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Modeling and feature assessment of the sleep quality among chronic kidney disease patients

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ABSTRACT

Chronic Kidney Disease (CKD) is a progressive and irreversible loss of kidney function. Data mining concepts may be used in assessing and predicting CKD-related issues to obtain hidden clinical information for a reliable and effective decision-making process. These advanced learning methods would identify the relationships and patterns that will help classify factors that affect the poor sleep quality of CKD patients. Poor sleep quality is a critical issue for CKD individuals, negatively affecting immunity, cognitive functions, and emotional demonstrations. This study aims to find the factors affecting the sleep quality of CKD patients. Decision tree-based methods are used to identify the impact of each feature to predict sleep quality. The predictive results are compared with different classification models as well. Furthermore, two re-sampling techniques, Synthetic Minority Oversampling and Random Oversampling, are also used to reduce the impact of the imbalanced nature of the data set. We further discuss how these results agree with the clinically relevant features determined by the physicians.

1. Introduction

Chronic Kidney Disease (CKD) is a gradual and irreversible loss of kidney function in the long term and is one of the most common diseases in adult age. According to the KDIGO definition, the term “CKD” includes markers of kidney damage or decrease of estimated glomerular filtration rate ($GFR < 60ml/min/1.73m^2$) for > 3 months [1]. The treatment for CKD focuses on slowing the progress of kidney damage, usually by controlling the underlying cause. Crossing several GFR categories (Table 1), CKD can progress to a kidney failure category (G5), which is fatal without artificial filtering (dialysis) or a kidney transplant.

Decreased sleep quality is typical in CKD patients and is associated with reduced health-related quality of life [2]. Poor sleep quality due to sleep disorders such as insomnia, obstructive sleep apnoea, restless leg syndrome, and excessive daytime sleepiness [3–6] have been reported to be associated with CKD [7,8], in particular those undergoing dialysis [9]. The autonomic imbalance has also been proposed as a crucial mechanistic factor for poor sleep quality with the progression of CKD [10]. Development of cognitive and physical impairment is another major issue with CKD patients [11,12]. For older adults, emerging evidence suggests low sleep quality increases the risk of developing cognitive im-

pairment and dementia [13]. However, the prevalence of “poor sleep quality” in CKD patients is not yet really known; hence there is increasing attention on measuring the sleep quality of these patients.

This study aimed to find the external factors affecting the sleep quality of patients where the sleep quality is measured using the Pittsburgh Sleep Quality Index (PSQI) [14] in 105 CKD patients (101 patients after removing missing value columns) in Sri Lanka. The PSQI is a commonly used measure of sleep quality. This self-administered questionnaire assesses the quality of sleep during the previous month. It contains 19 self-rated questions yielding seven domains [15] shown in Table 3. Each domain is scored from 0 to 3, the sum of which causes a global PSQI score between 0 and 21, where the higher scores indicate lower sleep quality. The PSQI helps identify “good sleepers” and “poor sleepers.” A global PSQI score > 5 indicates that a person is a “poor sleeper” having severe difficulties in at least two areas out of seven or moderate challenges in more than three areas.

Many studies are found in the literature based on similar objectives, but some results are conflicting. According to one of the findings in the literature [16], there is no difference in the quality of sleep between patients with early kidney disease (G2) and kidney failure (G5) in a developing country; hence, sleep quality is independent of the GFR category.

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Table 1
GFR (Glomerular Filtration Rate) categories in CKD.

GFR category	GFR ml/min/1.73m ²	GFR category name
G1	≤ 90	Normal to increased GFR
G2	60 – 89	Mildly reduced
G3a	45 – 59	Mildly to moderately reduced
G3b	30 – 44	Moderately to Severely reduced
G4	15 – 29	Severely reduced
G5	< 15 or treated by dialysis	Kidney failure

Without evidence of kidney damage, GFR category G1 or G2 will not fulfill the criteria for CKD.

Table 2
Demographics and clinical variables of the total study sample and according to quality of sleep.

