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CARDIOMYOPATHY PREDICTION IN PATIENTS WITH PERMANENT VENTRICULAR PACING USING MACHINE LEARNING METHODS

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Abstract. Pacing-induced cardiomyopathy is a notable issue in patients needing permanent ventricular pacing. Identifying risk groups early and swiftly preventing the ailment can reduce patient harm. However, current prognostic methods require clarity. We employed machine learning to develop predictive models using medical data. Three algorithms — decision tree, group method of data handling, and logistic regression — formed models that forecast pacing-induced cardiomyopathy. These models displayed high accuracy in predicting development, signifying soundness. Factors like age, paced QRS width, pacing mode, and ventricular index during implantation significantly influenced predictions. Machine learning can enhance pacing-induced cardiomyopathy prediction in ventricular pacing patients, aiding medical practice and preventive strategies.

Keywords: permanent ventricular pacing, risk factors, artificial intelligence, forecasting, machine learning.

INTRODUCTION

Right ventricular myocardial pacing remains dominating method in providing medical care to patients with various potentially fatal bradyarrhythmias, even though at the beginning of the 21st century, a relation between this form of cardiac pacing and the left ventricular contractility impairment [1], as well as deterioration of clinical outcomes in the distant period [2; 3].

According to data from various sources, the incidence of pacing-induced cardiomyopathy (PICM) in patients with conventional right ventricular pacing and with preserved initial left ventricle ejection fraction (LVEF) ranges from 7.5 to 26% [4–10].

The risk of heart failure hospitalizations (HFH) and overall mortality are significantly higher among patients with PICM, as was shown in a large retrospective study by Sung Woo Cho et al. [10]. Though in patients with initially reduced systolic function of the left ventricle and high burden of ventricular pacing, the factors of deterioration of the clinical outcomes are well established [3], in patients with preserved LVEF, they have not yet been fully studied. Along with the wide availability and significant global experience of using this method of cardiac pacing in clinical practice, there is a growing number of publications focusing on the adverse effects of right ventricular myocardial pacing (and investigating risk factors that led to them), one of which is the development of the so-called pacing-induced cardiomyopathy, which is characterized by a decrease in the left ventricle contractility and negative remodeling of the heart chambers, The identification of risk factors and prediction of PICM development in patients with an implanted pacemaker is an objective of significant importance for modern medicine, considering the appearance of modern physiological methods of cardiac pacing (such as conduction system pacing) which allow preventing or minimizing the negative consequences of right ventricular myocardial pacing [11–14]. It is important to note that machine learning and artificial intelligence are becoming more prevalent in healthcare, particularly in cardiology. These technologies have successfully predicted disease cases and identified pathologies [15]. However, studies that apply machine learning to indicate PICM were not found after analyzing various literature sources.

The primary focus of research in the intersection of cardiology and machine learning is centered around the prediction and diagnosis of diseases, including ischemic heart disease (IHD) [16; 17], HF [18], atrial arrhythmias [19; 20], and others, using data from patients' medical records, imaging, and biosignals. In the context of PICM, the scientific community focuses on studying risk factors and developing preventive measures [21; 22]. Thus, the use of machine learning can contribute to identifying patients at considerable risk of PICM, which will allow the introduction of prompt and effective therapeutic interventions or other invasive strategies. This study focuses on figuring out the possibilities of using the machine learning methodology to predict the development of PICM in patients with permanent ventricular pacing.

Specific tasks due to the urgency of the problem are determined by the following aspects:

1. Development of PICM prediction models based on various machine learning algorithms using the available medical dataset.

2. Comprehensive evaluation of constructed models using classification metrics including (but not limited to) accuracy, sensitivity, and specificity.

3. A detailed study of the importance of individual factors included in the model in the context of their influence on predicting PICM.

The objective of the study is the construction of detailed prognostic models for the development of PICM and the identification of critical factors that contribute to the occurrence of this complication.

