IEEE Access
Multidisciplinary | Rapid Review | Open Access Journal

Received 24 October 2023, accepted 21 November 2023, date of publication 23 November 2023,
date of current version 29 November 2023.

Digital Object Identifier 10.1109/ACCESS.2023.3336422

RESEARCH ARTICLE

Intensive Statistical Exploration to Identify Osteoporosis Predisposing Factors and Optimizing Recognition Performance With Integrated GP Kernels

RUHUL AMIN[1], MD. SHAMIM REZA[1], MD. MANIRUZZAMAN[2,3], MD. AL MEHEDI HASAN[4], (Member, IEEE), HYOUN-SUP LEE[5], SI-WOONG JANG [6], AND JUNGPIL SHIN[3], (Senior Member, IEEE)

[1]Department of Statistics, Pabna University of Science and Technology, Pabna 6600, Bangladesh
[2]Statistics Discipline, Khulna University, Khulna 9208, Bangladesh
[3]School of Computer Science and Engineering, The University of Aizu, Aizuwakamatsu 965-8580, Japan
[4]Department of Computer Science and Engineering, Rajshahi University of Engineering & Technology, Rajshahi 6204, Bangladesh
[5]Department of Applied Software Engineering, Dong-Eui University, Busanjin-gu, Busan 47340, Republic of Korea
[6]Department of Computer Engineering, Dongeui University, Busan 47340, Republic of Korea

Corresponding authors: Jungpil Shin (jpshin@u-aizu.ac.jp) and Si-Woong Jang (swjang@deu.ac.kr)

This work was supported in part by the Ministry of Science and ICT (MSIT), South Korea, under the Grand Information Technology Research Center Support Program supervised by the Institute for Information & Communications Technology Planning & Evaluation (IITP) under Grant IITP-2023-2020-0-01791; and in part by the Competitive Research Fund of The University of Aizu, Japan.

ABSTRACT Osteoporosis, a common skeletal disorder, necessitates the identification of its risk factors to develop effective preventive measures. It is crucial to identify the underlying risk factors and their relationships with the response class attribute. Different machine learning (ML) algorithms and feature selection approaches are used to estimate the risk of osteoporosis. However, ML-based algorithms may struggle to detect risk factors as well as grading of osteoporosis due to different measurement scale of data and their probability distributional assumptions. Violation of these assumptions and results interpretation may be improper in the presence of heteroscedasticity, or unequal variance in data. In this study, we seek to overcome distribution assumption constraints and improve the interpretability of our results by using rigorous statistical approaches, ensuring a robust and trustworthy study of osteoporosis risk variables. The study dataset consists of 40 clinical, lifestyle, and genetic attributes, allowing for a comprehensive analysis of potential risk factors associated with osteoporosis. In the analysis, after confirming the normality assumption using Kolmogorov-Smirnov and Shapiro-Wilk tests, independent t-test assess the factor ALT, FBG, HDL-C, LDL-C, FNT, TL, TLT, and URIC has a substantial impact on the risk of developing osteoporosis. The Mann-Whitney U test for the non-normal FN variable likewise showed a p-value of less than 0.05, indicating that this variable has a significant effect on the likelihood of developing osteoporosis. Based on the chi-square test p-values for the categorical factors, gender, calcium, calcitriol, bisphosphonate, calcitonin, COPD, CAD, and drinking have a severe significant risk of osteoporosis. For developing the predictive Gaussian Process (GPs) model, we proposed two customized integrated GP kernels into the analysis to enhance the modeling of complex relationships within the data. The proposed GP kernel model (modified kernel 2) outperforms the other individual kernels in this experiment and has the best accuracy score of 86.64% and AUC score of 86.63% on osteoporosis data. Moreover, a simulation study is also conducted to robustify the proposed model, the results are improved by different evaluation matrices ranging in accuracy from 0.60-11.41% and AUC from 0.50-11.60%.

INDEX TERMS Osteoporosis disease, statistical analysis, risk factor, Gaussian process kernel, prediction.

I. INTRODUCTION

Each disease has unique sign and symptoms that is determined by a specialized medical doctor; a symptom is evidence of diseases that is reported by a patient. When the protective mechanism in our bodies is unable to counteract any disruptive or harmful influences, diseases begin to emerge in our bodies [1]. The immune system is still robust in the early stages of human development, but it gradually deteriorates after that, and subsequently, the body develops a disease. Like several non-communicable diseases, osteoporosis is a non-communicable disease that affects bones and is characterized by decreased bone mineral density (BMD), lack of produced new bone, and different microstructures so those who are affected don't realize the full extent of the condition until it has progressed to the final stage of complexity. By measuring BMD with dual-energy X-ray absorptiometry, plain radiography, qualitative computerized tomography (CT) scan imaging, quantitative ultrasound densitometry (QUS), magnetic resonance imaging (MRI), X-ray, and several clinical attributes such as age, sex, height, weight, body mass index (BMI), etc., doctors attempt to identify osteoporosis, [2]. In the USA, there are 43.4 million people with low bone mineral density and 10.2 million cases of osteoporosis. It is expected that 13.2 million persons will have osteoporosis diagnoses and 57.4 million adults will have low bone mineral density [3].

At this time, both men and women over 50 years experience more than 9 million osteoporosis-related fractures each year globally. Notably, at least one osteoporotic fracture will occur in one out of every five men and one out of every two women in this age range [4]. Treatment of osteoporosis often consists of a combination of lifestyle modifications, appropriate medication, dietary changes, and so on that improve bone health and decrease the risk of fracture. Patients need muscle bearing to adapt to changes in their lives, and losing weight can help with bone health. Strength and bone density can be increased through walking and jogging. Regular vitamin D consumption moderated excessive alcohol and smoking, and taking dietary supplements like leafy greens, etc., are significant factors that might assist in promoting bone health and possibly avoiding osteoporosis [5]. Selective Estrogen Receptor Modulators (SERMs), hormonal replacement treatment (especially estrogen for postmenopausal women), and calcitonin hormone are some of the key medications that are used to supplement and improve bone health [6], [7]. There is vast relevance to the national interest of the osteoporosis study. In public health impact, Osteoporosis is now an intricate public health issue, especially in aging people [8]. This disease leads to bone fractures that produce a reduced quality of life, morbidity increased health-related costs, etc. Numerous studies demonstrate that low bone density is an important contributor to the development of osteoporosis. The understanding of bone biology that underlies the study of osteoporosis serves to empower the maintenance of bone health [9], [10]. Economically, osteoporosis has an impact on the economy both directly and indirectly. Osteoporosis patients require proper medical care, which can be costly and have an impact on our economy. If they don't get the proper care, people with osteoporosis experience long-term productivity losses.

It is crucial to remember that, even though treatment reduces the risk of developing osteoporosis, osteoporosis can still progress due to financial constraints, a lack of awareness, and a failure to follow lifestyle modifications, which are all essential first steps. However, researchers reported that osteoporosis is currently expanding quickly as a result of several risk factors. If osteoporosis is identified early, the risk of fracture and the financial burden on patients may be reduced. Different researchers use different methods to identify risk factors. Both statistical and machine learning (ML) methods are used to estimate the risk of osteoporosis as well as grading. In the development of ML area, to identify risk factors, traditional ML-based algorithms such as random forest (RF), gradient boosting, support vector machine (SVM), neural network (NN), decision tree (DT), filter, wrapper, embedding, LightGBM, and others have been widely used by researchers [11], [12], [13], [14]. Through these types of conventional ML-based algorithms, identifying significant risk factors and classifying data may be difficult. In terms of data distribution assumption, the majority of conventional ML-based algorithms do not follow the assumption of a probability distribution. They elucidate the relationship between the variable and the other instead of making assumptions. For optimum performance, several prominent algorithms need to have their hyperparameters tuned. A lack of adequate hyperparameters may prevent the ML-based algorithm from identifying the proper risk variables as well as classification. Traditional ML algorithms are unable to effectively interpret models, such as neural network models, even though they are strong algorithms. It's crucial to evaluate the underlying relationships between the risk factors while identifying them. The ML-based methods may be overfitting problems due to having a small dataset. Because it needs a large dataset to learn. With less dataset information, a sophisticated algorithm learns more from the training dataset, which causes overfitting and a failure to correctly identify the risk factor [15], [16].

Besides that, a bigger proportion of data in the real-world scenario exhibits complexity, particularly in medical data. Traditional ML-based algorithms like SVM, multiple kernel learning (MKL), DT, and others are constrained by their pre-defined frameworks, which reduces their flexibility to capture complicated patterns in the data [17]. But in terms of the Gaussian process (GPs), the kernel can capture non-parametric and non-linear relationships between the inputs and outputs. An individual kernel can be sensitive to the hyper-meters and kernel function choices made, which can cause complex data patterns to fail [18]. To take into account all of these considerations, this research work

The associate editor coordinating the review of this manuscript and approving it for publication was Yizhang Jiang.

combines a set of customized kernels (radial basis function (RBF), Matern, dot product, rational quadratic) and uses their find-tuned hyper-parameter to seize a wide range of patterns and relationships to generalize to unseen data and adapt to different data distributions, potentially improving the model's ability. To address these issues and other specific concerns, we applied a statistically supported methodology to identify risk factors. Specifically, we used the presented dataset to identify potential risk factors connected to the emergence of osteoporosis using some statistical techniques. Currently, evaluating osteoporosis patients requires a more modern method than the conventional one. Thus, this study provided a strategy that is effective for capturing probable osteoporosis risk factors in clinical data made up of various features, medical history, and laboratory tests in both men and women. The approach developed by this study intends to provide a more thorough and data-driven method for identifying those who are at risk for osteoporosis.

We seek to overcome distribution assumption constraints and improve the interpretability of our results by using statistical approaches, ensuring a robust and trustworthy study of osteoporosis risk variables. Incorporated the Kolmogorov-Smirnov and Shapiro-Wilk tests to evaluate whether continuous variables are normal. We applied the independent t-test to determine the significance of the risk of developing osteoporosis if the variables had a normal distribution. Moreover, the Mann-Whitney U test was used to determine significance when the variables did not follow a normal distribution. We employed a chi-square test to examine the impact of categorical variables on the occurrence of osteoporosis. Finally, we proposed customized integrated Gaussian Process (GP)-based kernels instead of using only individual kernels to predict osteoporosis patients. In comparison to individual kernels, the integrated GP-based kernel performs better in terms of model scalability, reducing the chances of overfitting, managing heterogeneous data, incorporating prior knowledge, and other factors [19]. By simulating a dataset and doing tests on the proposed model, we were able to validate it and determine its stability.