Feature	All	Good Sleepers	Poor Sleepers	p-value
Participants, n	101	32	69	-
Age - median (IQR)	61 (56–68)	64.5 (59.75–68.25)	60 (55–67)	0.0647
Creatinine (μmol/L) - median (IQR)	239.2 (166–429.7)	234.52 (169.5–291.14)	274 (166–610)	0.0702
haemoglobin (g/dL) - median (IQR)	10.9 (9–12.2)	11.6 (10.88–12.7)	10.1 (8.2–11.7)	0.0002
GFR category				0.0113
	G3, n(%)	9 (28.1)	23 (33.3)	
	G4, n(%)	16 (50)	15 (21.7)	
	G5, n(%)	7 (21.9)	31 (44.9)	
On haemodialysis	Yes, n(%)	0 (0)	21 (30.4)	0.0012
	No, n(%)	32 (100)	48 (69.6)	
Sex	Female, n(%)	14 (43.8)	22 (31.9)	0.3497
	Male, n(%)	18 (56.2)	47 (68.1)	
Employed	Yes, n(%)	11 (34.4)	12 (17.4)	0.1013
	No, n(%)	21 (65.6)	57 (82.6)	
Heart failure	Yes, n(%)	4 (4)	2 (2.9)	0.7986
	No, n(%)	30 (93.8)	67 (97.1)	
COPD	Yes, n(%)	1 (3.1)	5 (7.2)	0.7167
	No, n(%)	31 (10.3)	64 (92.8)	
GORD	Yes, n(%)	4 (12.5)	8 (11.6)	0.8418
	No, n(%)	28 (87.5)	61 (88.4)	
Depression	Yes, n(%)	1 (3.1)	0 (0)	0.6923
	No, n(%)	31 (96.9)	69 (100)	

P-values were calculated with the Mann-Whitney test and Pearson χ^2 test.

Table 3
Descriptive statistics for PSQI domains.

	Sleep Quality	PSQI Scores				P-value
		0	1	2	3	
Subjective sleep quality	Good (n, %)	3 (4.35)	20 (28.99)	32 (46.38)	14 (20.29)	1.4215e-9
	Poor (n, %)	17 (53.13)	13 (40.63)	2 (6.25)	0 (0.0)	
Sleep latency	Good (n, %)	4 (5.80)	11 (15.94)	20 (28.99)	34 (49.27)	7.1000e-9
	Poor (n, %)	20 (62.50)	4 (12.5)	5 (15.63)	3 (9.38)	
Sleep efficiency	Good (n, %)	14 (20.29)	12 (17.39)	20 (28.99)	23 (33.33)	1.4947e-9
	Poor (n, %)	28 (87.50)	4 (12.50)	0 (0.0)	0 (0.0)	
Sleep duration	Good (n, %)	17 (24.64)	10 (14.49)	16 (23.19)	26 (37.68)	1.7956e-8
	Poor (n, %)	28 (87.50)	4 (12.50)	0 (0.0)	0 (0.0)	
Sleep disturbance	Good (n, %)	0 (0.0)	33 (47.83)	33 (47.83)	3 (4.35)	5.6332e-5
	Poor (n, %)	2 (6.25)	28 (87.5)	2 (6.25)	0 (0.0)	
Use of sleep medications	Good (n, %)	64 (92.75)	0 (0.0)	2 (2.90)	3 (4.35)	0.2952
	Poor (n, %)	32 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Daytime dysfunction	Good (n, %)	21 (30.43)	35 (50.72)	10 (14.49)	3 (4.35)	0.0028
	Poor (n, %)	22 (68.75)	9 (28.13)	1 (3.13)	0 (0.0)	

P-values were calculated with Pearson χ^2 test.

Another supporting claim is that dialysis patients had poor sleep quality, as evidenced by their high median PSQI score [17]. Most statistical tools have been designed to study sleep quality and its predictors among dialysis patients. Using the p-values of statistical tests, it is shown that there are significant differences in sleep quality between sex, age, and duration of dialysis of CKD patients in Iran [18]. Using similar tools, it has also been stated that sleep quality decreases in the early kidney disease (G2) but does not appear to be associated with the subsequent GFR categories [19]. Moreover, [10] has concluded that CKD diabetic patients with poor sleep quality or low heart rate variability (HRV), but not sleep apnea, have a significantly increased risk for incidence of G5.

One can explain poor sleep as a short sleep duration (< 6 h). Sleep duration also can be assessed relative to other features of a CKD patient. In 2012, [18] claimed a conclusion saying that shorter (≤ 5 h) and longer (> 8 h) sleep duration and poor sleep quality (PSQI global score ≥ 6) were associated with patients in G5, considering CKD data in Japan [20]. A clinical analysis has shown that the sleep duration that was either < 6 or > 9 h were associated with a higher prevalence of CKD [21]. Ricardo et al. [8] has analyzed the associations of sleep duration and quality with CKD progression and has found that the high sleep fragmentation was associated with a higher risk for incident G5. A separate analysis [22] concludes that adequate sleep duration (average of seven hours) is

related to the increased health-related quality of life in predialysis CKD patients.

