Prediction of major adverse cardiac events in patients with multivessel coronary artery disease with an interpretable classification tree model based on coronary computed tomography angiography

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DOI: 10.33963/v.kp.98352

Received:
August 17, 2023

Accepted:
November 29, 2023

Early publication date:
December 21, 2023

INTRODUCTION

Cardiovascular diseases (CVD), the prevailing cause of death, contribute to almost one-third of all deaths around the world [1]. In 2030 CVD would cause more than 23 million deaths worldwide [2]. Patients with multivessel coronary artery disease (MVD) are particularly important due to their increased risk of acute coronary syndrome and sudden cardiac death [3]. According to our knowledge, currently there is no simple predictive model determining the occurrence of a major adverse cardiac event (MACE; cardiac death, myocardial infarction or unstable angina, stroke) during one year of follow-up in patients with MVD diagnosed by coronary computed tomography angiography (CCTA). Therefore, the aim of the study was to create a simple algorithm for the population of MVD patients that enables the risk estimation of MACE based solely on CCTA.

METHODS

Study population

We conducted a two-stage study in order to develop and test our model. In the first stage, 106 participants were enrolled after a hospitalization in the Cardiology Department of the Central Clinical Hospital in Lodz during the period 2020–2021. All the patients had MVD confirmed by invasive coronary angiography (ICA) after CCTA. Eligible patients were ≥18 years old, diagnosed with stable coronary artery disease (CAD) according to the European Society of Cardiology (ESC) guidelines [4]. Exclusion criteria were defined as permanent atrial fibrillation, acute coronary syndrome or stroke within the last 3 months.

In the second stage our model was validated using test external data to assess its reliability. For this purpose we collected another 52 CCTA records from patients admitted to the same department in 2022. The inclusion and exclusion criteria were the same. The only analyzed diagnostic method was CCTA. During follow-up, the specialist Heart Team classified patients into an appropriate treatment option of revascularization or conservative treatment taking into account patients' overall clinical condition and preferences as well as the ESC Guidelines.

The study complied with the Declaration of Helsinki and was approved by the local medical ethics committee. All the patients provided written informed consent prior to their participation in the study.

Analyzed parameters

All data collected from 106 patients was tested for correlation with the occurrence of MACE during one-year follow-up. A direct interview with each study participant or their family and medical data from one-year follow-up were the basis for the analysis. Survival data were based on the status in the central register of citizens.

CCTA was conducted on an outpatient basis in various computed tomography laboratories in the city of Lodz using iodine contrast agent and different at least 64-slice resolution CT scanners. Significant stenosis of the coronary artery was defined by the CCTA described as significant, critical, severe or >70% narrowing of the coronary artery lumen. Coronary artery calcium score was also measured in each CT scan.

ICA examinations were performed by one hemodynamic team. Significant stenosis of the coronary artery in ICA was defined as >50% narrowing in the left main (LM) coronary artery and >70% narrowing in the rest of the epicardial arteries [5]. ICA was performed ≤6 months after the CCTA on the same patient.

Prediction algorithm

After the first study stage a classification tree model was generated using the Classification and Regression Tree Algorithm based on the CT variables. Gini split criterion was used. Our dataset was evaluated using 5-fold cross-validation to assess the optimal tree depth. We revealed that the optimal depth of the tree is two (mean accuracy: 88% for the training dataset; 85% for the test dataset; Supplementary material, *Figure S1*). With increasing tree depth, the training dataset accuracy rose, however, the evaluated dataset accuracy declined, as an example of data overfitting.

Statistical analysis

The classification tree performance was assessed using the test cohort collected in the second stage of the study. Receiver operating characteristic (ROC) curve was also calculated. Demographic and laboratory data were analyzed as follows. The normality of continuous variable distribution was assessed using the Shapiro–Wilk test along with the evaluation of histograms. Numerical variables were presented using the mean with SD or median with interquartile range (IQR), qualitative variables were presented as numbers with an appropriate percentage. *P*-value <0.05 was considered statistically significant. Univariate logistic regression was applied to further compare the influence of factors on the risk of MACE. The results of the logistic regression are presented as odds ratio (OR) with a 95% confidence interval (95% CI). All calculations were carried out in Python 3.11 with the Scikit-learn 1.2.2 package for constructing the classification tree.