MATERIALS AND METHODS

In this research, we used anonymized data from patient examinations performed at the State Institution "M. Amosov National Institute of Cardiovascular Surgery" of the National Academy of Medical Sciences of Ukraine within the framework of the cooperation agreement with the National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute".

Before initiating the study, the M. Amosov National Institute of Cardiovascular Surgery performed a bioethical evaluation of the research protocol. We analyzed data on thirty-four patients, of which nine (26.5%) were diagnosed with PICM, which was determined with an LVEF of less than 45%. Left ventricle ejection fraction was within normal limits in the remaining twenty-five patients (73.5%).

The study included only those patients who met the following criteria: availability of echocardiographic data at the time of pacemaker (PM) implantation;

total percentage of ventricular pacing at the time of examination is not less than 90%; preserved LVEF at the time of implantation (≥ 50%); age restrictions patients (18–80 years at the time of implantation and control examination, respectively); this was to be a primary PM implantation without previous endocardial lead extractions or power source replacements.

For the study, the M. Amosov National Institute of Cardiovascular Surgery systematically collected and documented data, which included gender, age, the period from PM implantation to follow-up, as well as the main and concomitant diagnoses of the patients.

In addition, the data from echocardiographic and electrocardiographic studies were collected, as well as cardiac pacing parameters at two stages: at the time of hospitalization and during the control examination.

It is important to note that the used database has seventeen attributes, described in detail in Table 1.

Table 1. Attributes of the selected database

Attribute[1]	**Data type**	**Symbolic notation**
PICM	Binary	y
Gender	Binary	x_1
Age	Continuous integer	x_2
Time from pacemaker implantation to follow-up	Continuous integer	x_3
LVEF at the time of implantation	Continuous integer	x_4
LA diameter at the time of PM implantation	Continuous integer	x_5
Width of native QRS complex	Continuous integer	x_6
Width of paced QRS complex	Continuous integer	x_7
Presence of atrial arrhythmias (including AF)	Binary	x_8
Right ventricle pacing site	Binary	x_9
Structural heart diseases	Binary	x_{10}
Diabetes mellitus	Binary	x_{11}
Hypertension	Binary	x_{12}
Ischemic heart disease	Binary	x_{13}
Pacemaker type (single-chamber/dual-chamber)	Binary	x_{14}
Rate-adaptive pacing mode	Binary	x_{15}
Left ventricle EDI at the time of PM implantation	Continuous	x_{16}

The purpose of applying machine learning technologies was to find key input (independent) variables x that correlate with the presence of cardiomyopathy, represented as an output (dependent) variable y. Machine learning aims to identify patterns and relationships between variables through data processing. Machine learning algorithms are designed to explore dependencies in data and show trends that may not be clear. A substantial number of scientific developments confirmed this hypothesis, where authors considered tasks from various subject areas, including medicine [23–25].

[1] Accepted abbreviations: PICM — stimulation-induced cardiomyopathy; AP — artificial pacemaker; LVEF — left ventricular ejection fraction; LA — left atrium; AF — atrial fibrillation; EDI — end-diastolic index.

As can be seen from Table 1, the output variable y is dichotomous, which writes down the need to solve the classification problem.

Taking this into account, we decided to use three simple classification algorithms: decision tree [26], group method of data handling (GMDH) [27], and logistic regression [28].

Decision trees are one of the most convenient algorithms because of their visual interpretation and ability to oversee numerical and categorical data. They work by partitioning the space of input variables into regions corresponding to different classes of the output variable. However, they can be prone to overfitting, especially with complex data.

GMDH is an algorithm that creates a model based on a pairwise comparison of objects. Its main advantage is the high interpretability of the results, which supplies the possibility of a clear understanding of the classification mechanisms. However, due to high computational complexity, GMDH may only be effective for a small volume of data.

Logistic regression is a statistical algorithm commonly used to predict the probability of an event occurring by applying a logistic function. This method works well on two-class problems but can run into issues with non-linear relationships or many categorical variables.

