https://doi.org/10.35336/VA-2022-4-04

PREDICTORS OF PACEMAKER IMPLANTATION IN PATIENTS WITH MYOCARDIAL INFARCTION AND HEART BLOCK

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The **aim** of the study was to identify predictors of early and delayed pacemaker (PM) implantation in patients with myocardial infarction (MI) and heart block, allowing the development of models for predicting the feasibility of its implantation.

Methods. A randomized selection method was used to form a cohort of patients with MI complicated by cardiac conduction disorders. The first (control) group included 72 patients who did not have a PM implanted, the second (n=46) and third (n=68) groups consisted of patients with MI, having, respectively, indications for early (in the acute period of MI) and delayed (average after 3 years) PM implantation. All patients underwent endovascular revascularization of the infarct-dependent artery during hospitalization. Demographic, clinical, and morphological predictors of PM implantation in patients of the second and third groups were evaluated in comparison with the control group. Multiple logistic regression was used to identify factors associated with the need for PM implantation in the short term (hospital period) and in the long-term period.

Results. Factors that determine the expediency of a permanent PM in the acute period of MI at the hospital stage, delayed pacemaker implantation 3.2±1.9 years after myocardial infarction, as well as predictors that do not require a permanent PM throughout the entire observation period, were identified. The main factors that require permanent PM implantation in the acute period were identified: 3rd degree atrioventricular (AV) block in NSTEMI, GRACE score 96 or higher, development of 3rd degree AV block in MI of any localization except postero-inferior. Predictors for the need for PM implantation after 3.2±1.9 years (delayed period) were STEMI of anterior localization; at the same time, age had an inversely proportional relationship in predicting the fact of permanent pacing. The factors that determine the need for PM implantation are the presence of anterior MI, the multiple coronary artery lesions.

Conclusion. In the acute (hospital) period of NSTEMI, PM implantation is indicated at a high risk of adverse cardiovascular complications (GRACE scale of 96 points and above), in the presence of the 3rd degree AV block in any MI localization, except for the inferior one. Indications for permanent pacing 3.2±1.9 years after an acute coronary event are STEMI of anterior localization and multiple coronary artery lesions.

Key words: myocardial infarction; heart block; pacemaker; revascularization; predictors

Conflict of Interests: nothing to declare.
Funding: none.
Received: 28.03.2022 **Revision received:** 03.06.2022 **Accepted:** 27.06.2022
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For citation: Bryukhanova IA, Gorbunova EV, Mamchur SE. Predictors of pacemaker implantation in patients with myocardial infarction and heart block. *Journal of Arrhythmology*. 2022;29(4): 26-32. https://doi.org/10.35336/VA-2022-4-04.

According to the numerous data of Russian and international literature, the leading causes of the mortality and disability in a special cardiovascular continuum are the acute coronary syndrome (ACS) and verified myocardial infarction (MI) [1]. Despite the widely used modern methods of revascularization (percutaneous coronary intervention, coronary artery bypass grafting), mortality from MI and its complications remains high. It is known that the key events complicating the course of acute MI [2] are life-threatening cardiac arrhythmias, usually manifesting with sudden cardiac death, which determine an unfavorable clinical prognosis. Structural component of sudden cardiac death are ventricular arrhythmias (83%) and heart block (17%) [3]. Bradyarrhythmias complicating the MI are clinically polymorphic. Sinoatrial block often complicates the myocardial infarction, primarily of the inferior localization (about 30-40% of cases) and is prognostically favorable [4].

An important problem of the MI is atrioventricular (AV) block of varying degree [5], which determine the immediate and long-term prognosis in patients with high cardiovascular risk. The timing of the onset of AV blocks, the severity, the duration of atrioventricular conduction disturbance persistence - are determined by the severity and volume of the affected myocardium [6] and determine the indications for temporary and permanent pacing, which differ in different specialized surgical centers [7].

The currently existing modern clinical guidelines regulating the indications and timing of permanent pacing in myocardial infarction complicated by heart block have level C evidence [7]. There are no data supported by randomized clinical trials (level of evidence A and B). It should be noted that it remains relevant to identify predictors of permanent pacing in acute and late periods of MI complicated by heart block.