The remaining parts of the papers are as follows: Section II is on literature review, which presents a detailed review of several osteoporosis works and a summary. Section III presents research materials and methods in detail. Experimental results and discussion section illustrated in section IV. The conclusions and future actions are described in section V.

II. LITERATURE REVIEW

To accurately diagnose osteoporosis, several extensive research has been conducted on it. Lee et al. [20] conducted a study by using data from dental panoramic radiographs and skeletal bone mineral density. At the Korea University Ansan Hospital, the primary study was carried out among 680 patients between 2009 and 2018. By WHO guidelines, osteoporosis, and normal grading are carried out using a T-score. They employed four deep-learning models as convolution neural network (CNN), visual geometry group (VGG-16), transfer learning model from VGG-16 (VGG-16-TR), and fine-tuning with the transfer learning (VGG-16-TR-FT) model to accurately predict osteoporosis patients. They showed that the highest accuracy of 84.0% was obtained by VGG-16-TR-FT. Using a huge amount of clinical data and an ML-based algorithm, Engles et al. [21] also proposed an ML-based method for predicting osteoporotic patients. They trained LR (forward and backward selection), RF, SVM, random undersampling boost (RUSBoost), Super learner, and extreme gradient boosting (XGBoost) with 10-fold cross-validation and obtained the highest AUC of 70.4%.

Faysal et al. [22] conducted a cross-sectional study entitled 'Treatment and diagnosis pattern of osteoporosis in Bangladesh' on 107 osteoporosis patients. Their intended targets were several public and private hospitals in various regions of Bangladesh (Dhaka, and Comilla). With the help of the pre-designed questionnaire, they gathered information about their social demographic profile and the results of their physical therapy. The majority of patients, 83%, state that they are unaware of osteoporosis. Post-menopausal women have the highest rate of osteoporosis risk, at 10.4%, and are most frequently treated with bisphosphonates (hormone replacement therapy, calcium supplements, etc.) to prevent the disease. According to their research, a calcium-rich diet, vitamin D supplements, and physical activity are the most useful supplements. To diagnose osteoporosis, 50.0% utilized a bone mineral density test, 30.3% used a serum calcium test, and 15.4% used a serum creatinine test.

Ali et al. [9] conducted a cross-sectional study on 526 adults Bangladeshi people based on risk factors such as age, BMI, smoking habit, physical activity, education, previous disease (diabetes, cardiovascular disease, etc.) history, Quantitative Ultrasound (QUS) bone health test, etc. The osteoporosis stage is figured to be characterized by the T-score. About 43.2% of female respondents and 30.3% of male respondents are at risk for osteoporosis. According to their statistical research, seeing as the p-value is less than 0.05, adults over 50 with chronic health conditions are at a high risk of developing osteoporosis. Age and gender are the two main risk factors for developing osteoporosis. Shim et al. [23] investigated 1792 postmenopausal Korean women who participated in the Korea National Health and Nutrition Examination Surveys (KNHANES) V-1 and V-2 (2010-2011). They proposed a backward stepwise feature selection method on the total number of 19 raw data and achieved the best performance of their proposed method. With the use of k-nearest neighbor (KNN), DT, RF, gradient boosting machine (GBM), SVM, ANN, and LR, they were able to achieve performance scores of 0.713, 0.685, 0.734, 0.728, 0.728, 0.743, and 0.727. In another study, Kim et al. [24] conducted by using the National Health and Nutrition Examination Surveys (KNHANES) V-1 dataset. In their proposed approach, they identified the important features using the conventional embedded technique. They proposed SVM, RF, ANN, LR, Osteoporosis self-assessment

tool (OST), the customized Gaussian kernel function of SVM classifier (penalty parameter 100 for penalty parameter C, and 10 for scaling factor sigma) produces the maximum accuracy score of 76.7% and AUC of 82.7% when using the 10-fold cross-validation methodology. Yamamoto et al. [25] studied 1699 hip radiograph x-ray image data at a general hospital between 2014 and 2021 to classify osteoporosis. ResNet18, ResNet34, ResNet50, ResNet101, and ResNet152 are the five pre-trained models they employed. Among all models, the ResNet50 model prediction performance achieved an accuracy score of 0.812.

D. Devikanniga et al. [26] employed two image datasets, including lumbar spine and femoral neck datasets, with 10-fold cross-validation to classify osteoporosis in a healthy person. They proposed the monarch butterfly optimization-based artificial neural network (MBO-ANN) classifier. The proposed method for the lumbar spine dataset resulted in the accuracy, specificity, and sensitivity of 97.9% $\pm$ 0.14, 98.33% $\pm$ 0.03, and 95.24% $\pm$ 0.08, respectively, and 99.3% $\pm$ 0.16%, 99.2% $\pm$ 0.13 and 100, respectively, for femoral neck dataset.

Wani et al. [27] worked on knee X-ray images as well as osteoporosis-related clinical factors such as age, gender, previous fracture history, height, lifestyle habits, or other pathology through personal interviews. The dataset was collected from different regions of India. By the collaborative team of Unani, and Panchakarma Hospital, Srinagar, JK, India, and its sister branches of different areas of Kashmir from 21-12-2019 to 31-12-2019 the dataset was collected. In their approach, they applied many deep transfer-learning models namely AlexNet, VGG-16, VGG-19, and ResNet. The AlexNet achieved the best accuracy of 91.1%.

Iliou et al. [28] studied on taken the primary data set which was collected from one of the University hospitals in Greece's Orthopedic Clinical Information System of Alexandroupolis. This dataset contained only 4 diagnosis risk factors namely age, height, weight, and sex. They have taken an approach to categorize osteoporosis and non-osteoporosis based on the T-score using twenty ML-based algorithms. Instead of standard T-score 3 grading, they coded only 2 grads. If the T-score is less than -2.5 or equal coded that the person developed osteoporosis and if the score is greater than -2.5 encoded that the person is normal. The radial basis function network (RBFNetwork), naive Bayes tree (NBtree), reduced error pruning tree (REFtree), and locally weighted learning (LWL) achieved an accuracy of 71.44%, 71.22%, 70.40%, 68.70%, respectively.

Lin et al. [29] conducted a retrospective study between 2011 to 2018 at Wan Fang Hospital, in Taipei, Taiwan. Their process investigated 196 patients as a whole. They developed several ML predictive models, including ANN, LR, RF, and SVM, to predict osteoporosis patients. Among all classifiers, RF achieved the highest accuracy score of 75.0%, and LR achieved the highest AUC value of 73.1%. Huang et al. [30] obtained 172 CT scan images from 40-year-old patients from two Chinese hospitals. With their proposed approach, the authors used the Python PyRadiomics module to extract features from the photos. Then, to predict the risk of osteoporosis, the important features are chosen using the Mann-Whitney U test and the LASSO algorithm. They used six ML-based classifiers, including LR, RF, SVM, XGBoost, GNB, GBM, and accomplished accuracy scores of 0.80, 0.80, 0.71, 0.72, 0.80, and 0.81, respectively. With an accuracy of 0.81 and an AUC of 0.86, the gradient-boosting machine has demonstrated superior performance in predicting the risk of osteoporosis.

Bui et al. [31] studied osteoporosis to predict the risk of osteoporosis in Vietnamese people. The study materials were collected from Hanoi Medical University Hospital (July 2018 to February 2021) health information system database. For the feature selection approaches they used the chi-square test p-value and for model development used four ML models such as LR, SVM, NN, and RF using hyperparameter tuning. The Brier score, F1-score, precision, recall, and AUC score are used to evaluate the performance of the model. In their proposed first phase, LR, SVM, NN, RF, and osteoporosis self-assessment tool (OSTA) model achieved an AUC score of 0.832, 0.831, 0.854, 0.832, and 0.654, respectively. The RF method achieves the best AUC score using the validation protocol, which ranges from (0.825-0.881). Table 1 presents a detailed summary of the literature review.

III. MATERIALS AND METHODS

A. PROPOSED METHODOLOGY

A comprehensive process has been taken to build a Gaussian Process (GP) model that is incredibly precise and predictive. As part of an overall strategy, we employ a variety of techniques to undertake in-depth statistical analyses. We have thought about the specifics in detail within the recommended framework. As a starting point, we acquired the BMD dataset from the Harvard University Dataverse repository. We check for missing values when performing exploratory data analysis (EDA). We impute using the mean value of the variable if any features of the dataset have missing values. We scaled the dataset using the standardization technique, treating features fairly. This makes it easier to adhere to the assumptions about the Gaussian distribution, provide consistent feature weight, improve convergence, reduce the risk of overfitting, and so more. To apply the proposed statistical methodical analysis, we divided the dataset into continuous variables and categorical variables after confirming the processing of the dataset. Then, to determine whether the continuous data distribution is normal, we apply the Kolmogorov-Smirnov and Shapiro-Wilk tests. If the data have a normal distribution, we applied the t-test; if not, we used the Mann-Whitney U tests. For categorical data, the chi-square test is employed. This approach ensures accurate statistical analysis based on dataset distribution. Based on the p-values, we included every variable; if the p-value was lower than 0.05, we selected the variable for model fitting further. For dataset splitting, 5- and 10-fold cross-validation were utilized. For developing the patient classification model, we finally used our proposed

TABLE 1. Summary of the literature review on several work performance(in %).

