used as the meta-regressor. This study builds 3 types of ensemble model using the selected base models to get the best predictive ensemble model and work on the test dataset. Table 5 shows the comparative performance of each of the models for the 5-folds cross validation with the RMSE value.

Table 5 Comparative performance of different ensemble models in 5-folds cross validation.

Folds	Models		
	LR + SVR	LR + SVR+ RF	LR+ SVR+ RF+ XGBTREE
Fold 1	8.67257	8.68374	8.66089
Fold 2	8.67040	8.71205	8.70357
Fold 3	8.68717	8.66863	**8.65620**
Fold 4	8.70307	8.66755	8.66919
Fold 5	8.72441	8.69391	8.68605

The lowest RMSE value is selected as the best result. Table 5 shows that, LR + SVR + RF + XGBRTREE is the final model for prediction as it achieves the lowest RMSE value with 8.65620 in fold 3. Table 6 presents the overall performance of the proposed model on the test dataset.

Table 6 Performance of proposed models on test set.

Model	LR+ SVR	LR + SVR + RF	LR + SVR + RF + XGBTREE
RMSE	8.605	8.598	8.58459

The result revealed that the ensemble model of the four models performed better. The final ensemble model is also better than the base models. Table 7 shows the comparison among the base models and proposed model. Each of the models was used to make prediction on test dataset.

Table 7 Comparison of the proposed model with base models.

Models	R-squared	RMSE	Mean Survival
LM	0.25052	8.59	11.26
SVM	0.23408	8.78	9.53
RF	0.23493	8.75	11.28
XGBTree	0.249014	8.60	11.29
Proposed Model	0.250515	8.58	11.3

This table proves that the proposed model performs better and its mean survival months are same as the actual dataset. Fig. 5 depicts the performance comparison among the base models and the proposed model on evaluation metrics RMSE.

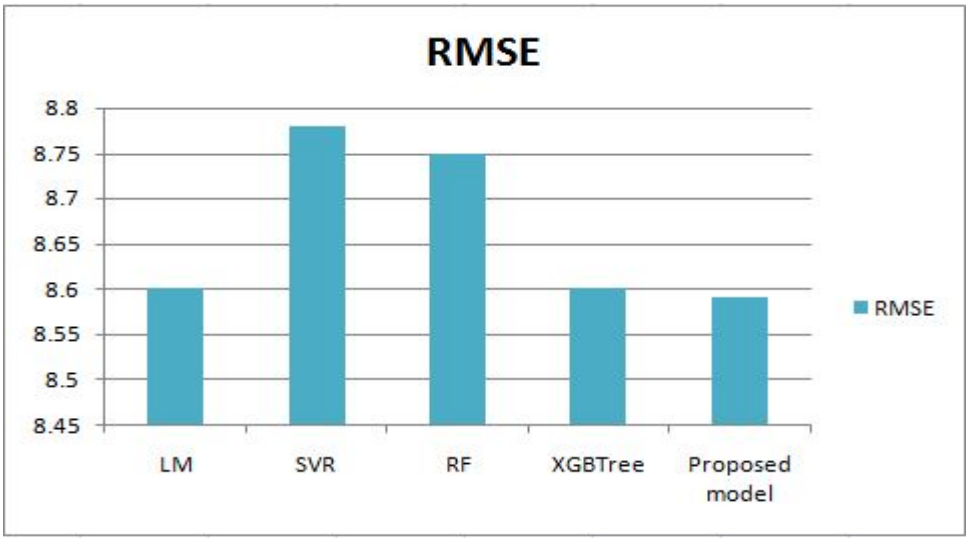


Fig. 5 Comparison of various algorithms on the basis of RMSE.

We tried to predict the survivability of the training dataset with the proposed model as well as the test dataset. Table 8 shows the statistical comparison of the predicted months with the training dataset and test dataset.

Table 8 Statistical comparison between the proposed model and actual dataset survivability.

