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Original Article

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Evaluation of vascular, pathologic, demographic and radioanatomic characteristics of hypertensive patients by conventional angiography

Abstract

Aim: Hypertension is a widespread cardiovascular disease and a major risk factor for heart conditions. This study aimed to identify vascular, pathological, demographic, and radioanatomical differences between hypertensive patients undergoing conventional coronary angiography and healthy individuals, using Machine Learning (ML) algorithms.
Materials and Methods: A retrospective analysis was conducted on coronary angiography images from 109 hypertensive patients (Group 1) and 96 healthy individuals (Group 2), aged 20–80 years. Diameters of the proximal, middle, crux, distal, posterolateral (PL), and posterior descending (PD) branches of the right coronary artery (RCA) were measured with right anterior oblique (RAO) cranial projection. Measurements of the left coronary artery (LMCA), proximal anterior interventricular artery (LAD), and proximal circumflex artery (CX) were obtained using left anterior oblique (LAO) caudal projection. Selected biochemical parameters were also retrieved from the hospital archive.
Results: ML algorithms achieved hypertension prediction accuracies ranging from 0.73 to 0.85. SHAP analysis of the Random Forest (RF) model indicated that the PL branch of the RCA had the greatest radioanatomical impact, while estimated glomerular filtration rate (eGFR) was the most significant biochemical predictor.
Conclusion: The findings demonstrate that hypertension can be predicted with high accuracy by combining coronary artery diameter measurements with biochemical parameters through ML algorithms. This integrative approach highlights the potential of modern computational methods in cardiovascular risk assessment.

Keywords: Hypertension, conventional angiography, coronary artery diameter, machine learning algorithms

INTRODUCTION

Hypertension is defined as having a systolic blood pressure of at least 140 mmHg and/or a diastolic blood pressure of at least 90 mmHg. It has been demonstrated that this constitutes a significant risk factor for the development of cardiovascular diseases (CVD). Hypertension is the most common and treatable cause of myocardial infarction, heart failure, aortic dissection, stroke, chronic renal failure and peripheral vascular disease. However, it is also a chronic disease with a high mortality rate due to the severe complications it causes (1).

In 1959, coronary angiography was first performed by Mason Sones. After this date, the coronary angiographic method has developed rapidly since then. With these developments, coronary angiography has been accepted as the gold standard for visualization of coronary arteries (2). MacAlpin et al. In their 1973 study published under the title "Human coronary artery size during life", MacAlpin et al. measured normal coronary artery diameters using coronary angiography technique for the first time (3). In left ventricular hypertrophy caused by a pathologic condition such as hypertension, it has been reported in angiographic studies that the mass of the left ventricle increases and that epicardial coronary artery diameters also increase. It has also been reported that coronary artery diameters vary between populations (4,5).

Hypertension is a disease that increases with age, causes hypertrophy of cardiac vessels, has a population-specific character and causes differences in blood biochemical parameters. The general pathophysiology is the inability of the kidney to excrete sodium at normal blood pressure. Glomerular filtration rate (eGFR) is therefore an important biomarker. Then endocrine factors, central nervous system disorders, vascular disorders, genetic factors can be shown. The first diagnosis is generally made with automated blood pressure measuring instruments. In treatment, an approach protocol should be applied according to the cause of hypertension in the individual (6,7).

Machine learning (ML) algorithms are a sophisticated form of data analysis technique that facilitates the automated construction of predictive models through the utilisation of algorithms that enable machines to acquire knowledge from data. It is a modern classifier widely used in engineering and has been gradually integrated in healthcare (8). ML can be used in many important health problems such as forensic identification, early disease prediction, improvement of medical diagnosis protocols (8,9).

The objective of the present study was to analyze the vascular, pathological, demographic and radioanatomical changes between hypertensive patients undergoing conventional coronary angiography and healthy individuals using ML algorithms, a current methodology in the healthcare field.