Author	Dataset	Approach	Performance (%)
et al. [20]	BMD & Dental panoramic radiography data	CNN, VGG16, VGG16-TR, **VGG16-TR-FT**	0.840
Yamamoto et al. [25]	Hip radiography image data	ResNet (18, **34**, 50, 101, 152)	0.809
Faysal et al. [22]	Clinical attributes data	Cross-sectional study	Not available
Ali et al. [9]	Clinical attributes data	Cross-sectional study	Not available
Wani et al. [27]	Knee x-ray image & Clinical attributes dataset	**AlexNet**, VGGNet-16, ResNet, VGGNet-19	90.91
Iliou et al. [28]	Clinical attributes dataset	**RBFNetwork**, NBTree, REPTree, LWL	71.74
Shim et al. [23]	KNHANES-V1 and V2	KNN, DT, RF, GBM, SVM, ANN, **LR**	74.9
Lin et al. [29]	Wan Fang Hospital, Taiwan clinical data	ANN, LR, **SVM**, RF	75.00
Huang et al. [30]	CT scan images	LR, RF, SVM, XGBoost, GNB, **GBM**	0.81
Bui et al. [31]	Health Information System Clinical database	LR, SVM, NN, **RF**, OSTA	0.85
Kim et al. [24]	KNHANES-V1	**SVM**, RF, ANN, LR, OST	76.70
Devikanniga et al. [26]	Lumber spine & Femoral neck image data	MBO-ANN for Lumber spine	97.9
Engels et al. [21]	Clinical attributes data	LR, **RUS Boost**, Super learner, XGBoost	70.4

Bold indicates the results of the proposed method.

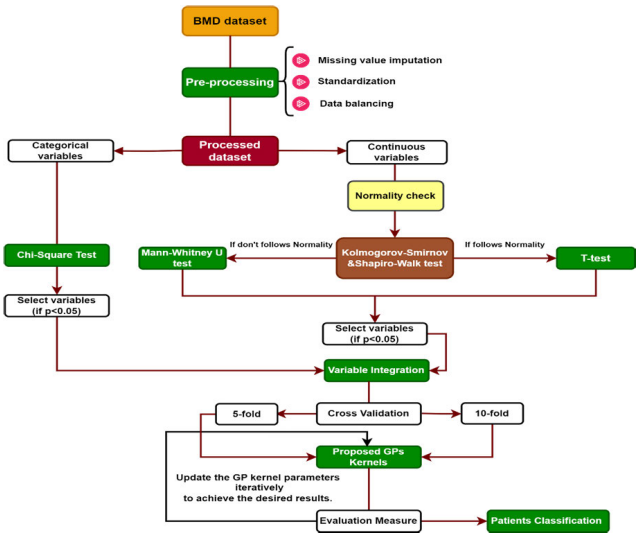


FIGURE 1. Proposed research workflow diagram for the detection of patients with osteoporosis.

GP kernel. Fig. 1 shows the complete design of the study in detail.

B. BONE MINERAL DENSITY (BMD) DATASET

To perform our research, we acquired the BMD dataset from the Harvard Dataverse repository [32]. This dataset was published on 17 December 2022 and is freely accessible to all research enthusiasts. This dataset contained 40 variables where osteoporosis is identified as a target variable and the remaining variables are risk factors for osteoporosis. Several osteoporosis works have been done in previous research work for the risk factor identification or closely associated with developing the risk of osteoporosis. The details are discussed in the literature review section. Researchers found various risk factors through the study such as age and gender [33], height, weight, and body mass index [34], [35], lumber spine [36], [37], femoral neck [38], telomere length [39], aspartate aminotransferase (AST), alanine aminotransferase (ALT) [40], bone marrow density [41], creatinine [42], uric [43], fasting blood glucose, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol [44], calcium [45], potassium [46], magnesium [47], calcitriol [48], bisphosphonate [49], calcitonin [50], hypertention [51], chronic obstructive pulmonary disease [52], diabetes mellitus [53], hyperlipidaemia [54], hyperuricemia [55], coronary artery disease [56], chronic kidney disease [57], smoking, drinking [58]. The details of the BMD dataset description are shown in Table 2.

C. DATA PRE-PROCESSING

We examine the missing values during the initial stage of dataset preprocessing. We found different variables with missing values only in continuous variables. There are 36 missing values in age, 34 missing values in height, 34 in BMI, 2 in ALT, 2 in AST, 1 in Bun, 3 in CREA, 16 in FBG, 17 in HDL-C, 14 in LDL-C, 2 in Ca, 5 in P, and 3 in Mg. All missing values are replaced using their respective means. The Standardization method is used to scale the continuous variables. We then check the balance set by looking at the target variable count number. There is a moderate imbalance in the target variable, as shown by the fact that out of 1537 patients, 568 (37%) have osteoporosis and 969 (63%) are at no risk. Due to the imbalance in this dataset, results may be erroneous or biased in a way that benefits the dominant class [59]. We applied the SMOTE (synthetic minority oversampling technique) balance technique to overcome these major difficulties [60], [61].

D. STATISTICAL ANALYSIS AND FEATURE SELECTION

To identify potential risk factors for getting the disease using statistical analysis, we executed several statistical tests on this dataset. In the first step, the Kolmogorov-Smirnov test; $D = |F(x) - S(x)|$, and Shapiro-Walk test; $S = \left(\frac{\sum_{i=1}^{n}(c_i x_i)^2}{\sum_{i=1}^{n}(x_i-\bar{x})^2}\right)$ is used to check the normality for the continuous [62]. Secondly, for continuous variables, we utilized the independent t-test (parametric) to identify the risk factor if the variable had a normal distribution; otherwise, we used the Mann-Whitney U test; $V_1 = n_1 n_2 + \frac{n_1(n_1+1)}{2} - Q_1$, $V_2 = n_1 n_2 + \frac{n_2(n_2+1)}{2} - Q_2$ (non-parametric) for non-normal distribution. The chi-square test; $\chi^2 = \sum \frac{(O-E)^2}{E}$ was employed in the second method for categorical variable selection [63]. Then, the p-value from the t-test, and chi-square test is considered to identify the risk factor, which

TABLE 2. Demographic information of bone mineral density dataset.

Variable names	Missing values	Osteoporosis	Non-osteoporosis	p-value
Total, n (%)	203	568 (36.96)	969 (63.04)	
Age (in years), Mean±SD	36	60.61±12.74	59.40±12.80	0.074
Height, Mean±SD	34	165.89±8.14	165.77±7.91	0.776
weight, Mean±SD	34	67.23±11.78	67.10±11.90	0.838
BMI, Mean±SD	34	24.32±3.26	24.30±3.29	0.924
ALT, Mean±SD	2	20.55±12.39	25.31±18.42	<0.001
AST, Mean±SD	2	22.24±9.29	22.91±9.54	0.182
BUN, Mean±SD	1	5.67±2.05	5.58±3.86	0.585
CREA, Mean±SD	3	74.27±27.49	73.79±24.56	0.726
FBG, Mean±SD	16	5.15±1.13	5.43±1.71	0.002
HDL-C, Mean±SD	17	1.27±0.38	1.23±0.37	0.040
LDL-C, Mean±SD	14	2.51±0.88	2.64±0.90	0.007
Ca, Mean±SD	2	2.24±0.21	2.23±0.12	0.632
P, Mean±SD	5	1.03±0.17	1.04±0.22	0.267
Mg, Mean±SD	3	0.86±0.101	0.86±0.09	0.734
L14, Mean±SD	—	1.13±0.19	1.13.0.18	0.781
L1.4T, Mean±SD	—	0.54±1.57	0.55±1.49	0.821
FN, Mean±SD	—	0.75±0.10	0.93±0.12	<0.001
FNT, Mean±SD	—	2.12±0.80	0.81±0.97	<0.001
TL, Mean±SD	—	0.82±0.11	1.00±0.13	<0.001
TLT, Mean±SD	—	-1.77±0.88	-0.43±0.99	<0.001
URIC, Mean±SD	—	339.17±90.25	353.34±100.15	0.006
Calcium, Yes, n (%)	—	148 (9.64)	78 (5.07)	0.030
Bisphosphonate, Yes, n (%)	—	65 (4.23)	940 (61.14)	<0.001
Gender, Male, n (%)	—	348 (22.64)	597 (38.84)	0.030
Calcitriol, Yes, n (%)	—	192 (12.50)	71 (24.47)	<0.001
Calcitonin, Yes, n (%)	—	77 (5.01)	11 (0.72)	<0.001
HTN, Yes (%)	—	327 (21.29)	515 (33.53)	0.093
COPD, Yes, n (%)	—	184 (11.98)	195 (12.68)	<0.001
DM, Yes, n (%)	—	194 (12.63)	312 (20.30)	0.093
Hyperlipidemia, Yes, n (%)	—	214 (13.93)	387 (25.19)	0.380
Hyperuricemia, Yes, n (%)	—	90 (5.85)	178 (11.59)	0.431
CAD, Yes, n (%)	—	153 (9.95)	159 (10.34)	<0.001
CKD, Yes, n (%)	—	27 (1.76)	32 (2.08)	0.153
Smoking, Yes, n (%)	—	143 (9.31)	253 (16.47)	0.686
Drinking, Yes, n (%)	—	97 (6.31)	253 (16.47)	<0.001

SD: Standard deviation; COPD: Chronic Obstructive Pulmonary Disease; CAD: Coronary Artery Disease; CKD: Coronary Kidney Disease.

is defined as a probability under the hypothesis that, if the p-value is less than 0.05 (p<0.05) represents the variable has no significant impact (null hypothesis) on the development of osteoporosis if the value is greater than 0.05 (p>0.05), we assume that the variable has a considerable impact (alternative hypothesis) on osteoporosis. Finally, we select significant risk factors with a p-value of less than 0.05 to build the osteoporosis prediction model; those with a value higher than that are thought to have no likelihood of developing the disease.