The aim of the study was to identify the predictors of early and delayed pacemaker (PM) implantation in patients with myocardial infarction and heart block, allowing to develop the models for predicting the feasibility of PM implantation.

METHODS

A retrospective analysis of electronic cases and outpatient records of patients with MI complicated by heart block was carried out. A random selection method was used to form a cohort of patients with prior MI complicated by cardiac conduction disorders. The first (control) group included patients (n=72) who did not have a PM implanted, the second (n=46) and third (n=68) groups consisted of patients with myocardial infarction with indications for early (hospital period) and delayed (during 3.2±1.9 years after MI) PM implantation, respectively. During hospitalization all patients underwent a temporary pacemaker and endovascular revascularization of the infarct-dependent artery.

The following parameters were considered as predictors of the PM implantation: gender, age, GRACE scale points, the form of the acute coronary syndrome (MI with ST segment elevation (STEMI), MI without ST segment elevation (NSTEMI), MI localization (anterior, posterior or other localization), type of arrhythmia (sick sinus node syndrome, AV block of the 2nd and the 3rd degree), complicated by a rhythm disorder (atrial fibrillation, ventricular extrasystole, other rhythm disturbances), the presence of Morgagni-Adams-Stokes attacks, severity of heart failure in MI according to Killip, MI in anamnesis, diabetes mellitus, arterial hypertension, severity of coronary artery lesions (single-vessel and multiple lesions), TIMI scale for assessing coronary blood flow. Qualitative (nominative) indicators were analyzed in the form of binary measurements.

An optimal set of predictors was selected to predict implantation in the acute period of MI. We studied the factors that determine the use of a PM 3.2±1.9 years after the index event.

Statistical analysis

Logistic regression, the Quasi-Newtonian method of estimation, was used to identify the factors for the need for pacemaker implantation. For a more visual representation of the quality of the resulting model, a Receiver Operator Curve (ROC) analysis was carried out. The quality of the resulting model was assessed using the following indicators: sensitivity (number of patients who underwent PM implantation, classified correctly / number of all patients who underwent permanent pacing), specificity (number of patients who did not undergo PM implantation, classified correctly / number of patients who did not undergo pacemaker implantation) and the area under the curve (AUC). This indicator serves as an indicator of the effectiveness of the model obtained as a result of the ROC analysis. For the obtained AUC values, the standard error and the boundaries of the 95% confidence interval (CI) were determined. The level of critical significance was taken as 0.05.

The indicative parameters of the constructed model of PM implantation adequacy were Pearson's $\chi 2$ and p-level. In the case of a significant logistic regression, the initial (with a cutoff level 0.5) efficacy parameters (specificity and sensitivity), as well as the regression coefficient B, standard error, p-level, odds ratio (OR) with a 95% confidence interval, Wald's $\chi 2$ separately for the constant and each predictor. Using B-coefficients of predictors and a constant, a mathematical formula was built to determine the need for implantation of a device in a patient in the hospital and long-term periods. Next, a ROC analysis was carried out with the construction of a graph of the ROC curve and the determination of AUC. Using the results of the ROC analysis, the optimal cut-off threshold was calculated to determine the need for pacemaker implantation in the patient. Statistical analysis was carried out using R v.4.0.3 programming language.

RESULTS

An analysis of clinical and anamnestic data revealed important criteria that determine the need for pacemaker implantation in patients in the acute period of MI associated with cardiac conduction disorders.

A significant direct dependence of the need for a permanent pacemaker on the numerical value (in points) of the GRACE scale (OR=1.07 [1.02-1.19]), the presence of 3rd degree AV block (OR=11.9 [3, 37-42.3]) and an inverse relationship with the fact that the patient has an MI of lower localization (OR = 0.082 [0.026-0.26]), presented in Table 1.