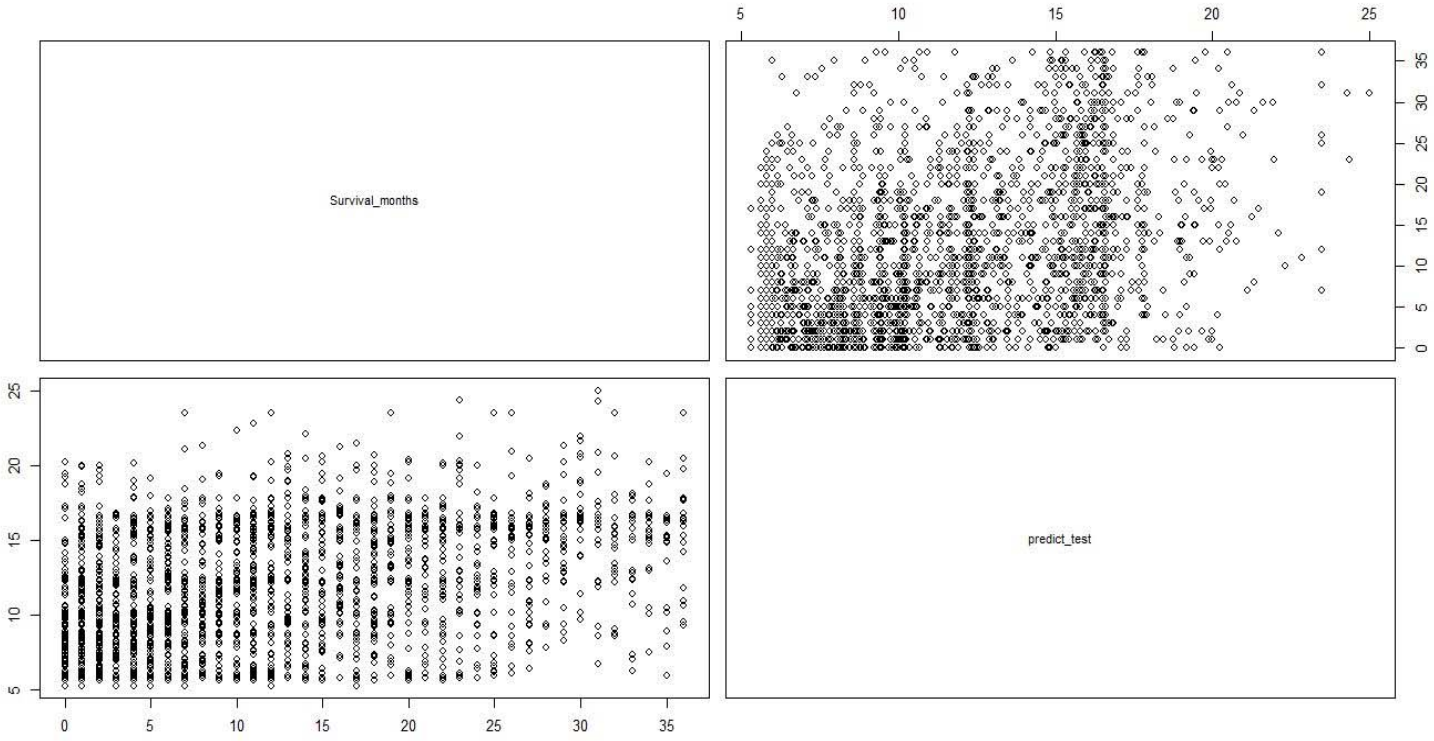
	Training Dataset	Prediction on Training Dataset	Test Dataset	Prediction on Test Dataset
Mean Survival	11.3	11.36	11.3	11.3
Standard Deviation	9.5641	4.13207	9.54638	4.15734

Table 8 shows that the mean survival time for both the training dataset and test dataset are 11.36 and 11.3 which are same as the actual survival months. The RMSE of the proposed model is a little bit lower than the sd of the both training set and test set. Fig. 6 presents the scatter plot of the actual survival months and proposed ensemble models survival month correlations.