E. PROPOSED GP KERNELS STRATEGY

The multivariate Gaussian normal distribution is broadly generalized by the Gaussian Process (GP). This process is a parametric and all underlying independent variables in this parametric process will have a normal distribution for it to function. However, the abnormal data distribution in the real world makes this assumption very challenging. The GP works very effectively when the dataset has a normal distribution or is very near to it. GP permits various hyperparameters instead of using only the mean and covariance matrix of multivariate Gaussian normal distribution. Suppose we have data points $x_1, x_2, \ldots, x_n$ drawn from normal distribution $f(x_i)$ where $i = 1, 2, \ldots n$. If we want to classify any data point using the GP of some target variables $Y = y_1, y_2, \ldots, y_m$. The GP process specifies the mean function $\mu(x)^i$ and kernel covariance function by $K(x_i, x_j)$, which is defined as a kernel function [64]. There are several kernels used in the GP process namely RBF, constant kernel, white noise, dot product, Matern, rational quadratic kernel, etc. Using these kernels GP model is built to perform on a specific dataset to classify any data point. Nowadays, the GP-based model is widely used for classification over various domains and obtained outstanding performances [65], [66]. To build a better model, the researcher can use the find-tuned strategy to modify the kernel hyperparameters. Changing kernel hyperparameters, integrating, and creating a product of many kernels with each other are some of the multiple ways we used in this work to design a better GP model. This study uses the four well-known GP kernels, including the RBF, dot product, Matern, and rational quadratic kernels. The integration of the proposed kernels is graphically depicted in Fig. 2. The customized GP kernels are as follows;

$$\text{RBF} = C * \exp\left(-\frac{||x_n - x_m||^2}{2L^2}\right) \tag{1}$$

where L is the length scale

$$\text{Dot product} = C * (\sigma\ (x_n * x_m)) \tag{2}$$

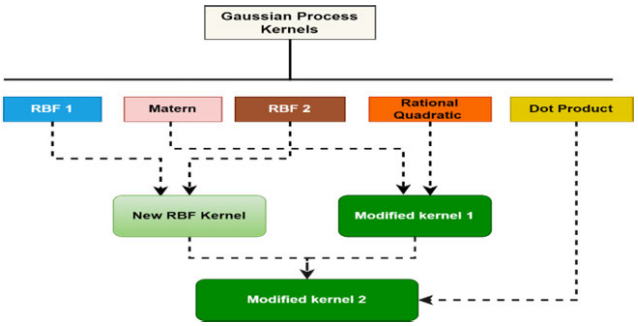


FIGURE 2. Two proposed GP classifier framework.

where σ is the hyperparameter that controls the scale of the product.

$$\text{Matern} = C * \frac{1}{\Gamma(\nu)\, 2^{\nu-1}} * \left(\frac{\sqrt{2\nu}}{L} d_1(x_n, x_m) \right)^{\nu} * K_{\nu} \left(\frac{\sqrt{2\nu}}{L}\, d_2(x_n, x_m) \right) \tag{3}$$

d_1 and d_2 is the Euclidean distance i.e., $d_1, d_2 = \sqrt{\sum_{i=1}^{n}(x_i - y_i)^2}$, $K_{\nu} = K_{\beta}\left(\rho \cdot \|x - x'\|\right)$ is the second kind of modified Bassel function, and Γ is the gamma function which is utilized in the kernel formula to define as a normalizing factor.

$$RQ = C * \left(1 + \frac{||x_n - x_m||^2}{(2aL^2)} \right)^{a} \tag{4}$$

where L is the scale for length and a is the large and small weight scale variation. Using these kernel functions, we proposed composite kernels by combining the individual modified kernels.

$$\begin{aligned} \text{Modified kernel\_1} = {} & C * \frac{1}{\Gamma(\nu)\, 2^{\nu-1}} * \left(\frac{\sqrt{2\nu}}{L} d_1(x_n, x_m) \right)^{\nu} \\ & + K_{\nu} * \left(\frac{\sqrt{2\nu}}{L}\, d_2(x_n, x_m) \right) \\ & + C * \left(1 + \frac{||x_n - x_m||^2}{(2aL^2)} \right)^{a} \end{aligned} \tag{5}$$

$$\begin{aligned} \text{Modified kernel\_2} = {} & (C * (rbf_1 * rbf_2)) \\ & + (C * \text{Modified kernel\_1}) \\ & + (C * \sigma\, (x_n * x_m)) \end{aligned} \tag{6}$$

where C is a different, predetermined constant value that is utilized to adjust the hyperparameter tuning to establish a consistent model. rbf_1 and rbf_2 are the two same kernel functions of equation one.

IV. RESULTS AND DISCUSSION

In this section, we've outlined the entire process of identifying risk factors for both continuous and categorical data, proposed modified Gaussian process kernel results as well and validated the model strength. The strategic approach to risk factor identification and the selection criteria are based on p-values. The GP kernel findings demonstrated the classification of osteoporosis patients' prediction model and insights.

A. NORMALITY CHECK USING KOLMOGOROV-SMIRNOV AND SHAPIRO-WILK TEST

Our dataset contains two different types of variables: continuous and categorical. In our proposed approach, we first use the Shapiro-Wilk and Kolmogorov-Smirnov tests at a 5% level of significance to assess the normality of continuous variables in our dataset, taking into account all linked variables with osteoporosis (class; osteoporosis=1) and non-osteoporosis (class; non-osteoporosis=0) patients. The variable of the dataset is assumed to have a normal distribution if the p-value is less than 0.05 ($p<0.05$). Notably, based on these two statistical tests, all the variables have normal distributions, except the femoral neck variable for osteoporosis patients ($p=0.200$). Then, using the 95% confidence interval for mean equality, we perform the t-test for normal distribution to find risk factors, and for the non-normal distribution of the femoral neck variable, we run the Mann-Whitney U test. The t-test takes into account variance equality and non-equality. This analytical approach aids in the selection of appropriate statistical analysis methods. Parametric techniques are frequently more effective and illuminating when the data is normally distributed. Other specialized procedures or non-parametric methods may be needed for non-normal data. Also, this method might make dataset comprehension, interpretative competencies, model validity, and data transformation simpler. Table 3 provides specific information about the data's normality using two proposed tests.

B. STATISTICAL ANALYSIS AND FEATURE SELECTION FOR OSTEOPOROSIS PATIENTS

Statistical feature selection aids in identifying the most important features and ignoring the unimportant ones, which increases model performance, decreases overfitting, prevents multicollinearity, and increases data complexity [67]. As we dig a bit deeper into the demographic and clinical context, we find that there are 969 cases of non-osteoporosis and 586 cases of osteoporosis in the whole dataset. We evaluated the continuous variables and estimated the mean and standard deviation for both cases. The frequency and percentage of categorical variables are estimated for the two groups. The dataset contains a total of 203 missing values, as shown in Table 2. Among all the variables, we found that continuous variables were the ones that had the majority of the missing values. Among them, 92% of the missing values were found for age, height, weight, BMI, FBG, HDL-C, and LDL-C. The average age (60 years) and BMI (24) of people with osteoporosis and non-osteoporosis are nearly identical. Approximately one-fourth of the male patients were afflicted by the disease. The average mean and standard deviation of CREA, P, Mg, L14, L1.4T, and other variables

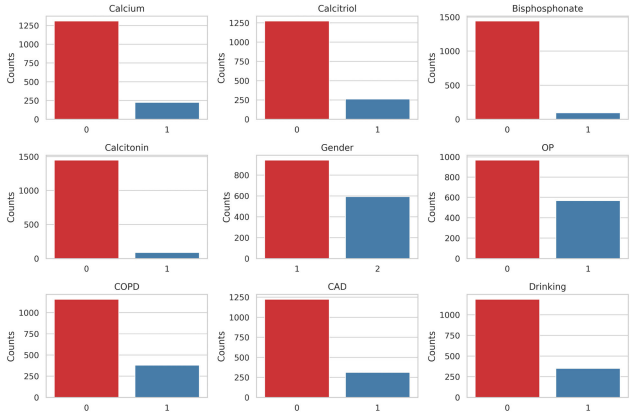


FIGURE 3. Bar diagram for each categorical variable.

are nearly equal for both cases. Approximately, six to nine percent of osteoporosis patients confess to having a bad habit, such as smoking or drinking. Respondents 601 and 268 among 1537 patients acknowledged having hyperlipidemia and hyperuricemia, which may likely be ignorable ($p<0.05$) for the diseases in terms of genetic features. However, in our proposed dataset, ALT, FN, FNT, TLT, TL, calcium, calcitriol, bisphosphonate, calcitonin, COPD, and CAD, drinking p-values is <0.001 indicate that there is a severe significant risk of osteoporosis. The selection of additional variables has a considerable impact on the likelihood of developing osteoporosis disease. The p-values in Table 2 demonstrated the significance of developing osteoporosis. Fig. 3 shows a bar chart for each categorical variable, which includes calcium, calcitriol, bisphosphonate, calcitonin, gender, OP, COPD, CAD, and drinking. Aside from gender, the x-axis shows whether or not the patients are taking the medicine, impacted by any incidence, and so on, and the y-axis shows the frequency of the related patients. The gender variable displays the frequency of male and female patients who took part in the study. In Fig. 4, a scatter plot for every pair of continuous variables illustrates how correlations, trends, and patterns in multivariate data can be found. They may offer insights that aren't immediately seen from individual scatter plots or summary data alone, such as how various factors interact with one another. The paired graph shows that the maximum of the pair variables is independent of each other, implying that changes in one variable have no substantial impact on the other. As a result, there may be a particular constraint, condition, or characteristic. Each continuous variable's hold univariate histogram is represented by the diagonal subplot.

C. PERFORMANCE OF GP MODEL FOR PREDICTING OSTEOPOROSIS PATIENTS

For developing the predictive GP-based model, we employed the 5-fold and 10-fold CV to each kernel and its integrated custom kernels. We considered the accuracy, precision, recall, F1-score, and AUC to evaluate the performance of the proposed model. Both the 5-fold and 10-fold CV techniques

TABLE 3. Kolmogorov-Smirnov (KS) and Shapiro-Walk (SW) test for normality check.