RESULTS AND DISCUSSION

Figure 1A illustrates the algorithm that was created using the cohort of the first study stage. The parameter with the greatest significance in the MACE classification was the presence of LM significant stenosis. The second parameter with slightly lower significance was the presence of left anterior descending artery (LAD) significant stenosis.

The assessment of the second study stage cohort using the same classification tree demonstrated an accuracy of 84.5%, with a sensitivity of 80.0% and specificity of 86.5%, confirming that our algorithm exhibits a similar effectiveness on the external data. The confusion matrix in our second stage cohort is presented in Figure 1B.

Therefore, we propose a classification tree model which is simple to interpret (Figure 1C). The model is based solely on the LM significant stenosis as the first algorithm step, and the LAD significant stenosis as the second algorithm step. Despite its simplicity, the model accuracy was 87.7%, with sensitivity 71.4% and specificity 91.7% on our training data with the area under the receiver operating characteristic curve: 0.86 (95% CI, 0.80–0.92).

The first study group was predominantly male (n = 69.8%). The average age of the study population was 69.42 (8.28) years, and the mean body mass index: 27.91 (4.44) kg/m^2. Chronic heart failure, chronic kidney disease and diabetes mellitus type 2 were diagnosed in 52.8%, 18.9% and 35.8% of the group, respectively. The detailed characteristics are presented in Supplementary material, *Tables S1* and *S2*.

Other features that influence the risk of MACE in patients with MVD, in addition to the CCTA stenosis described above, are as folows: presence of heart failure (odds ratio [OR], 3.6; 95% CI, 1.20–10.71; *P* = 0.02), elevated creatinine level (OR, 2.81; 95% CI, 1.23–6.37; *P* = 0.01), elevated N-terminal pro-B-type natriuretic peptide level (OR, 1.77; 95% CI, 1.13–2.76; *P* = 0.01), elevated troponin level (OR, 4.52; 95% CI, 1.81–11.28; *P* = 0.001), history of COVID-19 infection (OR, 3.37; 95% CI, 1.04–10.90; *P* = 0.04) and the history of myocardial infarction (OR, 6.85; 95% CI, 2.12–22.13; *P* = 0.001). The detailed characteristics are presented in Supplementary material, *Table S3*.

Stenosis of the LM is a significant cause of stenocardia in patients with CAD [6]. Based on many current studies that prove the LM stenosis to be an independent indicator of an increased morbidity and mortality among patients with CAD [7, 8], the algorithm we developed may be an efficient tool for predicting the risk of MACE in patients with MVD.

CCTA is gaining in importance. According to the study by Rudziński et al. [9] which evaluated the long-term efficacy and safety of CCTA vs. ICA as the first-line imaging test in stable patients with a high clinical probability of obstructive CAD, no significant differences were found between both methods in MACE occurrence or long-term safety.

Study limitations

The study was conducted as a single-center retrospective study with a relatively small group of participants. All of these factors may lead to an increased risk of selection bias and accidental findings in relation to the factors correlating with the study endpoint.

CONCLUSIONS

Summarizing, we created the classification tree to predict the risk of MACE in patients with MVD in one-year observation. If confirmed on a larger sample size, these findings may provide an interpretable tool for the risk stratification of MACE using only CCTA results. In our study the significant stenosis of the LM and the LAD are the most statistically significant factors associated with a one-year risk of MACE in patients with MVD.