From the figure it can visible that, there is a positive partial relationship between these survival months. In Fig. 6 it can be seen that the actual survival months is around 0 to 36, where the proposed model predicts in a range of 0 to 25 months approximately. The survival months 0 to 25 in the actual dataset has the highest frequency, it can be a reason that our model can predict around 25 months.

An ensemble model with regression algorithms is proposed in this study which predicts the survivability (months) of the lung cancer patients. The collected data are analyzed and relevant features are selected for further processing. The training set is used as the input for training each model and the performance of each of the base models are calculated. The best 4 model's outputs were selected as input to ensemble using stacking method.

Fig. 6 Scatter plot of actual and proposed predicted ensemble.



The proposed ensemble model performs better than the base models in predicting the test dataset survivability. The model is compared with some other regression algorithms such as Gradient Boosting Machine, Extreme Gradient Boosting Linear, Principal Component Regression and K-Nearest Neighbor which are applied on the same dataset and Table 9 presents the comparison result according to the RMS value.

Table 9 proves that the proposed model gives much better performance than the regression algorithms. This works is also compared with some existing work. Table 10 shows the comparison among proposed method and existing works which had been used regression techniques for prediction.

Table 9 Performance comparisons of single regression algorithms and proposed model.

Model Name	RMSE
XGBLinear	8.924
Gradient Boosting Machine	8.59
Principal Component Analysis	8.76
K-Nearest Neighbor	8.954
Proposed Ensemble Model	8.58459

Table 10 Comparison of RMSE with previous studies.

Studies	**No. of Attributes**	**Algorithm**	**Evaluation Metrics**
(Lynch et al., 2017)	18	Used GBM, LR, RF, DT, SVM and their weighted ensemble algorithm.	RMSE= 15.32
(Bartholomai and Frieboes, 2018)	13	Used RF for classify the dataset into three classes & LR, GBM, RF and their ensemble model for regression.	RMSE= 10.52
Proposed Method	12	Ensemble of MLR, SVR, RF, XGBTree using stacking technology with meta-learner GBM.	RMSE= 8.58459

Lynch et al. (2017) proposed an ensemble model using linear regression, support vector machine, random forest, decision tree and gradient boosting machine and these models weighted ensemble model. The most accurate model was GBM with RMSE value 15.32 and the predicted months are ~30, where actual survival months are ~72. JA Bartholomai and HB Frieboes divided the dataset into three classes on survival months (0-6, 7-24 and >24 months) using random forest classification algorithm. Then they predicted survivability using LR, GBM, RF regression algorithm and their ensemble model for each class (Bartholomai and Frieboes, 2018). This work gained 10.52 RMSE for the class 0-6 months, RMSE 15.65 for 7-24 months class and RMSE 20.51 for >24 months. Our proposed model used dataset of survival months 0- 35 and it can predict ~25 months with RMSE 8.58459. From the result above, our proposed model can perform better in terms of lung cancer survivability prediction. The proposed approach was a 2-level ensemble model and the proposed model had better accuracy compared to not only the base models but also some single regression algorithms and existing works.

4 Conclusion

In this paper, we used a combination of Multiple Linear Regression, Support Vector Machine, Random Forest And Extreme Gradient Boosting Tree algorithms with stacking technology for constructing a lung cancer survivability prediction model. We illustrated the effectiveness of the proposed method using 5-fold cross validation, R-squared and RMSE. This study aims to build a regression model which can predict lung cancer patients survivability more accurately with reduced the RMSE value. Although the results showed that this

method improved a little bit compared with the base models and the previous works, it has been shown the improvement of the models for further developing suitable models.

As for further work, we plan to investigate the survivability of different lung cancer patients for long term survival months with regression algorithm. Also analyzing the combination of different classifiers with gradient boosting-based classifiers ensemble would be of interest.

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