Variable names	Class	KS test		SW test	
		Statistic	p-value	Statistic	p-value
Age	0	0.079	<0.001	0.973	<0.001
	1	0.076	<0.001	0.977	<0.001
Height	0	0.078	<0.001	0.988	<0.001
	1	0.064	<0.001	0.991	0.002
Weight	0	0.045	<0.001	0.993	<0.001
	1	0.046	0.006	0.993	0.009
BMI	0	0.030	0.040	0.991	<0.001
	1	0.045	0.008	0.990	0.001
ALT	0	0.164	<0.001	0.695	<0.001
	1	0.135	<0.001	0.761	<0.001
AST	0	0.187	<0.001	0.747	<0.001
	1	0.175	<0.001	0.679	<0.001
BUN	0	0.243	<0.001	0.328	<0.001
	1	0.138	<0.001	0.819	<0.001
CREA	0	0.130	<0.001	0.679	<0.001
	1	0.169	<0.001	0.666	<0.001
FBG	0	0.215	<0.001	0.608	<0.001
	1	0.173	<0.001	0.735	<0.001
HDL-C	0	0.085	<0.001	0.879	<0.001
	1	0.091	<0.001	0.892	<0.001
LDL-C	0	0.033	0.014	0.984	<0.001
	1	0.048	0.004	0.991	0.002
Ca	0	0.044	<0.001	0.993	<0.001
	1	0.148	<0.001	0.526	<0.001
P	0	0.112	<0.001	0.710	<0.001
	1	0.071	<0.001	0.902	<0.001
Mg	0	0.062	<0.001	0.959	<0.001
	1	0.064	<0.001	0.937	<0.001
L14	0	0.032	0.021	0.983	<0.001
	1	0.048	0.003	0.981	<0.001
L1.4T	0	0.050	<0.001	0.979	<0.001
	1	0.054	<0.001	0.976	<0.001
FN	0	0.038	0.002	0.990	<0.001
	1	0.033	0.200	0.994	0.031
FNT	0	0.048	<0.001	0.990	<0.001
	1	0.049	0.002	0.991	0.002
TL	0	0.034	0.010	0.995	0.003
	1	0.040	0.031	0.981	<0.001
TLT	0	0.042	<0.001	0.994	<0.001
	1	0.054	0.001	0.979	<0.001
URIC	0	0.038	0.002	0.989	<0.001
	1	0.073	<0.001	0.970	<0.001

BMI: Body Mass Index; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; BUN: Blood Urea Nitrogen; CREA: Creatinine; FBG: Fasting Blood Glucose; HDL-C: High-density Lipoprotein Cholesterol; LDL-C: low-density lipoprotein cholesterol; Ca: Calcium; P: Phosphorus; Mg: Magnesium; L14 and L14.T: Lumber Spine Measurement; FN: Femoral Neck; TL: Thoracic and Lumbar; TLT: Telomere Length.

were used for the BMD dataset. We sought to construct an integrated GP-based kernel by utilizing a trial-and-error approach in which we fitted the best GP's kernel parameters. Our proposed modified GP-based kernel 2 provides better performance scores (accuracy: 86.12%, precision: 84.13%, recall: 89.06%, F1-score: 86.52%, and AUC: 86.13%) compared to the individual GP kernels for 5-fold CV. Notably, the Matern kernel performs poorer than all other kernels. The accuracy score reached 86.64%, while the overall performance matrix increased by 3.43-6%, indicating an improved ability to recognize osteoporosis patients correctly. The AUC value increased by 3.92-5.26%, demonstrating the superior validity of the model and discriminative power. Consistent and utile results have been obtained for all

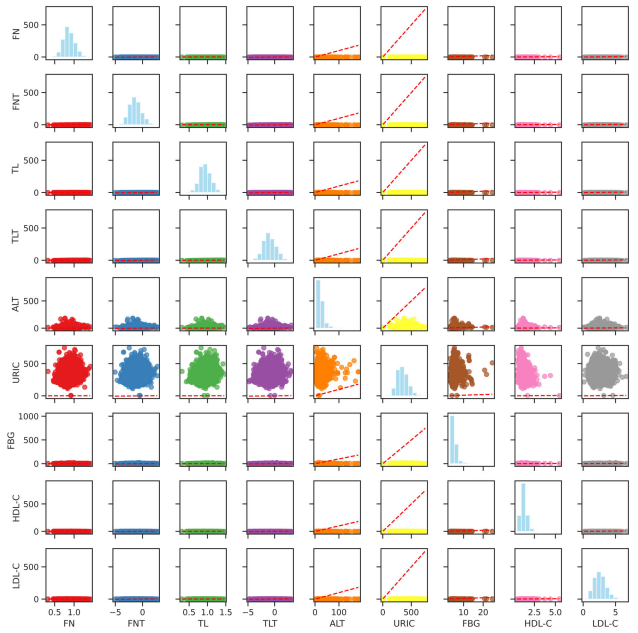


FIGURE 4. Scatter plot for continuous variables.

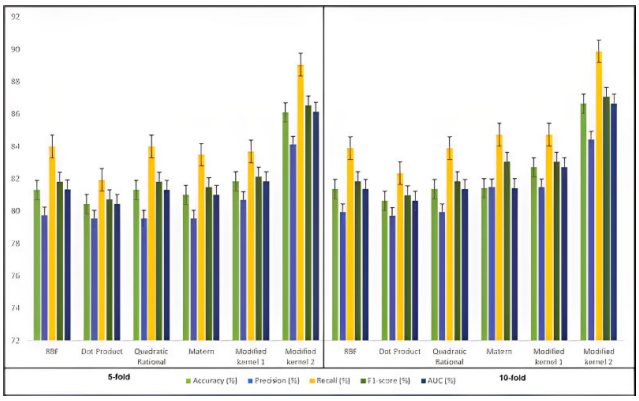


FIGURE 5. BMD dataset individual modified GP-based kernel multiple bar chart with the two protocols.

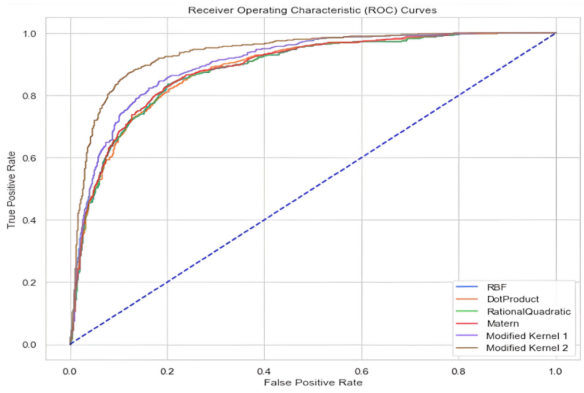


FIGURE 6. ROC curve of proposed GP-based kernels.

modified kernel performances. Detailed findings for the proposed BMD dataset performance are shown in Table 4.

Fig. 5 shows the visualization of the two proposed protocol results for the BMD dataset. However, these findings demonstrate that the proposed modified integrated GP-based kernel may be used to develop a more dependable and accurate model on the provided dataset. The ROC curve of the GP-based kernels for both individuals and integrated kernels is shown graphically in Fig. 6. In all of the distinct curves, modified kernel 1 covered nearly 83.00%, and our proposed modified kernel 2 covered nearly 87.00% of the total area. This study showed that the proposed integrated modified GP-based kernel 2 had better classification power than other individual GP-based kernels and conventional ML-based algorithms.

D. VALIDATION OF THE PROPOSED MODEL

To validate our proposed GP model, we generated simulation data using the Python sci-kit-learn library to make a classification framework 'make classification'. We generated 1,000 observations where 18 features are set up as an independent feature and one feature is a binary class target feature. We set a strategic plan by setting up 5 features informative, 3 are redundant, and 2 are repeated features to reduce noise, improve model efficiency, and generalization. We trained a GP-based model with a 5-fold and 10-fold CV for the simulated dataset and an outstanding performance score was obtained for a 10-fold CV. Especially, the GP-based model achieved 89.30% accuracy, 89.34% precision, 89.65% recall, 89.41% F1- score, and an AUC of 89.30%. Our proposed modified GP kernel outperformed individual kernels in those simulation results, demonstrating the potency of our developed model. These results demonstrated how well the integrated GP-based model handles the data and produces reliable predictions. The simulation results of the proposed GP-based framework are displayed in Table 5.

E. BENCHMARKING WITH SIMILAR EXISTING STUDIES

In this section, we assess the performance results for classifying osteoporosis patients based on potential risk factor identification with similar existing research work. There are several studies conducted to identify the prominent risk factor and classify the osteoporosis patient which is discussed in the literature review section. Table 6 provides a detail overview of the benchmarking studies with our proposed study. Shim et al. [23] conducted a study with 1792 patients and 19 possible risk factors. They used traditional LR-based backward stepwise variable selection to identify the potential risk factors. After that, these selected features are fed into seven ML-based algorithms (KNN, DT, RF, GBM, SVM, ANN, and LR) to predict osteoporosis patients. The highest AUC of 74.30% was achieved by ANN. Lin et al. [29] used two intensive statistical approaches (the chi-square test and the t-test) to identify the significant risk factors for osteoporosis patients. Despite using a parametric test, they did not take into account any assumptions about data distribution. The performance scores (accuracy: 71.70% and AUC: 70.90%) were obtained by the ANN classifier.

TABLE 4. Performance (in %) of proposed GP-based kernels performance for the BMD dataset.

Protocol	GP Kernels	Accuracy	Precision	Recall	F1-score	AUC
5-fold	RBF	81.32	79.75	84.00	81.82	81.33
	Dot Product	80.44	79.56	81.94	80.73	80.44
	Quadratic Rational	81.32	79.56	84.00	81.82	81.32
	Matern	81.01	79.55	83.49	81.47	81.01
	Modified kernel 1	81.84	80.70	83.69	82.12	81.85
	Modified kernel 2	86.12	84.13	89.06	86.52	86.13
10-fold	RBF	81.37	79.94	83.90	81.84	81.37
	Dot Product	80.65	79.72	82.35	80.98	80.65
	Quadratic Rational	81.37	79.94	83.90	81.84	81.37
	Matern	81.42	81.47	84.73	83.05	81.43
	Modified kernel 1	82.71	81.47	84.73	83.05	82.71
	Modified kernel 2	**86.64**	**84.44**	**89.88**	**87.06**	**86.63**

Bold value indicate the results of proposed method.

TABLE 5. Performance (in %) of proposed GP kernels for simulation data.

Protocol	GP Kernels	Accuracy	Precision	Recall	F1-score	AUC
5-fold	RBF	87.50	85.82	90.04	87.86	87.49
	Dot Product	77.89	78.89	77.80	78.09	77.70
	Quadratic Rational	87.50	85.82	90.04	87.86	87.48
	Matern	87.70	86.00	90.44	88.11	87.68
	Modified kernel 1	87.80	86.46	89.84	88.09	87.79
	Modified kernel 2	88.70	88.12	89.65	88.85	88.79
10-fold	RBF	87.60	86.21	90.04	87.96	87.59
	Dot Product	77.90	77.93	78.90	78.20	77.90
	Quadratic Rational	87.60	86.21	90.04	87.96	87.59
	Matern	87.80	86.25	90.64	88.22	87.78
	Modified kernel 1	87.90	86.38	90.44	88.27	87.89
	Modified kernel 2	**89.30**	**89.34**	**89.65**	**89.41**	**89.30**

Bold value indicate the results of proposed method.