RESULTS

Before building PICM prediction models, we divided the patient sample into a train (80%, or twenty-seven patients) and a test (20%, or seven patients) using a stratification method, which preserves the class ratio between subjects in each sample. We measured the performance of each algorithm by its accuracy (proportion of correctly classified patients), sensitivity (proportion of correctly classified patients with pathology), and specificity (proportion of correctly classified healthy patients) [29]. The performance of the selected classification algorithms is presented in Table 2.

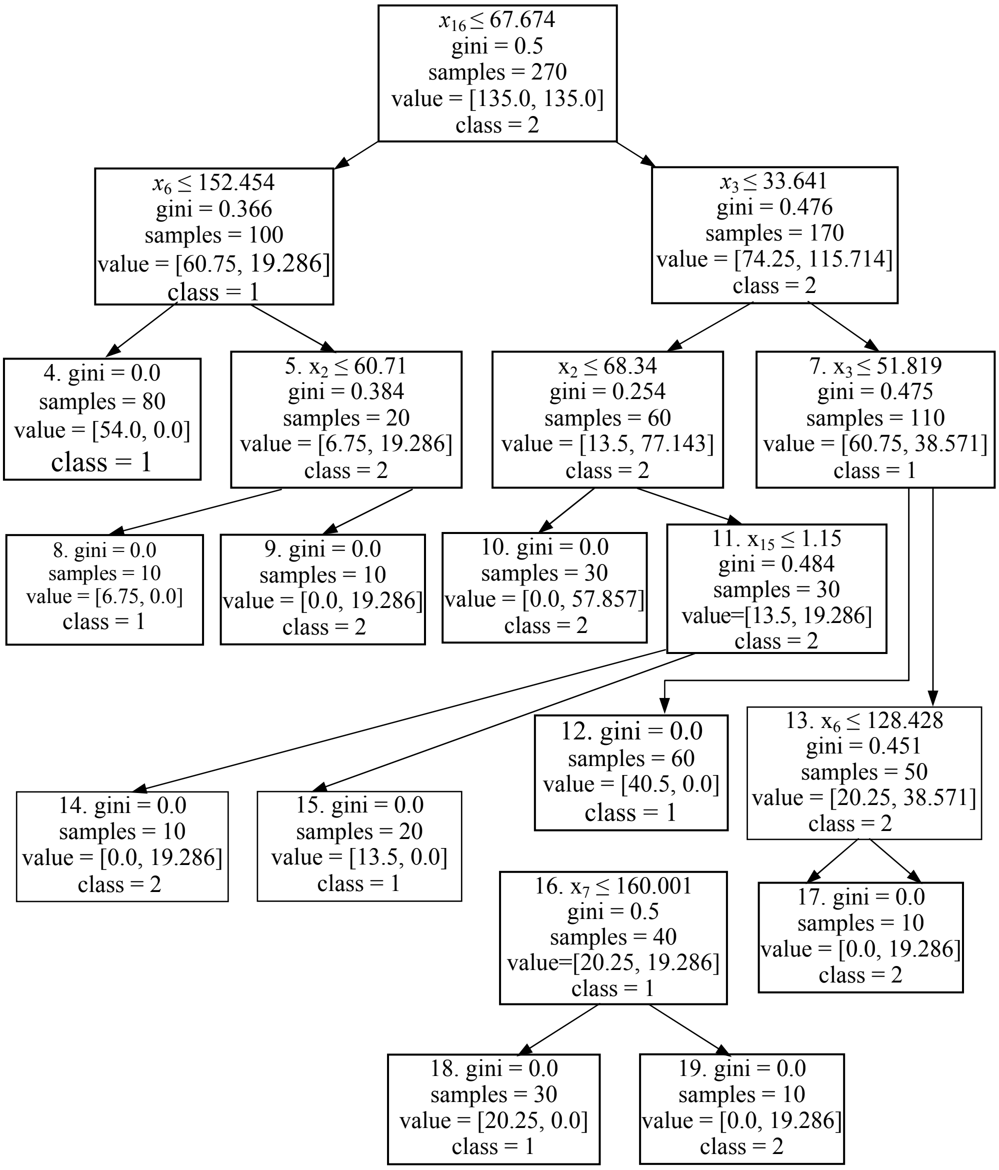
Table 2. Evaluation of the constructed PICM prediction models by classification metrics