When dealing with patient data or diagnosis information, one of the major problems raised is the class imbalance issue; that is the fact that one class (majority class) is represented by a much larger number of instances than the other class (minority class) [23]. Medical data sets usually have class imbalance problems; therefore, the predictions can be biased towards the majority class [24]. Another issue with this data set is the smaller sample size. This can affect machine learning models and lead to over-fitting.

To reduce the impact of the class imbalances, we used two re-sampling techniques, Random over-sampling [25] and Synthetic Minority Over-sampling Technique (SMOTE) [26]. Random over-sampling is an earlier method, which involves supplementing the training data with multiple copies of some of the minority instances. Instead of duplicating every sample in the minority class, some of them may be randomly chosen with replacement. This method has already been proven to be robust. SMOTE is one of the most common techniques for re-sampling, which creates synthetic data points by considering the k nearest neighbors (in feature space) of a randomly selected data point. We discuss these methods in detail in Section 2.

To find the relevant features for the quality of sleep of CKD patients, we mainly use decision tree models [27,28] due to the easy interpretability. The results are compared with four existing binary classification methods, Logistic Regression (Logit) [29], Linear Support Vector Machine (SVM-linear) [30,31], Random Forest (RFC) [32], and Light Gradient Boosting (Lgbm_c) [33]. These classification models are then evaluated using commonly-used performance measures, accuracy, recall, precision, F1-score, AUC, and kappa statistics. The higher the values of each measure, the better the performance of the model at distinguishing between the poor and good classes. The kappa coefficient can be negative, which implies no effective agreement between the two classes, or the agreement is worse than random.

The rest of this paper is organized as follows. Section 2 will detail the data and methods used in the experimental design. Section 3 presents the results and the interpretations. Section 4 of this paper is concluded with a summary and a discussion of its contributions and limitations.

2. Methodology

2.1. Data set

Data were collected from 101 CKD patients (65 male) in the Colombo South Teaching Hospital, Sri Lanka. The data set consists of 12 features (four numerical and eight categorical) other than the target variable, i.e., "Quality of sleep". Detailed information about the features is shown in Table 2.

Out of 101 instances, 69 (68.3%) were identified as poor sleepers (majority class) according to the PSQI. For this study, data were collected from patients in three GFR categories, G3 (G3a, G3b), G4, and G5, where 21 (20.8%) patients from G5 were on a special treatment (regular haemodialysis). Early kidney disease patients were not included in the data. The serum creatinine test is done to assess kidney function, which measures creatinine level in a patient's blood and estimates how well the kidneys filter. Chronic obstructive pulmonary disease (COPD) and Gastro-oesophageal reflux disease (GORD) are also included as features to assess the impact on sleep quality.

2.2. Statistical tests

The analysis focuses on comparing the two independent groups, "good sleepers" and "poor sleepers." Normality assumptions for each attribute for both groups were tested using the Shapiro-Wilk test. Normality assumptions were violated in continuous grouped features; hence in Table 2, the distributions were presented as medians and inter-quartile

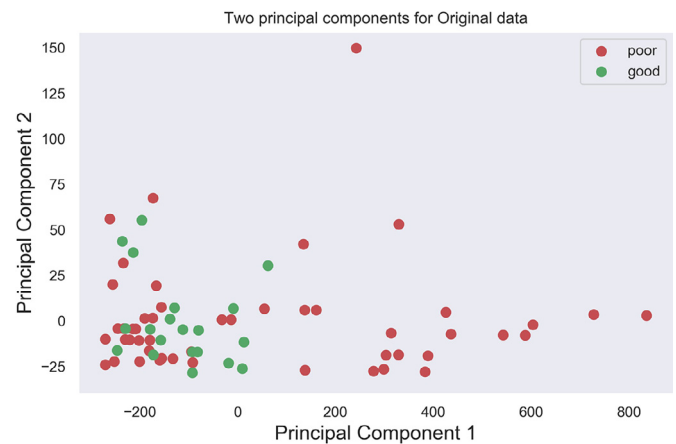


Fig. 1. Classification for first two principal components for original data.

ranges (IQRs). Categorical variables for each group were presented as a percentage share of the obtained data.

We used a nonparametric Mann-Whitney U test on each numerical feature to determine whether the underline distributions of two groups (poor sleepers/ good sleepers) are equal. Then, a chi-square fit test for two independent variables is used to compare two categorical variables in a contingency table to check if the data fits. Statistical tests were done using Python libraries: Pandas and Scipy.