TABLE 6. Several osteoporosis recognition performances (in %) compared against our proposed performance.

Author	Technique	Accuracy	AUC
Shim et al. [23]	KNN, DT, RF, GBM, SVM, ANN, LR	74.90	74.30
Lin et al. [29]	ANN, RF, LR, SVM	71.70	70.90
Huang et al. [30]	GNB, RF, LR, GBM, XGBoost, SVM	81.00	86.00
Bui et al. [31]	LoR, RF, NN, SVM	—	84.50
Bui et al. [68]	OSTA and OSTC	—	73.9
Kim et al. [24]	SVM, RF, ANN, LR, OST	76.70	82.70
Kokkotis et al. [13]	LR, SVM, NB, KNN, DT, RF, XGBoost	71.71	—
Tanphiriyakun et al. [69]	RF, GB, LR, SVM, NB, MLP, and KNN	69.00	70.00
Proposed study	**Modified GP classifier**	**86.64**	**86.63**

Bold value indicate the results of proposed method.

Huang et al. [30] used 172 CT scan images and then applied the PyRadiomics package in Python to extract the features. Two statistical tests namely the Mann-Whitney U test and the least absolute shrinkage and selection operator (LASSO) algorithm were used to reduce the dimension of the dataset. Following that, GBM achieved the greatest accuracy of 81% and AUC-ROC of 86% among the classic ML algorithms (GNB, RF, LR, GBM, XGBoost, and SVM). They utilized image data but did not employ an algorithm for handling image data, which was why information might be lost when extracting features. Bui et al. [31] introduced four ML-based algorithms (LoR, RF, NN, SVM), and finally, an AUC score of 84.50% was achieved by the RF algorithm. Bui et al. [68] performed a retrospective investigation with 797 postmenopausal Vietnamese women. They proposed two strategies (OSTA and OSTC) to anticipate osteoporosis patients. They solely employed the AUC score to compare their research, and they came up with final scores of 70.9 to 73.9 for the OSTA method and 68.7 to 71.6 for the OSTC approach. Kim et al. [24] utilized SVM, RF, ANN, LR, and the osteoporosis self-assessment tool (OST) to predict postmenopausal women's osteoporosis. SVM attained an accuracy rate of 76.7% and an AUC rate of 82.70%.

Kokkotis et al. [13] combined the use of the filter, wrapper, and embedding approaches for risk identification. Implementation of the seven ML-based algorithms (LR, SVM, NB, KNN, DT, RF, and XGBoost) and the greatest accuracy of 71.71% was obtained by LR. Tanphiriyakun et al. [69] used the RF, GB, LR, SVM, NB, MLP, and KNN classifiers after completing several pre-processing steps using a statistical technique, and RF ultimately achieved the best training accuracy of 0.69 and AUC of 0.70. Our proposed intensive statistical exploration for risk factor identification and utilization of the GP-based-kernel for osteoporosis patients' classification performed the best accuracy score of 86.64% and AUC score of 86.63%. The fact that these results were

better than those from previous studies of a similar nature highlights the effectiveness of our approach. However, our research highlights the significance of carefully analyzing statistical data and data features before using ML-based algorithms. Statistical ML-based algorithms fared better than conventional ML-based approaches in this particular context of classifying osteoporosis patients, demonstrating its promise for medical research and diagnostics.

V. CONCLUSION AND FUTURE WORK

It is challenging to early detection of risk factors in enabling prompt interventions and individualized healthcare approaches. This research improved osteoporosis patient recognition through the incorporation of intense statistical approaches with an inventive integrated GP kernel to identify risk factors and construct a prediction model. In our comprehensive evaluation, Kolmogorov-Smirnov and Shapiro-Wilk are used to check normality for the continuous variables. Then the t-test is used for normal data and others are tested by the Mann-Whitney U test. The chi-square test is used to test for categorical variables. The following variables including ALT, FBG, HDL-C, LDL-C, FN, FNT, TL, TLT, URIC, gender, calcium, calcitriol, bisphosphonate, calcitonin, COPD, CAD, and drinking identified as risk factors based on p-values ($p<0.05$) by the proposed rigorous assessment.

The proposed GP kernel 2 model boosted an upscale accuracy of 86.64% and a highly esteemed AUC of 86.63% on the proposed BMD dataset. It increased 14.94 % better performances than state-of-the-art results showcasing its superiority over traditional methods in terms of predictive power. We validate the proposed model with a simulation study to show the effectiveness of our approach, the prediction score reaches 89.30% by the proposed framework. However, in the future work plan, through the analysis of medical imaging, we ought to assess bone microarchitecture and spot anomalies. Using an extensive range of powerful deep-learning models, we can automatically learn hierarchical characteristics from images and produce accurate and reliable predictions. For a precise diagnosis, it is necessary to combine multi-modal data from different populations with radiography, clinical history, and genome-wide association studies (GWAS) in conjunction with bioinformatics.

REFERENCES

[1] B. Zhang et al., "Deep learning of lumbar spine X-ray for osteopenia and osteoporosis screening: A multicenter retrospective cohort study," *Bone*, vol. 140, Nov. 2020, Art. no. 115561.

[2] J. Smets, E. Shevroja, T. Hügle, W. D. Leslie, and D. Hans, "Machine learning solutions for osteoporosis—A review," *J. Bone Mineral Res.*, vol. 36, no. 5, pp. 833–851, 2021.

[3] N. C. Wright, A. C. Looker, K. G. Saag, J. R. Curtis, E. S. Delzell, S. Randall, and B. Dawson-Hughes, "The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine," *J. Bone Mineral Res.*, vol. 29, no. 11, pp. 2520–2526, Nov. 2014.

[4] L. Wang, J. Jiang, Y. Li, J. Huang, R. Wang, Y. Liang, C. He, and S. Liu, "Global trends and hotspots in research on osteoporosis rehabilitation: A bibliometric study and visualization analysis," *Frontiers Public Health*, vol. 10, Nov. 2022, Art. no. 1022035.

[5] A. Bhatnagar and A. L. Kekatpure, "Postmenopausal osteoporosis: A literature review," *Cureus*, vol. 14, no. 9, pp. 1–15, Sep. 2022.

[6] K. N. Tu, J. D. Lie, C. K. V. Wan, M. Cameron, A. G. Austel, J. K. Nguyen, K. Van, and D. Hyun, "Osteoporosis: A review of treatment options," *Pharmacy Therapeutics*, vol. 43, no. 2, p. 92, 2018.

[7] S.-S. Li, S.-H. He, P.-Y. Xie, W. Li, X.-X. Zhang, T.-F. Li, and D.-F. Li, "Recent progresses in the treatment of osteoporosis," *Frontiers Pharmacol.*, vol. 12, Jul. 2021, Art. no. 717065.

[8] G. Leeson, "The situation of the elderly in Denmark," *Danish Med. Bull.*, vol. 39, no. 3, pp. 220–223, 1992.

[9] M. Ali, Z. Uddin, and A. Hossain, "Prevalence and patterns of risk of osteoporosis in Bangladeshi adult population: An analysis of calcaneus quantitative ultrasound measurements," *Osteology*, vol. 1, no. 4, pp. 187–196, Oct. 2021.

[10] M. Z. Islam, A. A. Shamim, H. T. Viljakainen, M. Akhtaruzzaman, A. H. Jehan, H. U. Khan, F. A. Al-Arif, and C. Lamberg-Allardt, "Effect of vitamin D, calcium and multiple micronutrient supplementation on vitamin D and bone status in Bangladeshi premenopausal garment factory workers with hypovitaminosis D: A double-blinded, randomised, placebo-controlled 1-year intervention," *Brit. J. Nutrition*, vol. 104, no. 2, pp. 241–247, Jul. 2010.

[11] A. Sarkar, M. Z. Khan, M. M. Singh, A. Noorwali, C. Chakraborty, and S. K. Pani, "Artificial neural synchronization using nature inspired whale optimization," *IEEE Access*, vol. 9, pp. 16435–16447, 2021.

[12] H. Esmaily, M. Tayefi, H. Doosti, M. Ghayour-Mobarhan, H. Nezami, and A. Amirabadizadeh, "A comparison between decision tree and random forest in determining the risk factors associated with type 2 diabetes," *J. Res. Health Sci.*, vol. 18, no. 2, p. 412, 2018.

[13] C. Kokkotis, S. Moustakidis, G. Giakas, and D. Tsaopoulos, "Identification of risk factors and machine learning-based prediction models for knee osteoarthritis patients," *Appl. Sci.*, vol. 10, no. 19, p. 6797, Sep. 2020.

[14] M. Wang, X. Li, M. Lei, L. Duan, and H. Chen, "Human health risk identification of petrochemical sites based on extreme gradient boosting," *Ecotoxicology Environ. Saf.*, vol. 233, Mar. 2022, Art. no. 113332.

[15] H. Suresh and J. Guttag, "A framework for understanding sources of harm throughout the machine learning life cycle," in *Proc. Equity Access Algorithms, Mech., Optim.*, 2021, pp. 1–9.

[16] E. Christodoulou, J. Ma, G. S. Collins, E. W. Steyerberg, J. Y. Verbakel, and B. Van Calster, "A systematic review shows no performance benefit of machine learning over logistic regression for clinical prediction models," *J. Clin. Epidemiol.*, vol. 110, pp. 12–22, Jun. 2019.

[17] S. Karamizadeh, S. M. Abdullah, M. Halimi, J. Shayan, and M. J. Rajabi, "Advantage and drawback of support vector machine functionality," in *Proc. Int. Conf. Comput., Commun., Control Technol. (ICT)*, Sep. 2014, pp. 63–65.

[18] H. Liu, Y.-S. Ong, X. Shen, and J. Cai, "When Gaussian process meets big data: A review of scalable GPs," *IEEE Trans. Neural Netw. Learn. Syst.*, vol. 31, no. 11, pp. 4405–4423, Nov. 2020.

[19] P. S. Palar, L. R. Zuhal, and K. Shimoyama, "Gaussian process surrogate model with composite kernel learning for engineering design," *AIAA J.*, vol. 58, no. 4, pp. 1864–1880, Apr. 2020.