Classifier	Train (80%)			Test (20%)		
	Accuracy	Sensitivity	Specificity	Accuracy	Sensitivity	Specificity
Decision tree	1.000	1.000	1.000	1.000	1.000	1.000
GMDH	1.000	1.000	1.000	1.000	1.000	1.000
Logistic regression	0.852	0.857	0.850	1.000	1.000	1.000

Using the *scikit-learn* (the Python library), we implemented the classification model (Figure) based on the decision tree method. The tree has a depth of five and consists of nine leaves.

According to the data presented in Table 2, this model shows 100% accuracy on the test sample, indicating its reliability and the absence of overfitting phenomena.

Six input variables: x_3, x_6, x_7, x_2, x_{15}, and x_{16}, were used in the model and are illustrated in the tree (Fig. 1). We expressed each variable's impact through the tree's weights: $x_3 = 0.303$, $x_6 = 0.193$, $x_7 = 0.146$, $x_2 = 0.127$, $x_{15} = 0.118$, $x_{16} = 0.113$. The weighting coefficients were figured out using the Gini index [26]. It considers the number of times each variable was used to split the data and how effective this split was. The final weighting of each variable is a normalized value based on the overall reduction in the Gini index caused by each variable. A variable with a higher importance value is considered more "important" to the model.



Decsion tree model

Applying the GMDH, we generated a model for which the formula below is given:

$$y = 0.001x_{16}^2 - 0.0009x_7x_{16} - 0.643x_{13}x_{14} - 0.006x_2x_{12} - 0.006x_{12}x_{16} -$$

$$- 0.031x_9x_{15} + 0.0003x_7^2 + 0.018x_4x_{12} - 0.519x_{11}x_{12} - 0.736$$

We conducted the training process by using *GMDH Shell DS* software. As shown in Table 2, the results show that the GMDH model is completely accurate in testing, indicating no model overfitting. This model includes ten independent variables, namely: $x_{16}, x_{13}, x_7, x_{14}, x_{12}$, x_{11}, x_4, x_2, x_9, and x_{15}. The weight of each of these variables is found based on the change in the model's predicted values when replacing the variable's actual values with its average value. As a result, the following variable weights were obtained: $x_{16} = 83.7\%$, $x_{13} = 53.9\%$, $x_7 = 53.2\%$, $x_{14} = 39.7\%$, $x_{12} = 33.4\%$, $x_{11} = 30.8\%$, $x_4 = 17.6\%$, $x_2 = 6.4\%$, $x_9 = 1.6\%$, $x_{15} = -0.2\%$.

In the third step, we applied a logistic regression model. The general form of the logistic model is defined by formula:

$$p = \frac{1}{1 + e^{-y}},$$

where p is the calculated probability of occurrence of a given event (PICM in this context); e is the basis of natural logarithms (2.713); y is the linear regression equation. The following logistic regression model was obtained:

$$y = -0.065x_2 + 0.044x_7 - 1.758x_{15} + 0.119x_{16} - 8.179.$$

We conducted the training procedure using the *scikit-learn* package of the *Python* programming language. The complexity of this model is four. Interestingly, this model includes variables also used in the earlier models: x_2, x_7, x_{15}, and x_{16}.

DISCUSSION

While analyzing constructed models for predicting pacing-induced cardiomyopathy based on the data in Table 2, it was found that only the logistic regression model failed to present an ideal result for the entire sample (with a classification accuracy of 85.2% in the train, despite 100% accuracy in the test). The observed phenomenon can be explained by the intrinsic simplicity of the logistic model in contrast to the other comparable models utilized in the research.