P -values for each test are shown in Table 2. According to the statistical test results, only four features, creatinine, haemoglobin, GFR category, and haemodialysis, are associated with the sleep quality of CKD patients with a 0.05 level of significance. In Section 3, we will compare the classification results with these statistical test results.

We also conducted hypothesis tests to determine the PSQI domains most responsible for the difference in sleep quality. In the related literature, [34] found that falling asleep is a more prevalent problem than staying asleep, while [35] found that daytime sleepiness may be more problematic than sleep disturbances. In our analysis, the P -values in Table 3 depicts that, other than the use of sleep medications, all six other domains are associated with the sleep quality of CKD patients with a 0.05 level of significance.

2.3. Re-sampling techniques

The cleaned data set was divided into training (70%) and testing (30%) data for evaluating the model performances. As with many medical data sets, this training data set also suffered from two major problems in machine learning: small sample size and class imbalance. The training set has only 70 instances with 2 : 5 imbalance rate, where the majority class represents the patients with poor sleep quality. Fig. 1 shows how the first two principal components of actual data points scatter around in a two-dimensional space.

Then we applied two re-sampling techniques to the data. The random over-sampling duplicates randomly chosen minority class instances until it reaches the majority class observations. The scatter plot would be the same as for Fig. 1 as new points lie on top of the same previous points.

We also synthesized data using another technique called SMOTE. SMOTE works by selecting minority instances in the feature space, drawing a line between them, and drawing a new sample at a point along that line. For example, first, it chooses a random point from the minority class. Then it finds k nearest neighbors for that point. A random neighbor is chosen, and a synthetic instance is created at a randomly selected point between the two points in the feature space. The scatter plot for the first two principal components of SMOTE data is shown in Fig. 2, and the new instances from the minority class can be clearly seen.

Table 4
Decision Tree model accuracy comparison for the selected feature set.

Classification Model	Re-sampling Technique	Accuracy	Recall	Precision	F1-score	AUC	Kappa
Decision_tree	Basic	0.4516	0.3333	0.3077	0.3200	0.4300	-0.1382
	RANDOM Over	0.5161	0.5833	0.4118	0.4828	0.5285	0.0530
	SMOTE	0.4839	0.5833	0.3889	0.4667	0.5022	0.0040

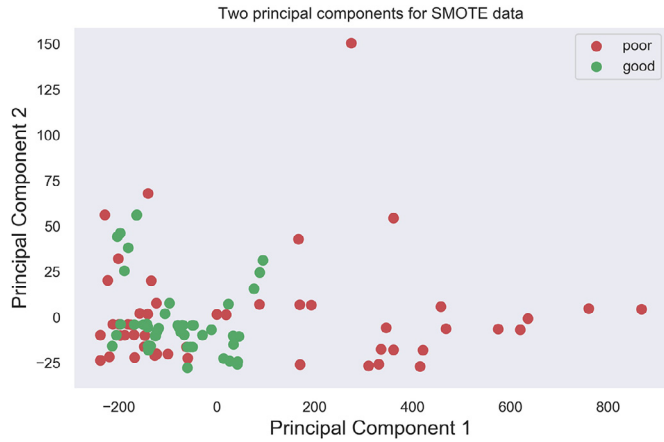


Fig. 2. Classification for first two principal components SMOTE data.

2.4. Decision trees

Decision trees are a machine learning method that uses a series of decisions about individual features to make a prediction, for instance. During decision-making using a decision tree, multiple features participate, and it is necessary to consider the importance and relevance of each feature. Hence, having the most beneficial feature at the root node, the tree traverses downwards by splitting into branches and internal nodes using several splitting measures like Entropy, Information Gain, Gini Index, etc. This leads to a decrease in impurity and uncertainty and yields better classification at each node.

Gini Index, also known as Gini impurity, calculates the probability of incorrectly classifying a specific feature when selected randomly. To compute the Gini index for a set of items with J classes, suppose $i \in 1, 2, \dots, J$, and p_i is the fraction of items labeled with class i in the set, then Gini Index can be expressed as:

$$\text{Gini Index} = 1 - \sum_{i=1}^n p_i^2.$$

The Gini index varies between 0 and 1, where 0 implies that all elements belong to a certain class and 1 indicates that the elements are randomly distributed across various classes. In this study, we used a categorical variable decision tree as we have a categorical target variable, quality of sleep, that is divided into categories, good and poor. One of the main advantages of using decision trees for this analysis is that the outputs are easy to read and interpret without requiring statistical knowledge.