The general characteristics of the constructed model testify to its effectiveness: Pearson's χ^2=61.2; p=0.0001. Regression coefficients are used to build a model for determining the need for PM implantation in the acute period of MI. To do this, it is necessary to enter the value of the indicators 'GRACE scale', '3rd degree AV block' and 'Posterior Wall MI' into the formula below:

Y1=EXP (Z1)/(1+EXP (Z1)) and

Z1=(-9.06+(X1×0.068)+(X2×2.48)+(X3×-2.5)),

where Y1 is the probability of the need for PM implantation in the early period of MI, which took values from 0 to 1. If the calculated indicator is less than 0.5, then the model determined the absence of the need for PM implantation in the early period, and with the value greater than or equal to 0.5 - testified to such a need; X1 - GRACE scale (points); X2 - presence of the 3rd degree AV block (no / yes); X3 - posterior wall MI (no / yes).

With an increase in the score on the GRACE scale in patients with 3rd degree AV block and MI of any localization, except for the inferior one, there was a higher probability of PM implantation in the early stages of MI.

Analysis of the obtained data showed that the constructed model was characterized by high sensitivity (78.3%) and specificity (84.7%). The AUC was 0.88, which indicated a high quality of the resulting model (Fig. 1a), the use of which is based on such indicators as the presence of the 3rd degree AV block, NSTEMI, the number

of points on the GRACE scale - made it possible to predict the need for a PM implantation in the acute period of MI in each patient individually.

Differences in the 'GRACE scale' indicators among the compared groups are also clearly visualized. Patients with persistent pacing in the acute period were associated with more severe MI according to the GRACE scale in comparison with the control group.

The median value of the GRACE scale was 137.5 (128.7; 146.0) points in patients of the second group. For the control group, this indicator corresponded to 123.5 (112.0; 134.5) points. The results of the study demonstrate that the 3rd degree AV block in NSTEMI and high values on the GRACE scale of any localization, except for the inferior one, are the main factors that determine the need for PM implantation in the early period of MI.

It should be noted that the presence of the 3rd degree AV block is an equivalent risk factor in terms of contribution for any localization of MI (except the inferior one). It has been shown that the more risk factors a patient has, the higher the risk of permanent pacing.

Comparative analysis of demographic and clinical and anamnestic data of the second group of subjects, requiring PM implantation for 3.2±1.9 years, and the first, control group, where permanent PM implantation was not performed, revealed a significant direct dependence of pacemaker implantation in the long-term period after ACS, namely NSTEMI (OR=3.61 [1.59-8.17]), the presence of anterior MI (OR=5.53 [1.95-15.6]), and inverse relationship with patient's age (OR=0.96 [0.93-0.99]).

Thus, integral parameters, namely NSTEMI, anterior MI localization, age of patients - characterize a comprehensive assessment of the probability of PM implantation in the delayed period (after 3.2±1.9 years). After calculating the integral parameters for predicting PM implantation, a multivariate binary logistic regression was built (Table 1).

The general characteristics of the constructed model testified to its effectiveness: Pearson's χ^2=20.5; p=0.001. The regression coefficients were used to build a model that determines the need for pacemaker implantation in the delayed period after MI. To do this, it was necessary to enter the values of the indicators 'Age', 'NSTEMI' and 'MI of the anterior wall' in the formula:

Y1=EXP(Z1)/(1+EXP(Z1)) and

Z1=(1.91+(X1×-0.041)+(X2×1.28)+(X3×1.71)),

where Y1 is the probability of the need for PM implantation in the delayed period, which took values from 0 to 1; if the calculated indicator is less than 0.5, then the model determined the absence the need for PM implantation on average 3 years after MI, and if the value is greater than or equal to 0.5 - the presence of such a need; while X1 is age (years); X2 - variant of ACS (STEMI / STEMI); X3 - MI of the anterior wall (no / yes).

It was found that with a decrease in age, as well as in patients with STEMI and anterior MI, there is a higher likelihood of PM implantation at a long-term period.

The constructed model was characterized by high sensitivity (72.1%) and specificity (66.7%). The AUC was 0.72, which indicates the high quality of the model that determines the need for PM implantation in the delayed period (Fig. 1b).

The results of the ROC analysis demonstrate the high ability of the model to predict the need for a permanent PM implantation on average 3 years after MI. The use of this model, based on the use of factors of STEMI of anterior localization and the age of patients, made it possible to reliably calculate the prognosis of PM implanta-

Table 1.