The developed decision tree model was structurally simple and included only six independent variables. While the results of the classification estimation are excellent, this model may be prone to misprediction of new data due to the limited initial sample size. The GMDH model wins here by incorporating ten independent variables for prediction. Additionally, the algorithm for constructing such a model allows non-linear combinations of variables, which sensitively increases their predictive power.

The identified combinations of factors influencing the PICM development align with the latest global publications. The three prediction models include the following independent variables: x_2 (patient's age), x_7 (width of paced QRS complex), x_{15} (rate-adaptive pacing mode), and x_{16} (left ventricular EDI at the time of PM implantation).

Among them, variable x_7 has a significant impact, especially in the decision tree (0.147) and GMDH (53.2%), with one of the highest weighting coefficients. There are also independent variables that were not included in any of the models, such as x_1 (patient gender), x_5 (LA diameter at the time of PM implantation), x_8 (presence of atrial arrhythmias), and x_{10} (structural heart diseases).

The modeling results obtained during the study open the possibility of predicting undesirable clinical consequences of right ventricular pacing based on combinations of the most informative factors. That makes it possible to prevent the influence of these factors or intervene at the stage of medical care provided, choosing more physiological cardiac pacing methods.

CONCLUSION

The study successfully developed models for predicting pacing-induced cardiomyopathy (PICM) based on various machine learning algorithms using an available medical dataset of thirty-four patients.

Methods used — including decision tree, group method of data handling (GMDH), and logistic regression — allowed robust predictive models to be created. On the test sample, all of them showed 100% prediction accuracy.

Obtained results demonstrated the high efficiency of the used machine learning algorithms in terms of the accuracy of the PICM prediction, the absence of overfitting, and the ability of the models to classify adequately normal and pathological states of patients.

A detailed study of values included in the models allows an understanding of their role in developing PICM.

The most significant data included in the models were patient age, paced QRS complex width, rate-adaptive pacing mode, and left ventricular end-diastolic index (EDI) at the time of pacemaker implantation.

The developed models can serve as a basis for further improving diagnostic and treatment technologies for PICM prevention strategies.

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INFORMATION ON THE ARTICLE

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ПРОГНОЗУВАННЯ КАРДІОМІОПАТІЇ У ПАЦІЄНТІВ З ПОСТІЙНОЮ ШЛУНОЧКОВОЮ ЕЛЕКТРОКАРДІОСТИМУЛЯЦІЄЮ ЗА ДОПОМОГОЮ МЕТОДІВ МАШИННОГО НАВЧАННЯ / Є.О. Перепека, В.В. Лазоришинець, В.О. Бабенко, І.В. Давидович, Є.А. Настенко

Анотація. Кардіоміопатія, спричинена кардіостимуляцією, є важливою проблемою для пацієнтів, які потребують постійної шлуночкової кардіостимуляції. Раннє виявлення груп ризику та швидка профілактика недуги можуть зменшити шкоду для пацієнтів. Однак сучасні методи прогнозування потребують доопрацювання. Застосовано машинне навчання для розроблення прогностичних моделей на основі медичних даних. Три алгоритми — дерево рішень, група оброблення даних та логістична регресія — сформували моделі, які прогнозують кардіоміопатію, спричинену кардіостимуляцією. Ці моделі показали високу точність у прогнозуванні розвитку, що свідчить про їх надійність. Ключові фактори, такі як вік, ширина QRS, режим кардіостимуляції та шлуночковий індекс під час імплантації, суттєво впливали на прогнози. Машинне навчання може покращити прогнозування кардіоміопатії, спричиненої кардіостимуляцією, у пацієнтів, які перебувають на шлуночковій електрокардіостимуляції, допомагаючи медичній практиці та профілактичним стратегіям.

Ключові слова: постійне ритмоведення шлуночків, фактори ризику, штучний інтелект, прогнозування, машинне навчання.