MATERIALS AND METHODS

This study was performed with the decision number 1388 of Karabük University Non-Interventional Local Ethics Committee (Approval date: May 16, 2023). It was performed by retrospectively evaluating the coronary angiography images of 205 subjects between the ages of 20 and 80 years who conducted to the Cardiology Outpatient Clinic of Medikar Hospital for a variety of reasons and undertook diagnostic coronary angiography between 2019 and 2023. Among the 205 participants, 109 were identified as having hypertension (Group 1), while 96 were cardiovascular disease-free individuals admitted to the cardiology department for various reasons (Group 2). Hypertension was defined according to the 2018 European Society of Cardiology/ European Society of Hypertension (ESC/ESH) guidelines as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, measured during clinical evaluation. In addition, individuals with a documented physician diagnosis of hypertension or those receiving antihypertensive treatment were classified as hypertensive. Exclusion criteria included irregular coronary artery anatomy, insufficient artery segments for measurement, and a history of bypass or other cardiac surgeries. Conventional angiography images were acquired using a General Electric Innova system.The arteria femoralis was preferred as the angiographic access site. Isoosmolar 350mh/200ml was used as contrast medium and 5-8 cc of contrast medium was injected in each coronary injection.

Image processing

Image scans were conducted on images acquired between 2019 and 2023. These images, stored in Digital Imaging and Communications in Medicine (DICOM) format, were transferred to a Windows-based personal workstation using the RadiAnt DICOM Viewer software. The diameter sizes of the proximal, middle, crux, distal, posterolateral (PL), and posterior descending (PD) branches of the right coronary artery (RCA) were measured using right anterior oblique (RAO) cranial imaging (Figure 1).

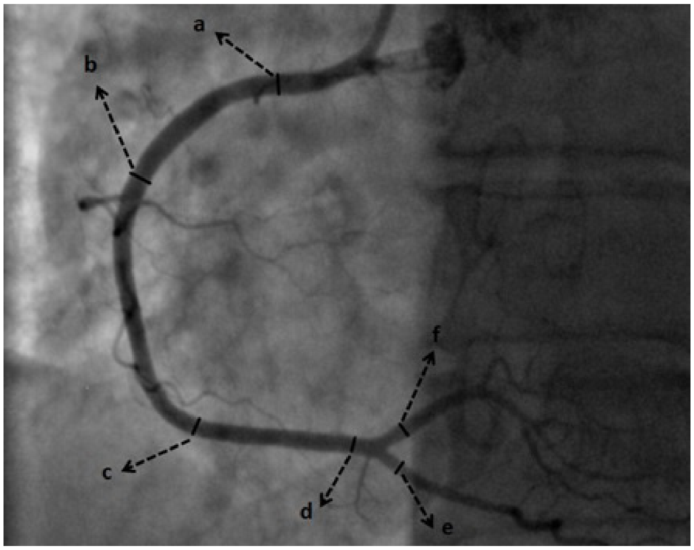

Figure 1. Measurement demonstration of A. coronaria dextra (a: RCA Proximal, b: RCA Middle, c: RCA Crux, d: RCA Distal, e: PD, f:PL).

Using images acquired through the left anterior oblique (LAO) caudal projection, left coronary artery (LMCA), anterior interventricular artery (LAD) proximal, circumflex artery (CX) proximal diameter measurements were made (Figure 2).

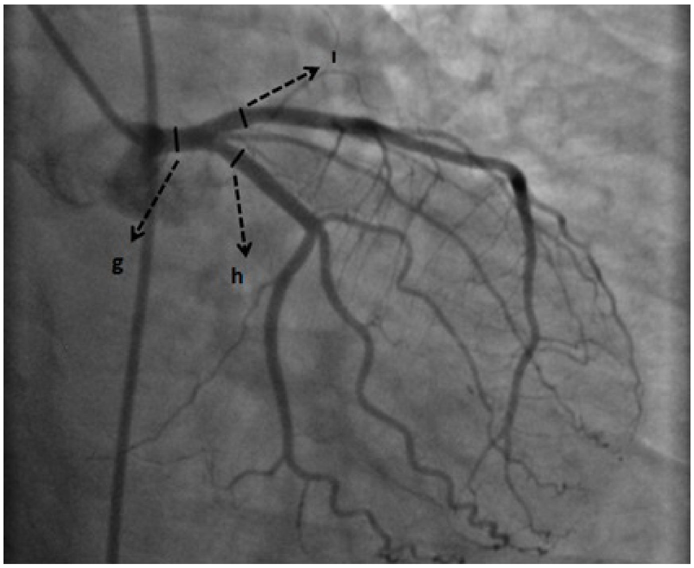

Figure 2. Measurement demonstration of a. coronaria sinistra (g: LMCA, h: CX Proximal, i: LAD Proximal)