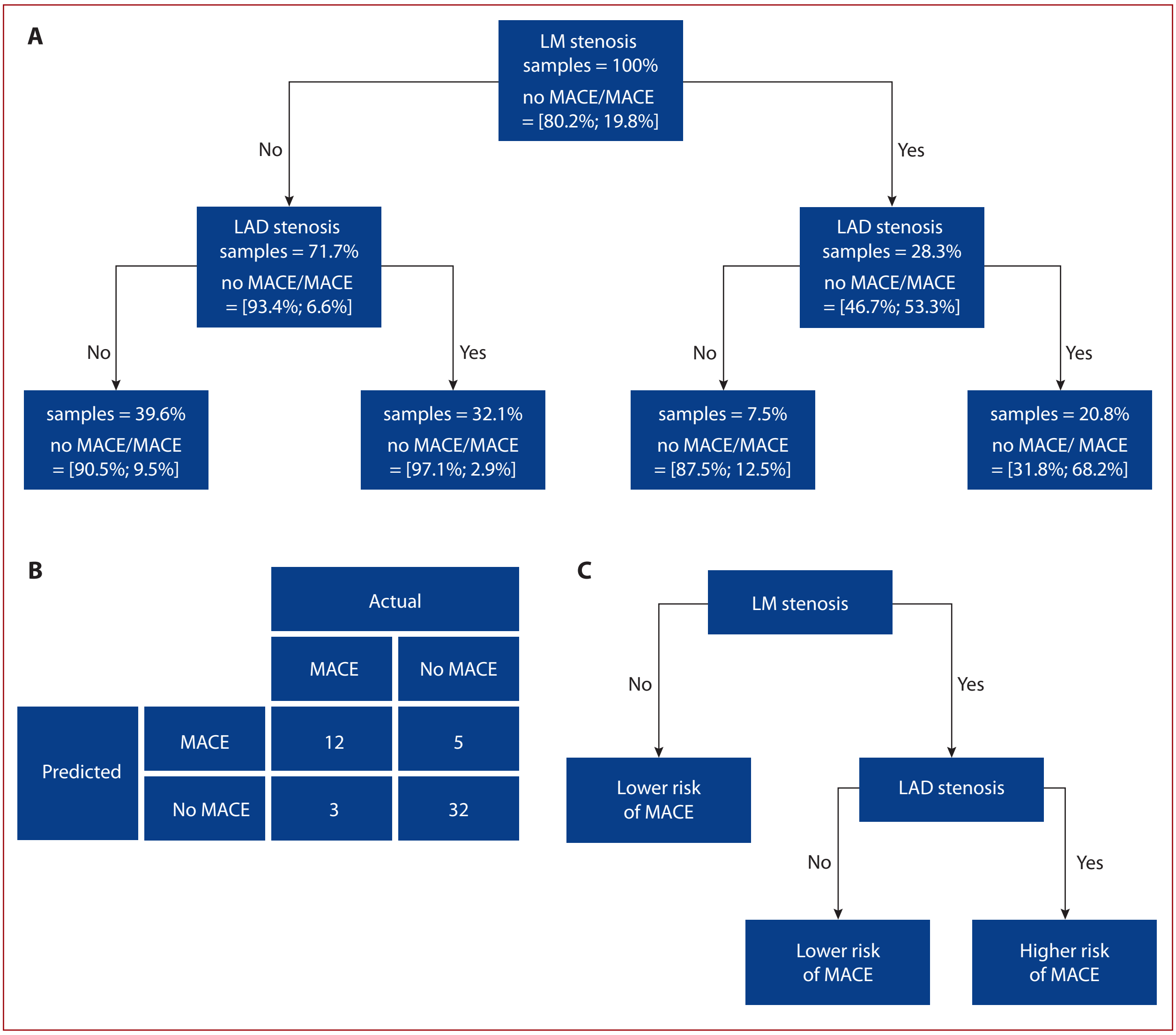

Figure 1. A. The major adverse cardiac event (MACE) classification algorithm on the basis of the cohort of the first study stage. **B.** The confusion matrix in the cohort of the second study stage. **C.** The classification tree model for prediction of MACE in patients with multivessel coronary artery disease (MVD) in one-year observation

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

Conflict of interest: None declared.

Funding: None.

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