3. Results

3.1. Decision tree classification

First, a decision tree classification model is fitted on a training set using four clinically relevant features determined by the physicians. They are creatinine, age, haemodialysis, and haemoglobin. The relevant accuracy matrices are appeared in Table 4. Random oversampling and SMOTE behave similarly; hence, the Decision tree classification results for the random over-sampling data when the depth is four is shown in Fig. 3.

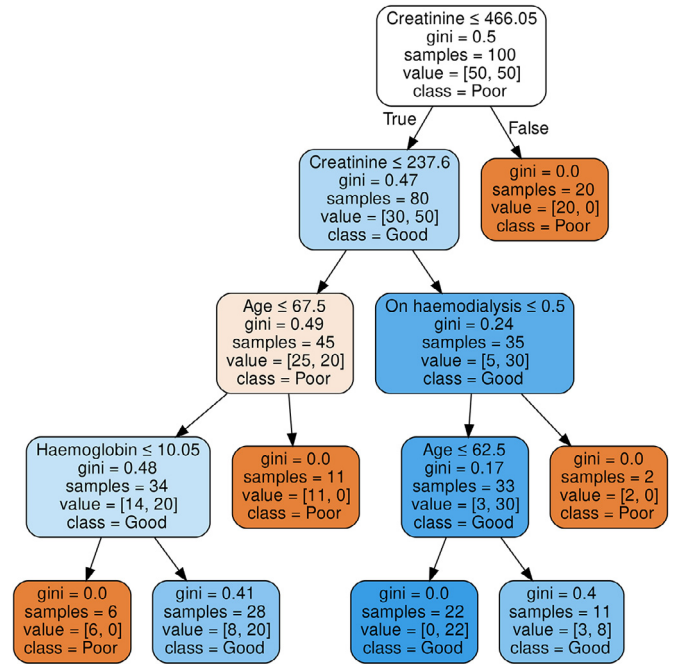


Fig. 3. Decision tree fitted on the random over-sampled CKD data. The maximum allowed depth for the tree was set to 4. Creatinine, age, haemodialysis and haemoglobin have been selected for the splits.

According to Fig. 3 the predicted sleep quality for any patient can be determined by tracing the path from the root of the tree (white node labeled “Creatinine ≤ 466.05”) to a leaf node. At each internal node, the decision to move to either child node is made by examining the condition at the node and moving either left or right depending on whether the condition is true for the patient. Thus, when the creatinine level ($\mu\text{mol/L}$) is greater than 466.05 or the creatinine level is less than 237.6, but the age is greater than 67.5, then we predict poor sleep quality. With the lower creatinine level, if the age is further below 67.5 and the haemoglobin rate (g/dL) is also below 10.05, they also have poor sleep quality. Haemodialysis patients whose creatinine level is also between 237.6 and 466.05 also have poor sleep quality. The same creatinine range for the non-haemodialysis patients whose age is below 62.5 years has a good sleep quality.

3.2. Comparing different classification methods

We then obtained results for the decision tree classifier with all the features, and the resultant tree is shown in Fig. 4.

The comparison is made by fitting models on the other four classification methods as well. The performance evaluation measures for each method with two different re-sampling techniques are shown in Table 5. For this specific training data set, the random over-sampling technique performs better with decision trees with the F1-score of 0.4828; still, the value is significantly low. Some reliable reasons for this will be discussed in Section 4. However, the SVM-linear model with SMOTE delivers better results over all the combinations we considered.

We analyzed 100 different random over-sampled training and test sets and observed the distribution of F1 scores in each trial to have ro-

Table 5
Classification model accuracy comparison for the training set.

Re-sampling Technique	Classification Model	Accuracy	Recall	Precision	F1-score	AUC	Kappa
Basic	Logit	0.3870	0.0833	0.1111	0.0952	0.3311	-0.3540
	SVM-linear	0.5806	0.2500	0.4286	0.3158	0.5197	0.0428
	Decision_tree	0.5484	0.4167	0.4167	0.4167	0.5241	0.0482
	RFC	0.5484	0.1667	0.3333	0.2222	0.4781	-0.0483
	Lgbm_c	0.5806	0.5000	0.4615	0.4800	0.5658	0.1296
	Logit	0.5161	0.5833	0.4118	0.4828	0.5285	0.0530
Over- sampling	SVM-linear	0.6129	0.5833	0.5000	0.5385	0.6075	0.2085
	Decision_tree	0.4839	0.3333	0.3333	0.3333	0.4561	-0.0877
	RFC	0.5161	0.4167	0.3846	0.4000	0.4978	-0.0043
	Lgbm_c	0.5483	0.4167	0.4167	0.4167	0.5241	0.0482
	Logit	0.4839	0.6667	0.4000	0.5000	0.5175	0.0313
SMOTE	SVM-linear	0.6452	0.6667	0.5333	0.5926	0.6491	0.2851
	Decision_tree	0.5161	0.5000	0.4000	0.4444	0.5132	0.0252
	RFC	0.5806	0.5000	0.4615	0.4800	0.5658	0.1296
	Lgbm_c	0.4839	0.4167	0.3571	0.3846	0.4715	-0.0553