[20] K.-S. Lee, S.-K. Jung, J.-J. Ryu, S.-W. Shin, and J. Choi, "Evaluation of transfer learning with deep convolutional neural networks for screening osteoporosis in dental panoramic radiographs," *J. Clin. Med.*, vol. 9, no. 2, p. 392, Feb. 2020.

[21] A. Engels, K. C. Reber, I. Lindlbauer, K. Rapp, G. Büchele, J. Klenk, A. Meid, C. Becker, and H.-H. König, "Osteoporotic hip fracture prediction from risk factors available in administrative claims data—A machine learning approach," *PLoS ONE*, vol. 15, no. 5, May 2020, Art. no. e0232969.

[22] A. Faysal, N. Tanjia, T. Fannana, M. Khalil, and M. Sayed, "Treatment and diagnostic pattern of osteoporosis in Bangladesh," *Int. J. Pharmaceutical Sci. Res.*, vol. 9, no. 3, pp. 1301–1306, 2018.

[23] J.-G. Shim, D. W. Kim, K.-H. Ryu, E.-A. Cho, J.-H. Ahn, J.-I. Kim, and S. H. Lee, "Application of machine learning approaches for osteoporosis risk prediction in postmenopausal women," *Arch. Osteoporosis*, vol. 15, no. 1, pp. 1–9, Dec. 2020.

[24] S. K. Kim, T. K. Yoo, E. Oh, and D. W. Kim, "Osteoporosis risk prediction using machine learning and conventional methods," in *Proc. 35th Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. (EMBC)*, Jul. 2013, pp. 188–191.

[25] N. Yamamoto, S. Sukegawa, K. Yamashita, M. Manabe, K. Nakano, K. Takabatake, H. Kawai, T. Ozaki, K. Kawasaki, H. Nagatsuka, Y. Furuki, and T. Yorifuji, "Effect of patient clinical variables in osteoporosis classification using hip X-rays in deep learning analysis," *Medicina*, vol. 57, no. 8, p. 846, Aug. 2021.

[26] D. Devikanniga and R. Joshua Samuel Raj, "Classification of osteoporosis by artificial neural network based on monarch butterfly optimisation algorithm," *Healthcare Technol. Lett.*, vol. 5, no. 2, pp. 70–75, Apr. 2018.

[27] I. M. Wani and S. Arora, "Osteoporosis diagnosis in knee X-rays by transfer learning based on convolution neural network," *Multimedia Tools Appl.*, vol. 82, no. 9, pp. 14193–14217, Apr. 2023.

[28] T. Iliou, C.-N. Anagnostopoulos, and G. Anastassopoulos, "Osteoporosis detection using machine learning techniques and feature selection," *Int. J. Artif. Intell. Tools*, vol. 23, no. 5, Oct. 2014, Art. no. 1450014.

[29] Y.-T. Lin, C.-Y. Chu, K.-S. Hung, C.-H. Lu, E. M. Bednarczyk, and H.-Y. Chen, "Can machine learning predict pharmacotherapy outcomes? An application study in osteoporosis," *Comput. Methods Programs Biomed.*, vol. 225, Oct. 2022, Art. no. 107028.

[30] C.-B. Huang, J.-S. Hu, K. Tan, W. Zhang, T.-H. Xu, and L. Yang, "Application of machine learning model to predict osteoporosis based on abdominal computed tomography images of the psoas muscle: A retrospective study," *BMC Geriatrics*, vol. 22, no. 1, p. 796, Oct. 2022.

[31] H. M. Bui, M. H. Ha, H. G. Pham, T. P. Dao, T.-T. T. Nguyen, M. L. Nguyen, N. T. Vuong, X. H. T. Hoang, L. T. Do, T. X. Dao, and C. Q. Le, "Predicting the risk of osteoporosis in older Vietnamese women using machine learning approaches," *Sci. Rep.*, vol. 12, no. 1, p. 20160, 2022.

[32] L. He, "Bone mineral density," Harvard Dataverse, Draft Version, UNF:6: ilNdf2IE/CFSiMVCHITnNg==, 2022, doi: 10.7910/DVN/UDZIJS.

[33] P. Pietschmann, M. Rauner, W. Sipos, and K. Kerschan-Schindl, "Osteoporosis: An age-related and gender-specific disease—A mini-review," *Gerontology*, vol. 55, no. 1, pp. 3–12, 2009.

[34] S.-M. Park, J. Park, S. Han, H.-D. Jang, J.-Y. Hong, K. Han, H.-J. Kim, and J. S. Yeom, "Underweight and risk of fractures in adults over 40 years using the nationwide claims database," *Sci. Rep.*, vol. 13, no. 1, p. 8013, May 2023.

[35] J. E. Compston et al., "Relationship of weight, height, and body mass index with fracture risk at different sites in postmenopausal women: The global longitudinal study of osteoporosis in women (GLOW)," *J. Bone Mineral Res.*, vol. 29, no. 2, pp. 487–493, Feb. 2014.

[36] P. Chen, P. D. Miller, N. C. Binkley, D. L. Kendler, M. Wong, and K. Krohn, "Use of lowest single lumbar spine vertebra bone mineral density T-score and other T-score approaches for diagnosing osteoporosis and relationships with vertebral fracture status," *J. Clin. Densitometry*, vol. 11, no. 4, pp. 525–531, Oct. 2008.

[37] H. Li, T. Sun, D. Han, W. Gong, W. Mao, X. Gan, D. Shu, Q. Zhou, L. Xu, L. Hou, M. Zhou, M. Cai, and X. Lai, "Risk factors of osteoporosis in elderly inpatients: A cross-sectional single-centre study," *Frontiers Aging*, vol. 4, May 2023, Art. no. 1126172.

[38] M. Jergas and H. K. Genant, "Spinal and femoral DXA for the assessment of spinal osteoporosis," *Calcified Tissue Int.*, vol. 61, no. 5, pp. 351–357, Nov. 1997.

[39] F. Wu, Y. Huang, J. Hu, and Z. Shao, "Mendelian randomization study of telomere length and bone mineral density," *Aging*, vol. 13, no. 2, pp. 2015–2030, Jan. 2021.

[40] H. J. Do, J.-S. Shin, J. Lee, Y. J. Lee, M.-R. Kim, D. Nam, E.-J. Kim, Y. Park, K. Suhr, and I.-H. Ha, "Association between liver enzymes and bone mineral density in Koreans: A cross-sectional study," *BMC Musculoskeletal Disorders*, vol. 19, no. 1, pp. 1–13, Dec. 2018.

[41] B. K. Park, K. Y. Yun, S. C. Kim, J. K. Joo, K. S. Lee, and O. H. Choi, "The relationship between renal function and bone marrow density in healthy Korean women," *J. Menopausal Med.*, vol. 23, no. 2, pp. 96–101, 2017.

[42] J. H. Huh, S. I. Choi, J. S. Lim, C. H. Chung, J. Y. Shin, and M. Y. Lee, "Lower serum creatinine is associated with low bone mineral density in subjects without overt nephropathy," *PLoS ONE*, vol. 10, no. 7, Jul. 2015, Art. no. e0133062.

[43] L. Chen, Y. Peng, F. Fang, J. Chen, L. Pan, and L. You, "Correlation of serum uric acid with bone mineral density and fragility fracture in patients with primary osteoporosis: A single-center retrospective study of 253 cases," *Int. J. Clin. Exp. Med.*, vol. 8, no. 4, pp. 6291–6294, 2015.

[44] L.-J. Gu, X.-Y. Lai, Y.-P. Wang, J.-M. Zhang, and J.-P. Liu, "A community-based study of the relationship between calcaneal bone mineral density and systemic parameters of blood glucose and lipids," *Medicine*, vol. 98, no. 27, 2019, Art. no. e16096.

[45] D. L. Kendler, G. M. Kiebzak, C. G. Ambrose, C. Dinu, S. Robertson, P. Schmeer, and J. L. Van Pelt, "Effect of calcium tablets on interpretation of lumbar spine DXA scans," *J. Clin. Densitometry*, vol. 9, no. 1, pp. 97–104, Jan. 2006.

[46] D. Granchi, R. Caudarella, C. Ripamonti, P. Spinnato, A. Bazzocchi, A. Massa, and N. Baldini, "Potassium citrate supplementation decreases the biochemical markers of bone loss in a group of osteopenic women: The results of a randomized, double-blind, placebo-controlled pilot study," *Nutrients*, vol. 10, no. 9, p. 1293, Sep. 2018.

[47] M. Rondanelli, M. A. Faliva, A. Tartara, C. Gasparri, S. Perna, V. Infantino, A. Riva, G. Petrangolini, and G. Peroni, "An update on magnesium and bone health," *BioMetals*, vol. 34, no. 4, pp. 715–736, Aug. 2021.

[48] W.-B. Xia, Z.-L. Zhang, H.-F. Wang, X.-W. Meng, Y. Zhang, G.-Y. Zhu, X.-P. Xing, J.-L. Liu, L.-H. Wang, Y. Jiang, S.-F. Weng, T. Xu, Y.-Y. Hu, W. Yu, and J.-P. Tian, "The efficacy and safety of calcitriol and/or caltrate D in elderly Chinese women with low bone mass," *Acta Pharmacologica Sinica*, vol. 30, no. 3, pp. 372–378, Mar. 2009.

[49] S. Conway, B. Oldroyd, A. Morton, J. Truscott, and D. Peckham, "Effect of oral bisphosphonates on bone mineral density and body composition in adult patients with cystic fibrosis: A pilot study," *Thorax*, vol. 59, no. 8, pp. 699–703, Aug. 2004.

[50] C.-Y. Hsiao, T.-H. Chen, T.-H. Chu, Y.-N. Ting, P.-J. Tsai, and J.-F. Shyu, "Calcitonin induces bone formation by increasing expression of Wnt10b in osteoclasts in ovariectomy-induced osteoporotic rats," *Frontiers Endocrinol.*, vol. 11, p. 613, Sep. 2020.

[51] N. Hijazi and Z. Alourfi, "Association between hypertension, antihypertensive drugs, and osteoporosis in postmenopausal Syrian women: A cross-sectional study," *Adv. Med.*, vol. 2020, pp. 1–6, Feb. 2020.