Biochemistry parameters;

In this study, patients' laboratory results—including glucose, sodium, potassium, calcium, creatinine, low-density lipoprotein (LDL), high-density lipoprotein (HDL), blood urea nitrogen (BUN), alanine aminotransferase (ALT), aspartate transaminase

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(AST), eGFR, triglycerides, total cholesterol and C-reactive protein (CRP) data were obtained from the hospital records and entered into an Excel database.

Machine Learning Algorithms

In this study, various ML algorithms were employed, including linear discriminant analysis (LDA), logistic regression (LR), quadratic discriminant analysis (QDA), decision tree (DT), random forest (RF), extra trees classifier (ETC), and k-nearest neighbors (k-NN), Gaussian naive Bayes (GaussianNB). Scikit-learn version 1.1.1 framework and Python version 3.9 programming language were used in ML modeling. Modeling was done using a computer with Monster Abra A7 V12.5 containing 8 GB of RAM and i5 processor. In ML modeling, the training set was determined as 80% and the test set was 20%. While 24 parameters created the input, inclusion in Group 1 and Group 2 was determined as the output. The performance criteria employed in this study included accuracy (Acc), specificity (Spe), sensitivity (Sen) and the F1 score (F1) (Equation 1).

$$Acc = \frac{TP}{TP + FN + FP + TN}$$

$$\text{Sen} = \frac{TP}{TP+FN}$$

$$\text{Spe} = \frac{TN}{TN+FP}$$

$$\text{F1} = 2\frac{Spe \times Sen}{Spe + Sen}$$

Equation 1. TP; True positive, TN; True negative, FP; False positive, FN; False negative

Statistical Analysis

The Anderson-Darling test was employed to ascertain the normality of the parameters. In the context of descriptive statistics, the mean and standard deviation were employed for data sets that conformed to a normal distribution. Conversely, for data sets that did not comply with a normal distribution, the median, minimum, and maximum values were utilised. The associations between groups and the strength of these relationships were assessed using the Pearson correlation test for normally distributed data and the Spearman's rho test for non-normally distributed data. Basic statistical analyses were conducted using the Minitab 17 software package.

RESULTS

Demographic Findings

The mean ages of female and male subjects in Group 1 were 68.39 ± 9.91 and 69.15 ± 10.14 years, respectively, whereas in Group 2 they were 59.48 ± 11.29 and 55.32 ± 11.83 years. A statistically significant difference in age distribution was observed between the groups ($p<0.05$).

Radioanatomic Findings and Biochemistry Findings

In this study, which was conducted on conventional angiography images and blood parameters of 109 individuals in group 1 and 96 individuals in group 2, it was found that the RCA proximal, LAD proximal and potassium parameters measured followed the normal distribution, while all other parameters did not comply with the normal distribution. Descriptive statistics of parameters complying with normal distribution are displayed in Table 1.

Table 1. Descriptive statistics of parameters complying with normal distribution

Parameters (unit)	Group	Mean ± Standard deviation
RCA proximal (mm)	1	2.17 ± 0.49
	2	2.01 ± 0.48
LAD proximal (mm)	1	2.63 ± 0.48
	2	2.53 ± 0.1
Potassium (mmol/l)	1	4.53 ± 0.56
	2	4.43 ± 0.47

RCA: A.coronaria dextra, LAD: A. interventricularis anterior. Group 1: Hypertensive patients, Group 2: Healthy individuals

The descriptive statistics pertaining to the radioanatomical parameters that demonstrate deviations from normality are delineated in Table 2.