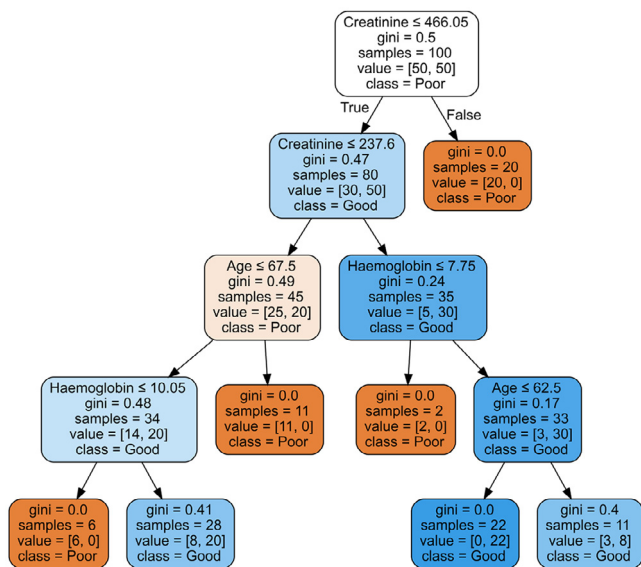


Fig. 4. Decision tree fitted on the random over-sampled CKD data with all features. The maximum allowed depth for the tree was set to 4.

bust results. The results are shown in Fig. 5, and it can be seen that Logit and SVM-linear classifiers obtained higher F1-scores in most of the situations.

3.3. Feature importance

To get remedies and pay attention to the lack of sleep issue of CKD patients, physicians must know the reasons. Hence, identifying the most important features affecting sleep quality is a crucial aspect of this study.

To achieve this task, we considered the feature importance, which was directly obtained from the classification model trained. We fitted each model on 100 random over-sampled training sets and computed the average feature importance, and ranked features accordingly. The mean of the ranks per each feature was also obtained. The results are shown in Table 6, which is sorted according to the rank of the means.

Decision tree-based modes (i.e., decision tree, RFC, and lgbm_c) select creatinine, haemoglobin, age, and sex as the top four important features, and that are three of the four features noted by the physicians. At the same time, the Logit model chooses haemodialysis, haemoglobin, employed, sex and creatinine. Most importantly, the SVM-linear model selects haemodialysis, GFR category, creatinine, and haemoglobin as the most important four features by agreeing on the same results obtained from the statistical analysis discussed in Section 2. However, on average,

haemoglobin, creatinine, haemodialysis, and sex are the most affected features identified by all the methods.

Then we used the Bland-Altman (B&A) plots [36] to determine the agreement between two pairs of quantitative rankings. Although the decision tree models didn't give us the highest accuracy, they have gained more interest among physicians because of their easy interpretability. Thus, we considered decision tree ranking as the base for this analysis. The plots in Fig. 6 are scattered above and below zero and within limits, suggesting that there is no consistent bias toward one approach. Also, the narrow limits in RFC and Lgbm_c reflect the minor mean difference between ranks with the decision tree classifier.

For further comparison, we also calculated the Euclidean distances between each classification model and decision tree classification using the equation below.

$$d(\mathbf{p}, \mathbf{q}) = \sqrt{\sum_{i=1}^n (q_i - p_i)^2}$$

where, $n = 12$, \mathbf{p}, \mathbf{q} are the two points in Euclidean n -space and q_i, p_i are Euclidean vectors, starting from the origin of the space.

The results in Table 7 also agree with the conclusion of the B&A plot in which RFC and Lgbm_c have obtained closer ranks with the decision tree model than with Logit and SVM-linear.