[52] D. Inoue, R. Watanabe, and R. Okazaki, "COPD and osteoporosis: Links, risks, and treatment challenges," *Int. J. Chronic Obstructive Pulmonary Disease*, vol. 11, pp. 637–648, 2016, doi: 10.2147/COPD.S79638.

[53] B. Liu, J. Liu, J. Pan, C. Zhao, Z. Wang, and Q. Zhang, "The association of diabetes status and bone mineral density among US adults: Evidence from NHANES 2005–2018," *BMC Endocrine Disorders*, vol. 23, no. 1, pp. 1–9, Feb. 2023.

[54] P. De Angelis, E. Rella, P. F. Manicone, G. Gasparini, V. Giovannini, M. G. Liguori, F. Camodeca, G. De Rosa, C. Cavalcanti, and A. D'Addona, "The effect of hyperlipidemia on peri-implant health: A clinical and radiographical prospective study," *BioMed Res. Int.*, vol. 2023, pp. 1–8, Apr. 2023.

[55] J. W. Lee, B. C. Kwon, and H. G. Choi, "Analyses of the relationship between hyperuricemia and osteoporosis," *Sci. Rep.*, vol. 11, no. 1, p. 12080, Jun. 2021.

[56] C. Khandkar, K. Vaidya, K. K. Galougahi, and S. Patel, "Low bone mineral density and coronary artery disease: A systematic review and meta-analysis," *IJC Heart Vasculature*, vol. 37, Dec. 2021, Art. no. 100891.

[57] M. P. Duarte, H. S. Ribeiro, S. G. R. Neri, L. S. Almeida, J. L. Viana, and R. M. Lima, "Global prevalence of osteoporosis in chronic kidney disease: Protocol for a systematic review," *Kidney Dialysis*, vol. 1, no. 1, pp. 47–52, Jul. 2021.

[58] S. Yuan, K. Michaëlsson, Z. Wan, and S. C. Larsson, "Associations of smoking and alcohol and coffee intake with fracture and bone mineral density: A Mendelian randomization study," *Calcified Tissue Int.*, vol. 105, no. 6, pp. 582–588, Dec. 2019.

[59] R. Yeasmin, R. Amin, and M. S. Reza, "Effect of integrated kernel PCA function on data sampling techniques for liver disease prediction," *BAUET J*, vol. 3, no. 2, pp. 40–47, 2022.

[60] D. Elreedy and A. F. Atiya, "A comprehensive analysis of synthetic minority oversampling technique (SMOTE) for handling class imbalance," *Inf. Sci.*, vol. 505, pp. 32–64, Dec. 2019.

[61] A. Kishor and C. Chakraborty, "Early and accurate prediction of diabetics based on FCBF feature selection and SMOTE," *Int. J. Syst. Assurance Eng. Manag.*, pp. 1–9, 2021, doi: 10.1007/s13198-021-01174-z.

[62] N. M. Razali and Y. B. Wah, "Power comparisons of Shapiro-Wilk, Kolmogorov-Smirnov, Lilliefors and Anderson-Darling tests," *J. Stat. Model. Anal.*, vol. 2, no. 1, pp. 21–33, 2011.

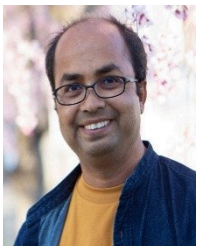
[63] J. E. Higgins and G. G. Koch, "Variable selection and generalized chi-square analysis of categorical data applied to a large cross-sectional occupational health survey," *Int. Stat. Rev./Revue Internationale de Statistique*, vol. 45, no. 1, pp. 38–51, Apr. 1977.

[64] J. Donnelly, S. Abolfathi, J. Pearson, O. Chatrabgoun, and A. Daneshkhah, "Gaussian process emulation of spatio-temporal outputs of a 2D inland flood model," *Water Res.*, vol. 225, Oct. 2022, Art. no. 119100.
[65] M. Maniruzzaman, N. Kumar, M. M. Abedin, M. S. Islam, H. S. Suri, A. S. El-Baz, and J. S. Suri, "Comparative approaches for classification of diabetes mellitus data: Machine learning paradigm," *Comput. Methods Programs Biomed.*, vol. 152, pp. 23–34, Dec. 2017.
[66] M. Maniruzzaman, M. A. M. Hasan, N. Asai, and J. Shin, "Optimal channels and features selection based ADHD detection from EEG signal using statistical and machine learning techniques," *IEEE Access*, vol. 11, pp. 33570–33583, 2023.
[67] H. K. Bhuyan, Dr. C. Chakraborty, S. K. Pani, and V. Ravi, "Feature and subfeature selection for classification using correlation coefficient and fuzzy model," *IEEE Trans. Eng. Manag.*, vol. 70, no. 5, pp. 1655–1669, May 2023.
[68] M. H. Bui, P. T. Dao, Q. L. Khuong, P.-A. Le, T.-T.-T. Nguyen, G. D. Hoang, T. H. Le, H. T. Pham, H.-X.-T. Hoang, Q. C. Le, and X. T. Dao, "Evaluation of community-based screening tools for the early screening of osteoporosis in postmenopausal Vietnamese women," *PLoS ONE*, vol. 17, no. 4, Apr. 2022, Art. no. e0266452.
[69] T. Tanphiriyakun, S. Rojanasthien, and P. Khumrin, "Bone mineral density response prediction following osteoporosis treatment using machine learning to aid personalized therapy," *Sci. Rep.*, vol. 11, no. 1, p. 13811, Jul. 2021.

RUHUL AMIN received the bachelor's degree in statistics from the Pabna University of Science & Technology (PUST), Pabna, Bangladesh, in May 2022. He joined the Deep Statistical Learning & Research Laboratory, PUST, in 2021, under the supervision of Dr. Shamim Reza. He is also working on liver disease diagnosis, handwritten digit recognition optimization, diabetes, and osteoporosis patient classification. His research interests include big data analysis, statistical learning algorithms, deep learning, health informatics, and the application of these techniques to the processing of medical images and healthcare data.

MD. SHAMIM REZA received the B.S. and M.S. degrees in statistics from Rajshahi University, Bangladesh, in 2007 and 2008, respectively, and the Ph.D. degree in natural science from the School of Mathematics, Peking University, Beijing, China, in 2019. Currently, he is an Associate Professor with the Department of Statistics, Pabna University of Science & Technology, Bangladesh. His research interests include multivariate data analysis, statistical learning algorithms, deep learning, and the application of these techniques to the processing of medical images and healthcare data.

MD. MANIRUZZAMAN received the B.Sc., M.Sc., and M.Phil. degrees in statistics from the Department of Statistics, University of Rajshahi, Rajshahi, Bangladesh, in 2013, 2014, and 2021, respectively. He is currently pursuing the Ph.D. degree with the Pattern Processing Laboratory, School of Computer Science and Engineering, The University of Aizu, Japan, under the direct supervision of Dr. Jungpil Shin. He became a Lecturer and an Assistant Professor with the Statistics Discipline, Khulna University, Khulna, Bangladesh, in September 2018 and November 2020, respectively. He has coauthored more than 40 papers published in widely cited journals and conferences. His research interests include bioinformatics, artificial intelligence, pattern recognition, medical images, signal processing, machine learning, data mining, and big data analysis.



MD. AL MEHEDI HASAN (Member, IEEE) received the B.Sc., M.Sc., and Ph.D. degrees in computer science and engineering from the Department of Computer Science and Engineering, University of Rajshahi, Rajshahi, Bangladesh, in 2005, 2007, and 2017, respectively. He became a Lecturer, an Assistant Professor, an Associate Professor, and a Professor with the Department of Computer Science and Engineering, Rajshahi University of Engineering & Technology (RUET), Rajshahi, in 2007, 2010, 2018, and 2019, respectively. Recently, he completed his postdoctoral research from the School of Computer Science and Engineering, The University of Aizu, Aizuwakamatsu, Japan. He has coauthored more than 130 publications published in widely cited journals and conferences. His research interests include machine learning, deep learning, bioinformatics, health informatics, computer vision, probabilistic and statistical inference, medical image processing, sensor-based data analysis, human computer interaction, operating system, computer networks, and security.

HYOUN-SUP LEE received the B.S., M.S., and Ph.D. degrees from Dong-Eui University, Pusan, South Korea, in 2004, 2006, and 2017, respectively. From 2012 to 2015, he was a CTO with Albam Company Ltd. Since 2014, he has been a Professor with the Department of Application Software Engineering, Dong-Eui University. His research interests include big data, data analysis, and artificial intelligence.

SI-WOONG JANG received the B.S., M.S., and Ph.D. degrees from Pusan National University, Pusan, South Korea, in 1984, 1993, and 1996, respectively. From 1986 to 1993, he was a Research Worker with Daewoo Telecom Company Ltd. Since 1996, he has been a Professor with the Department of Computer Engineering, Dong-Eui University, South Korea. His research interests include image processing, artificial intelligence, and the IoT.

JUNGPIL SHIN (Senior Member, IEEE) received the B.Sc. degree in computer science and statistics and the M.Sc. degree in computer science from Pusan National University, South Korea, in 1990 and 1994, respectively, and the Ph.D. degree in computer science and communication engineering from Kyushu University, Japan, in 1999, under a scholarship from the Japanese Government (MEXT). He was an Associate Professor, a Senior Associate Professor, and a Full Professor with the School of Computer Science and Engineering, The University of Aizu, Japan, in 1999, 2004, and 2019, respectively. He has coauthored more than 350 published papers for widely cited journals and conferences. His research interests include pattern recognition, image processing, computer vision, machine learning, human–computer interaction, non-touch interfaces, human gesture recognition, automatic control, Parkinson's disease diagnosis, ADHD diagnosis, user authentication, machine intelligence, handwriting analysis, recognition, and synthesis. He is a member of ACM, IEICE, IPSJ, KISS, and KIPS. He served as the program chair and as a program committee member for numerous international conferences. He serves as an Editor for IEEE journals, Springer, Sage, Taylor & Francis, *Sensors* (MDPI), *Electronics* (MDPI), and *Tech Science Press*. He serves as a reviewer for several major IEEE and SCI journals.