Table 2. Descriptive statistics of radioanatomical parameters that do not comply with normal distribution

Parameters (unit)	Group	Median (Minimum- Maximum)
RCA middle (mm)	1	2.55 (1.70-4.52)
	2	2.59 (1.32-4.77)
RCA crux (mm)	1	2.11 (1.21-3.73)
	2	1.97 (1.20-4.01)
RCA distal (mm)	1	2.05 (1.13-3.32)
	2	1.68 (0.91-3.03)
PL (mm)	1	1.48 (0.82-2.63)
	2	1.25 (0.61-2.21)
PD (mm)	1	1.41(0.89-2.45)
	2	1.27 (0.10-2.19)
LMCA (mm)	1	3.33 (1.89-4.91)
	2	3.22 (2.32-5.41)
CX proximal (mm)	1	2.45 (1.23-3.62)
	2	2.49 (1.66-4.27)

RCA: A. coronaria dextra, PL: Postero lateral, PD: Posterior descending, LMCA: A. coronaria sinistra, BUN: Blood urea nitrogen, CX proximal: Proximal circumflex artery. Group 1: Hypertensive patients, Group 2: Healthy individuals

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Descriptive statistics of biochemical parameters that do not follow a normal distribution are displayed in Table 3.

Table 3. Descriptive statistics of biochemical parameters that do not comply with normal distribution

Parameters (unit)	Group	Median (Minimum- Maximum)
Glucose (mg/dl)	1	125.00 (77.00-495.00)
	2	113.00 (73.00-453.00)
Sodium (mmol/l)	1	138.00 (130.00-145.00)
	2	138.00 (34.00-147.00)
BUN (mg/dl)	1	18.00 (10.00-42.00)
	2	15.00 (7.00-33.00)
LDL (mg/dl)	1	111.00 (21.00-212.00)
	2	117.50 (54.00-265.00)
HDL (mg/dl)	1	47.00 (25.00-129.00)
	2	40.75 (18.00-74.00)
Creatinine (mg/dl)	1	0.92 (0.48-2.04)
	2	0.87 (0.53-1.64)
Calcium (mg/dl)	1	9.30 (7.50-10.60)
	2	9.30 (8.10-30.00)
AST (U/L)	1	23.00 (9.00-156.00)
	2	21.50 (11.00-81.00)
ALT (U/L)	1	17.00 (5.00-81.00)
	2	21.00 (8.00-99.00)
EGFR (ml/dk)	1	75.00 (27.90-113.10)
	2	94.20 (44.20-128.60)
Triglyceride (mg/dl)	1	150.00 (52.00-731.00)
	2	147.50 (45.00-612.00)
CRP (mg/dl)	1	5.30 (0.10-325.70
	2	3.90 (0.10-192.40)
Total cholesterol (mg/dl)	1	174.00 (86.00-329.00)
	2	189.50 (108.00-316.00)

BUN: Blood urea nitrogen, LDL: Low density lipoprotein, HDL: High density lipoprotein, AST: Aspartate transaminase, ALT: Alanine aminotransferase, EGFR: Glomerular filtration rate. CRP: C-reactive protein. Group 1: Hypertensive patients, Group 2: Healthy individuals

The ML algorithms applied to parameters from Group 1 and Group 2 revealed that the LDA algorithm achieved the highest hypertension prediction accuracy of 0.85. Accuracy rates for the other algorithms ranged from 0.73 to 0.83 (Table 4).

The ROC curve of the LDA algorithm with the highest accuracy is shown in Figure 3.

The confusion matrix table of the LDA algorithm with the highest accuracy is shown in Figure 4. According to the LDA algorithm, 20 out of 23 patients who were hypertensive were predicted correctly. Of the 18 non-hypertensive individuals, 15 were predicted correctly.

The effect of the parameters on the outcome was evaluated using the SHAP analyzer of the RF algorithm, and it was determined that the highest contribution from the radioanatomical parameters was provided by PL, and from the biochemical parameters, eGFR had the highest contribution (Figure 5). Since the SHAP analyzer presents the 20 features with the highest contribution, parameters with relatively low importance values—such as RCA Crux, glucose, and total cholesterol were not included in the top 20 SHAP importance ranking and therefore were not visualized in the figure.