4. Discussion

Poor sleep quality is a critical issue with chronic kidney disease (CKD) patients, and it is also important to identify the factors that affect the quality of sleep. In this study, we use machine learning methods for extracting information from data arising from a study of CKD patients. Decision tree classification methods are commonly used machine learning classification methods, mainly due to easy implementation and straightforward interpretation of the results. Decision tree-based models, i.e., decision tree, RFC, and Lgbm_c identified creatinine, hemoglobin, age, and sex as the most important four features that affect the sleep quality of CKD patients. These are three of the four features noted by the physicians, whereas the four clinically relevant features determined by the physicians are creatinine, age, haemodialysis, and haemoglobin.

Two linear classification methods, Logit and SVM-linear, are also used to achieve the same objective, and SVM-linear strongly agreed with the statistical relationship results by identifying hemodialysis, GFR category, creatinine, and hemoglobin as the most important four features. However, haemoglobin, creatinine, haemodialysis, and sex are the most affected features identified by all the methods on average.

Traditional classification algorithms can perform poorly on imbalanced data sets and small sample size [37,38]. To avoid this class-imbalanced issue, two re-sampling techniques, random over-sampling

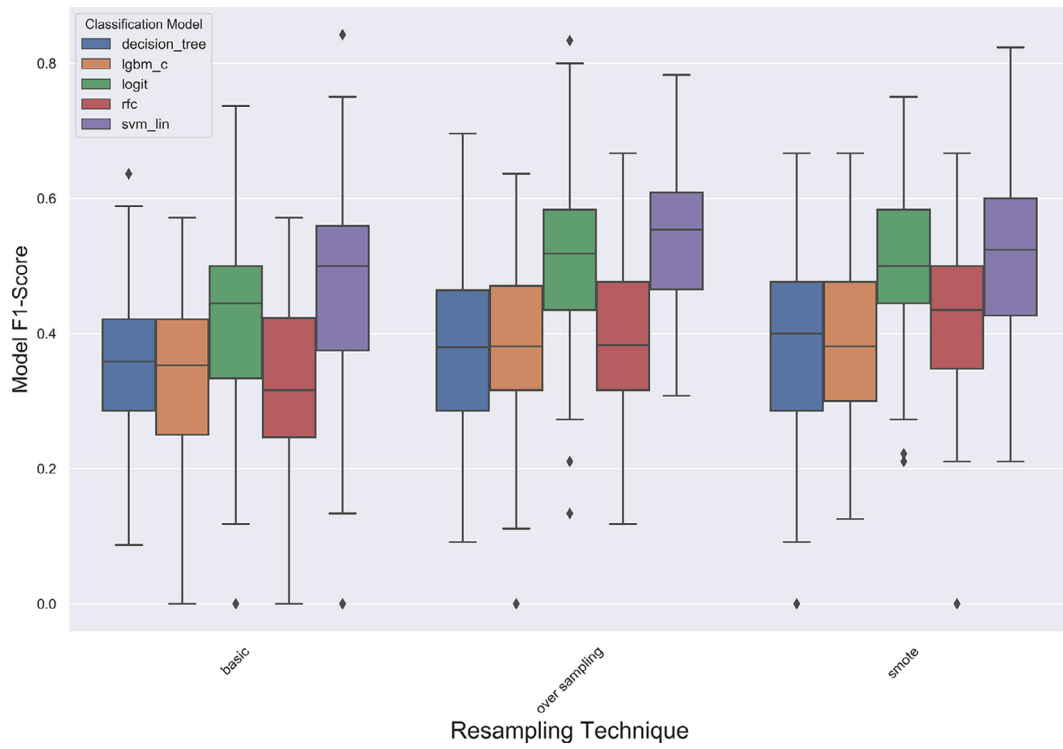


Fig. 5. F1-scores for different training sets.