Predictors of pacemaker implantation depending on the period of myocardial infarction complicated by heart block

Parameter	B coefficient	Standard error	p-value	OR	CI-	CI+	Wald's χ^2
Acute period of IM							
GRACE scale (points)	0.068	0.02	0.002	1.07	1.02	1.19	9.33
3rd degree AV block (no / yes)	2.48	0.64	0.0002	11.9	3.37	42.3	15.1
Inferior MI (no / yes)	-2.50	0.59	<0.0001	0.082	0.026	0.26	18.2
Constant	-9.06	3.04	0.003	0.0001	0.003	0.048	8.86
Long-term period of IM							
Age (years)	-0.041	0.02	0.02	0.96	0.93	0.99	5.24
ACS variant (STEMI / NSTEMI)	1.28	0.41	0.002	3.61	1.59	8.17	9.65
Anterior MI (no / yes)	1.71	0.53	0.001	5.53	1.95	15.6	10.6
Acute and long-term period of IM							
ACS variant (STEMI / NSTEMI)	1.59	0.38	0.00004	4.89	2.31	10.3	11.8
Anterior MI (no / yes)	2.45	0.49	0.000001	11.5	4.39	30.4	24.9
MCAL (no / yes)	0.78	0.38	0.04	2.18	1.03	4.61	4.27
Constant	-1.05	0.31	0.001	0.35	0.19	0.64	11.8

Note: B coefficient - regression coefficient; OR - odd ratio; CI- - lower border of 95% OR confidence interval; CI+ - upper border of 95% OR confidence interval; ИМ - myocardial infarction; GRACE scale - Global Registry of Acute Coronary Events; AV - atrioventricular; ACS -acute coronary syndrome; STEMI / NTEMI - MI with / without ST elevation; MCAL - multiple coronary artery lesion.

tion in the long-term period personally for each patient. It was found that patients with NSTEMI (compared with patients with STEMI) were significantly more common in the third group of delayed pacemaker implantation than in the control group (OR=3.61 [1.59-8.17]). The same pattern is observed in anterior MI with heart block (OR=5.53 [1.95-15.6]).

Differences in the 'age' indicator in the comparison groups indicate that in patients of the second group, the median value (lower; upper quartiles) of age was higher than in the control group; the average age of patients, which practically corresponded to this indicator in the third group of patients.

Therefore, the main predictors of PM implantation in the long-term period in patients with MI complicated by heart block were anterior STEMI; at the same time, age had an inversely proportional relationship in predicting the use of a permanent PM in the delayed period, namely, the older the age, the earlier the pacemaker was implanted.

A comparative analysis of the predictors of PM implantation in the early (second group of patients) and late periods after MI (the third group of subjects) was carried out in comparison with the control group, in which PM was not implanted, since conduction disturbances were of a transient nature.

A significant direct correlation was found between the expediency of PM implantation and the variant of ACS, namely NSTEMI (OR=4.89 [2.31-10.3]), anterior MI (OR=11.5 [4.39-30,4]) and the severity of coronary artery lesions, namely, multiple atherosclerotic changes (OR=2.18 [1.04-4.61]).

The obtained integral indicators: STEMI, anterior MI, multiple lesions of the coronary arteries, characterizing a comprehensive assessment of the probability of PM implantation, made it possible to build a multivariate binary logistic regression of the probability of PM implantation (Table 1).

An effective model (formula) was constructed that allows predicting the need for PM implantation in MI when compared with the control group, where a permanent PM was not performed (Pearson's χ^2=44.2; p=0.00001). The probability of using a permanent PM was calculated using the formula:

Y1=EXP(Z1)/(1+EXP(Z1)) and

Z1=-1.05+(X1×1.59)+(X2×2.45)+(X3×0.78),

where Y1 is the probability of the need for PM implantation, which takes values from 0 to 1; if the calculated parameter is less than 0.5, then the model determines that there is no need for a permanent pacemaker, and if the value is greater than or equal to 0.5, the presence of such necessary, Z1 - intermediate indicator EXP - exponential function, X1 - variant of ACS (STEMI / STEMI), X2 - anterior wall MI (no / yes), X3 - multiple coronary artery disease (no / yes).

Analysis of the results showed that the constructed model has a sensitivity 82%, and a specificity 59.7%, which indicates a high ability to predict the need for PM implantation (Fig. 1c).