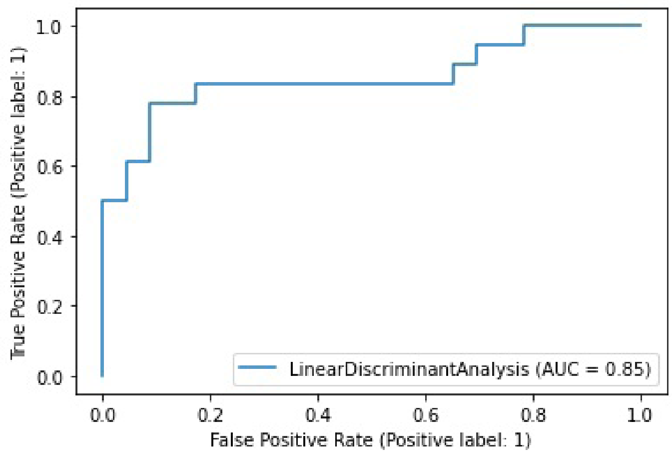

Figure 3. ROC curve of the LDA algorithm

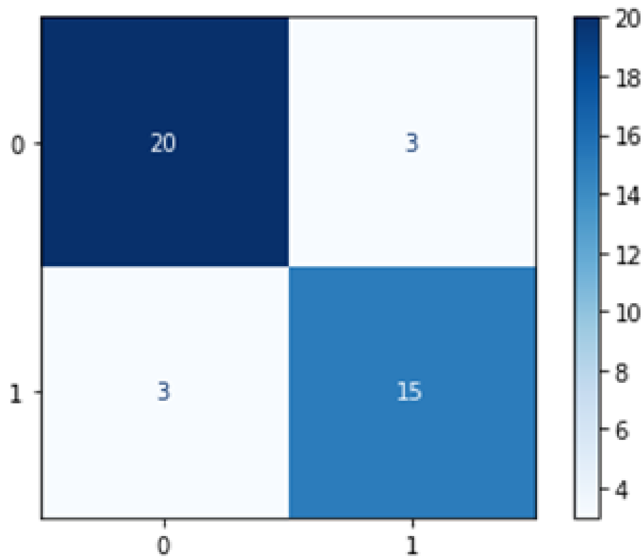

Figure 4. Confusion matrix table of the LDA algorithm

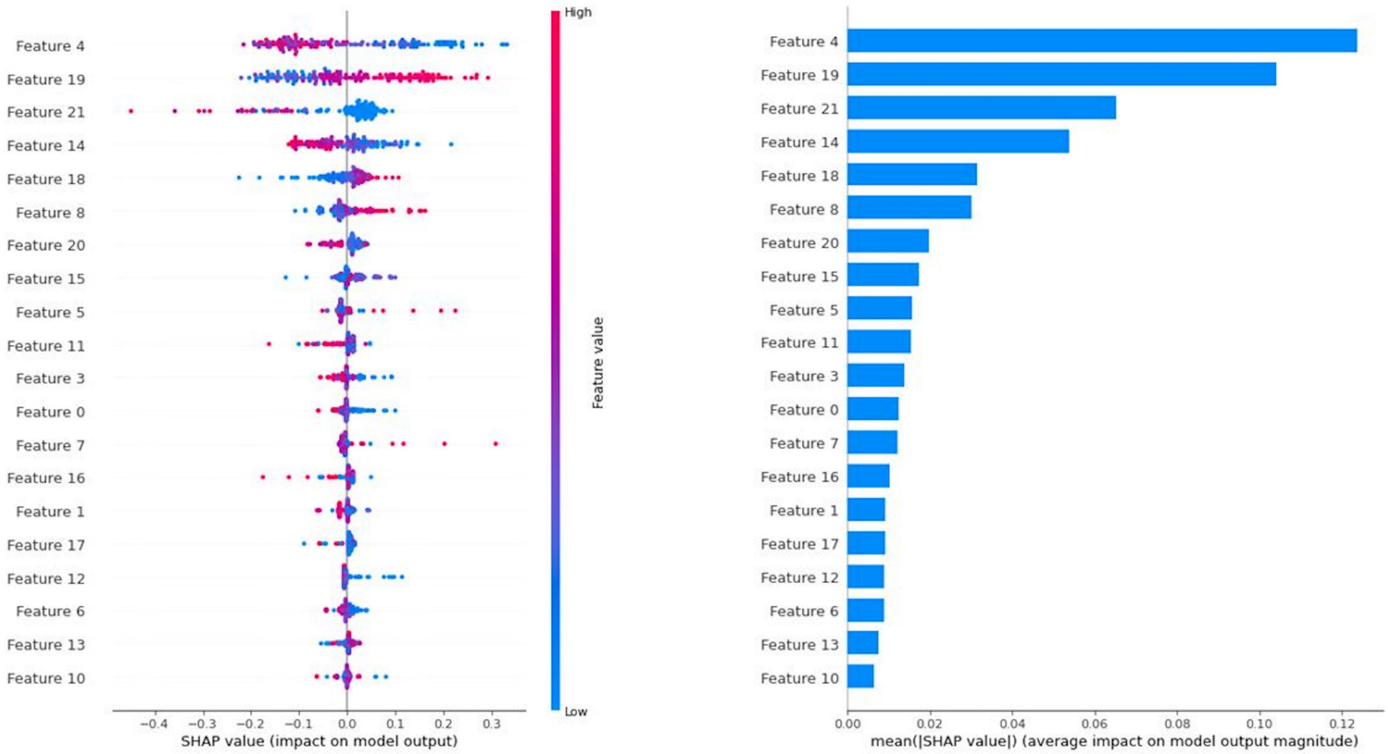

Figure 5. SHAP analyzer (Feature 0: RCA proximal, 1: RCA middle, 2: RCA crux, 3: RCA distal, 4: PL, 5: PD, 6: LMCA, 7: LAD proximal, 8: CX proximal, 9 : Glucose, 10: Sodium, 11: Potassium, 12: BUN, 13: LDL, 14: HDL, 15: Creatinine, 16: Calcium, 17: AST, 18: ALT, 19: eGFR, 20: Triglyceride, 21: CRP, 22: Total cholesterol)

Table 4. Performance criterion results of ML algorithms

Algorithms	Acc	Spe	Sen	F1 Score
LDA	0.85	0.85	0.85	0.85
LR	0.83	0.83	0.83	0.83
ETC	0.80	0.80	0.81	0.80
QDA	0.78	0.78	0.77	0.78
k-NN	0.78	0.80	0.78	0.78
RF	0.76	0.76	0.76	0.76
GaussianNB	0.76	0.77	0.76	0.76
DT	0.73	0.73	0.73	0.73

LDA: Linear discriminant analysis, LR: Logistic regression, ETC: Extra trees classification, QDA: Quadratic discriminant analysis, k-NN: k- nearest neighbor regression, RF: Random Forest, Gaussian NB: Gaussian Naïve Bayes, DT: Decision tree, Acc: accuracy, Spe: specificity, Sen: sensitivity

DISCUSSION

In this study, ML algorithms LDA, QDA, LR, RF, DT, ETC, Gaussian NB, k-NN methods were used to detect vascular, pathological and radioanatomical changes in hypertensive patients and healthy individuals who underwent conventional coronary angiography. As a result of transferring the obtained data to the algorithm, the highest hypertension prediction accuracy rate of 0.85 was obtained with the LDA method. In addition, the data were ranked in terms of the effects of the RF algorithm on the accuracy rate with the help of the SHAP analyzer. Among the available data, the radioanatomical parameter PL and the biochemical parameter eGFR were found to have the highest effect on the accuracy rate.

Coronary artery diameters may vary between populations due to ethnic and racial factors. This variation may also be due to hypertension, which is a pathologic condition. In left ventricular hypertrophy caused by hypertension, the mass of the left ventricle increases and coronary artery diameters may also increase (4,5). Hypertensive individuals may also have differences in blood parameters. Parameters such as eGFR, CRP, Triglycerides, Uric acid, Cholesterol may vary in the presence of hypertension (10-14).