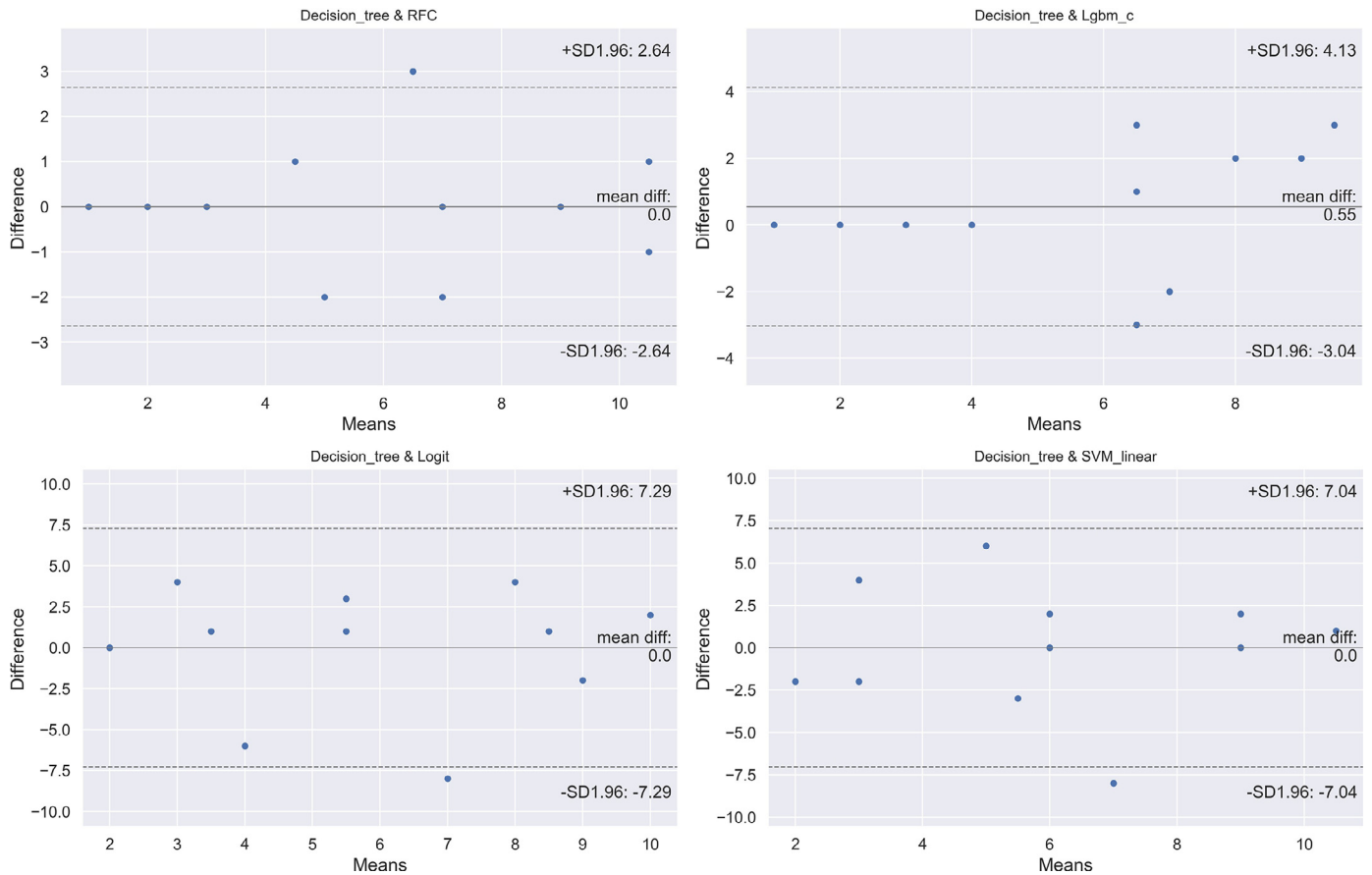


Fig. 6. Bland and Altman plot for data from the Table 6 by comparing Decision Tree with each classification model, with the representation of the limits of agreement (dotted line), from -1.96s to +1.96s.

Table 6
Rankings of average of feature importance for each classification methods.

Feature	Decision Tree	RFC	Lgbm_c	Logit	SVM_linear	Mean	Rank of means
Haemoglobin	2	2	2	2	4	2.4	1
Creatinine	1	1	1	7	3	2.6	2
On haemodialysis	5	4	8	1	1	3.8	3
Sex	4	6	4	3	7	4.8	4
Employed	7	7	6	4	5	5.8	5
GFR category	8	5	5	10	2	6	6
Age	3	3	3	11	11	6.2	7
Heart failure	6	8	8	5	6	6.6	8
GORD	9	9	7	8	9	8.4	9
Depression	10	11	8	6	8	8.6	10
COPD	11	10	8	9	10	9.6	11

Table 7
Euclidean Distances.

Classification model	Euclidean Distance with Decision Tree
Logit	12.3288
SVM-linear	11.9164
RFC	4.4721
Lgbm_c	6.3246

and SMOTE, were used. We remark that smaller sample sizes can reduce the power of the study, and by having more samples, we could achieve higher scores for performance evaluation measures.

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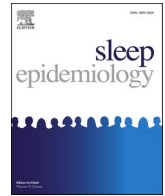
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