It should be assumed that in patients with STEMI and anterior MI, as well as with multiple lesions of the coronary arteries, there is a higher likelihood of PM implantation. MI of any localization (except anterior) and other types of coronary artery lesions (except for multiple) were associated with a lower risk of PM implantation.

The results of the ROC-analysis performed in patients with pacing and without permanent pacing in patients with MI with transient heart block showed a high predictive value of the model, the use of which this model, based on parameters of STEMI of anterior localization and the multiple coronary artery lesions, allows us to reliably calculate the expediency of using the PM individually in patients who have undergone MI. Thus, in patients with STEMI and anterior MI, as well as with multiple coronary arteries lesions, there was a higher probability of the need for a permanent PM (OR=4.89 [2.31-10.3]), (OR=11.5 [4.39-30.4]). MI of any localization (except anterior) and with other types of coronary artery lesions (except for multiple) was associated with a lower risk of a permanent PM.

Thus, a multivariate analysis of clinical and anamnestic data revealed predictors of PM implantation in patients with MI associated with heart block in the acute and long-term periods (3.2±1.9 years after the index event). An effective mathematical model has been developed to predict the need for PM implantation in patients with MI complicated by heart block, which can be used to reduce mortality from fatal cardiovascular events.

DISCUSSION

Despite significant progress in high-tech methods of myocardial revascularization, heart blocks associated with MI, being the main electrophysiological pattern of sudden cardiac death, worsen the immediate and long-term prognosis. Successful reperfusion, by reducing the degree and severity of irreversible changes in the conduction system

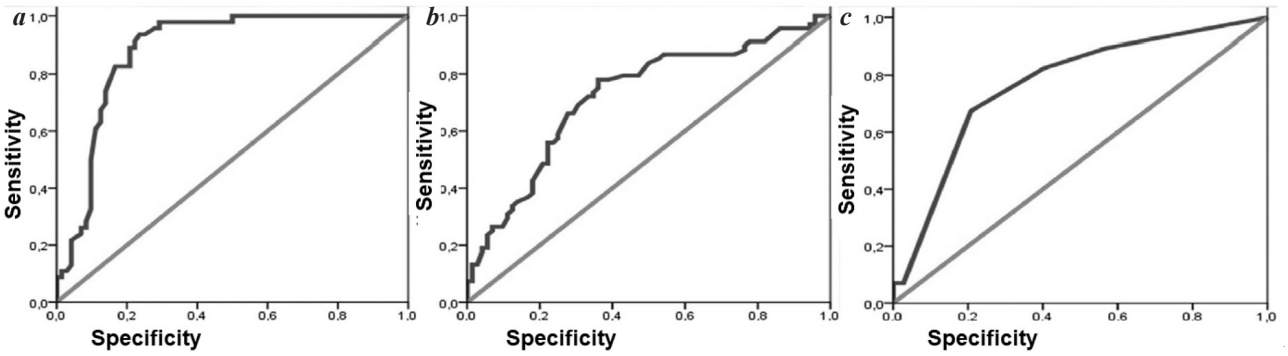

Fig. 1. ROC curves: a - in the first model without pacemaker implantation, b - in the second model with pacemaker implantation in the acute period of myocardial infarction, c - in the third model with delayed pacemaker implantation.

of the heart, contributes to the restoration of atrioventricular conduction [8], and reduces the risk of sudden cardiac death twice [9]. However, after a time due to chronic coronary insufficiency and the progression of degenerative changes in the conduction system of the heart, blockades recur and require constant chronotropic support, carried out with the help of a permanent PM.

The decision on the need for PM implantation is determined by the timing of the block, the duration of its persistence, and the risk of its progression [10]. According to B.Bacior [11], acute high-grade AV block, especially with fascicular lesions of the cardiac conduction system, are considered as a serious predictor of hospital mortality and poor long-term clinical prognosis and are an important criterion for the implantation of a permanent PM.

In our study, the development of complete AV block was the main predictor of permanent pacemaker implantation in the acute period of the index event; AV block of the 3rd degree was more common in the group of patients who underwent permanent pacing for MI at the hospital period than in the control group (OR=11.9 [3.37-42.3]).