Dodge et all. (15) reported that there were differences in the branches in the lower segments of the RCA compared to normal individuals in a study conducted in hypertensive individuals. In our study, we found that PL and PD, the subsegment branches of the RCA, and CX, the branch of the LMCA, had a high contribution to the identification of hypertensive patients according to the ML algorithm. We suggest that PD and PL, which are sub-segment branches of the RCA, and CX, which are branches of the LMCA, may cause differences in coronary arteries in hypertensive individuals compared to normal individuals in case of hypertension pathology.

eGFR is a blood value that indicates the glomerular filtration function of the kidney. It can be defined as a condition in which the glomerular filtration rate is permanently reduced enough to cause detectable changes in kidney function. This usually occurs when the filtration rate falls below 25 ml/min. In patients diagnosed with hypertension, renal function is evaluated both at diagnosis and during follow-up. The most reliable assessments are derived from measurements of glomerular filtration rate (GFR) and urinalysis, which reflect the flow rate of filtered fluid through the kidneys (7). In kidney diseases, the number of glomeruli decreases, but since the filtration demand remains the same, the blood flow per glomerulus increases, which may lead to hypertension due to hyperfiltration (16). eGFR is commonly utilized to evaluate kidney function, and declines in eGFR have been linked to the advancement of renal failure (17,18). In a study in the literature, it was reported that the occurrence of hypertension pathology in postoperative renal patients was associated with eGFR level (18). Hypertension has also been reported to decrease eGFR levels, and this decrease increases the risks associated with hypertension (19-21). In a study, multivariate LR analysis revealed a decrease in eGFR values in the presence of diabetes and hypotension (1,22). The relationship between hypertension and GFR is considered bidirectional in the literature. A decrease in GFR may contribute to the development of hypertension through mechanisms such as sodium retention and changes in renal hemodynamics, while long-term hypertension can also cause structural and functional damage to the renal vessels and glomeruli, leading to hypertensive nephropathy and a progressive decrease in renal filtration capacity. Therefore, hypertension and renal dysfunction can mutually exacerbate each other during the progression of the disease. In our study, eGFR was identified by ML algorithms as the biochemical parameter with the greatest contribution to predicting hypertension among the parameters analyzed, which supports our findings.

CRP is a type of acute phase reactant and the most important one. It expresses circulating cytokine functions and detects the level of interleukin-6. It is recognized as a risk marker for CVD. CRP levels have been reported to be elevated in coronary artery diseases. It has been found that circulating CRP levels in myocardial infarction are correlated with each other (23-26). During recent years, several studies have indicated a positive correlation between hypertension and CRP levels (27). Blood pressure has been shown to be related to CRP even in individuals who are prehypertensive according to the Joint National Comitee VII classification (27-29). CRP levels in hypertensive patients have also been associated with the development of vascular disease (13). In a study conducted in hypertensive patients, CRP level was found to be high. CRP level was found to be significant in hypertensive patients with both hypertension and diabetes ($p<0.01$) (26). Another study demonstrated that increased CRP levels above 3 mg/L, along with higher blood pressure categories, independently predicted the risk of future cardiovascular events. Additionally, CRP provided added prognostic information across all blood pressure ranges. Considerable evidence supports a link between hypertension and inflammation, with cross-sectional human studies demonstrating a correlation between CRP levels and blood pressure (23). In our study, CRP was the second biochemistry parameter in predicting hypertension disease after eGFR. We concluded that elevated CRP has an important place among the determinants of CVD. The main limitation of this study is the lack of diverse ethnic populations.

Limitations

Retrospective design may introduce selection bias and information bias. The study is a single-center study conducted at a single tertiary cardiology center. Therefore, the findings may not be fully generalizable to other populations or healthcare settings. Since all participants underwent diagnostic coronary angiography, there is potential for angiography-based selection bias. The study population does not represent the general healthy population, but rather individuals referred for cardiac evaluation.

CONCLUSION

The study found that the highest radioanatomical contribution to the prediction of hypertension was provided by the PL branch of the RCA and the highest biochemical contribution was provided by eGFR. We believe that this result will contribute to early diagnosis and early treatment of hypertension in clinical sciences.

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Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that there is no financial support.

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Ethical Approval

The study protocol received approval from the Karabük University Non-Interventional Local Ethics Committee (Approval date: May 16, 2023, Decision No: 1388).

Patient Consent

This study is retrospective and was conducted using existing archives. Therefore, an informed consent form is not required.

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