There is an opinion that there is a certain relationship between the need for PM implantation and the localization of MI. So, for example, according to S.A. Saiganova [12], AV block of the 3rd degree with lower MI develop in the first 24 hours, are caused by reversible ischemia of the perinodal tissue and are transient, hemodynamically insignificant and do not require a permanent PM [13]. This fact is consistent with the data of our study, where in the group of patients with permanent pacing in the acute period with lower myocardial infarction, the need for permanent pacing was significantly lower (OR=0.082 [0.026-0.26]).

The widely used GRACE scale, which is necessary to determine the risks and, accordingly, the timing of myocardial revascularization in NSTEMI, also determines the severity and volume of ischemic myocardial damage, which in turn determines the severity and irreversibility of organic changes in the conduction system of the heart, as well as the development of life-threatening hemodynamic disorders. In our study, it was shown that the numerical value of the GRACE scale in NSTEMI is an important predictor of permanent PM implantation in the acute period of MI. In patients of the study group, the median value of the GRACE scale was 137.5 [128.7; 146.0[points, while in the control group these indicators corresponded to 123.5 [112.0; 134.5] points, OR=1.07 [1.02-1.19]). The presence of complete AV block in MI of any localization, except of the lower one, indicates the expediency of PM implantation in the acute period with a GRACE score of 96 points and higher.

It is known that high-grade AV block is more likely to complicate the STEMI compared to NSTEMI (2.4% and 0.9%, respectively). However, in NSTEMI, the need for implantation of a permanent pacemaker is higher (30% versus 16%) [14], which is consistent with the data obtained in our study, which also revealed that an important predictor of implantation of a permanent pacemaker in the long-term period is the STEMI complicated by heart block. In the group with NSTEMI associated with high degree blocks, the need for PM implantation is more likely in the delayed period compared to the control group (OR=3.61 [1.59-8.17]).

Localization of MI is closely related to the volume of the affected myocardium and, as a rule, determines the severity and irreversibility of organic changes in the conduction system of the heart. It is known that acute AV blocks in anterior MI are often irreversible, associated with severe hemodynamic consequences (cardiogenic shock, pulmonary edema, sudden death) and, therefore, require constant chronotropic support [5]. Our study revealed that in the group of patients with anterior MI, the need for PM implantation in the delayed period was significantly higher compared to the control group (OR=5.53 [1.95-15.6]). The study also showed that the ACS variant, namely NSTEMI (OR=4.89 [2.31-10.3]), the presence of anterior MI (OR=11.5 [4.39-30.4]), are the main criteria for continuous cardiac pacing.

It should be noted that the severity of block in MI directly correlates with the volume of the affected myocardium, which, in turn, is determined by the degree and massiveness of coronary obstruction, as well as the presence of collateral blood flow. According to A.N. Osmolovsky [15], the multiple coronary artery lesions contribute to the development of chronic hypoperfusion of the cardiac conduction system and irreversible degenerative changes that predetermine the stability of hemodynamically significant conduction disorders.

According to our data, the multiple coronary artery lesions is an independent predictor of permanent pacemaker implantation. Thus, in the group with severe coronary disease, PMs were implanted significantly more often than in the control group (OR=2.18 [1.04-4.61]).

As a result of a multivariate regression analysis of demographic and clinical and anamnestic data, three prognostic models have been developed that determine the expediency of choosing the tactics of managing patients with MI complicated by heart block in the acute and long-term periods. It should be assumed that the use of these models in real clinical practice will reduce the risk of sudden cardiac death with timely PM implantation in patients with high cardiovascular risk, will justify the tactics of managing patients with MI complicated by heart block.

CONCLUSION

The identified predictors of the permanent pacemaker implantation in the acute (hospital) and long-term periods (during 3.2±1.9 years after MI) determine the indications for permanent pacing in patients with heart block in MI. In the acute (hospital) period of NSTEMI, pacemaker implantation is indicated at a high risk of adverse cardiovascular complications (GRACE scale of 96 points and above), in the presence of the 3rd degree AV block of any MI localization, except for the inferior one. Indications for permanent pacing 3.2±1.9 years after an acute coronary event are STEMI of anterior localization and multiple lesions of the coronary arteries.

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