SECTION 1. CARDIOLOGY

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1.1 Modeling of the quality of life and predictors of its deterioration in patients with myocardial infarction without ST-segment elevation

Myocardial infarction (MI) without ST-segment elevation (NSTEMI) remains one of the most dangerous manifestations of damage to the cardiovascular system in patients of any age category [1, 6, 7]. In addition to high mortality during the year, this pathology significantly affects quality of life indicators in the near and distant periods [2, 3, 8]. In our study, we analyzed indicators of quality of life according to the MIDAS-35 score.

We examined 200 patients with NSTEMI aged 38 to 80 (mean 62.0 ± 0.71, median – 62 and interquartile range – 55 and 70) years, who were hospitalized in the Municipal Non-Profit Enterprise "Vinnytsia Regional Clinical Medical and Diagnostic Center for Cardiovascular Pathology" with urgent indications [13, 14].

All patients were examined according to the NSTEMI protocol. Overall Quality of Life Assessment (QL) was performed according to the valid MIDAS-35 score © Oxford University Innovation Limited, 2002. All rights reserved [3], which was conducted on day 5-7 MI, in the general group of NSTEMI patients examined, ranged from 13.2 to 74.4 and averaged 38.6 (mathematical error of the average – 1.12), median – 37.9 and interquartile variation – 24.4 and 48.6, respectively. All of the research corresponds to the principles of the Declaration of Helsinki of the World Medical Association.

The basis of our analysis was the creation of a multiple linear regression model of QL of NSTEMI patients. Accordingly, the total score determined on the MIDAS-35 score on day 5-7 of NSTEMI was taken as the initial parameter of the model. It was established that an increase in the value of the total score predicted a deterioration, while its decrease – an improvement in the quality of life of these patients .

In order to select the most informative model variables (independent predictors), a preliminary Spearman rank correlation analysis of the initial parameter (total

MIDAS-35 score) with all clinical, instrumental and laboratory indicators, which represented the statistical matrix of the study, was conducted. The results of the analysis are given in table 1.

A direct moderate correlation was found with the degree of stenosis of the LCx in % according to the data of coronary angiography (CAG) (R=0.31, p<0.0001) and the size of the left atrium (LA) in mm (R=0.32, p<0.0001) [4, 5], and weak – with the presence of frequent ventricular extrasystoles (VE) (R=0.25, p=0.001) [9], the presence of paroxysms of ventricular tachycardia (VT) (R=0.24, p=0.002) [10], smoking (R=0.29, p=0.0002), ST2 level in plasma (R=0.18, p=0.02). In addition, a negative weak correlation of the value of the total score with the nature of diastolic dysfunction of the left ventricle (LV) was determined (R=-0.22, p=0.001) and the presence of biochemical association ST2 < 36 ng/ml + troponin I (Tp I) > 6 ng/ml in plasma (R=-0.23, p=0.003) [11, 12].

In order to increase the informativeness and adequacy of the model, as well as to simplify the use of independent predictors as prognostic factors, some factors were replaced with new ones that were not used by the previous statistical matrix, were calculated deliberately and showed a larger R with the original parameter (Table 2).

Table 1.

Spearman's rank correlation between the total MIDAS-35 score and various clinical, instrumental and biochemical indicators in NSTEMI patients

Total score on the MIDAS-35	Spearman R	P-value
The presence of frequent VE on the 1st day of MI (yes -1, no - 0)	0,25	0,001
The presence of VT paroxysms on the 1st day of MI (yes -1, no - 0)	0,24	0,002
History of smoking (yes - 1, no - 0)	0,29	0,0002
Degree of stenosis of LCx, %	0,31	<0,0001
LA, mm	0,32	<0,0001

Continuation of table 1

LV diastolic dysfunction (1 – impaired relaxation, 2 – pseudonormal type)	-0,22	0,001
ST2 level, ng/ml	0,18	0.02
Association ST2 < 36 ng/ml + Tp I > 6 ng/ml (yes – 1, no – 0)	-0,23	0,003

Thus, such individual variable models as the presence of frequent VE and the presence of VT paroxysms, which characterized the same pathophysiological process, namely the increase in electrical instability of the LV myocardium, were replaced by a total indicator that characterized the presence of frequent VE and/or VT paroxysms in first day of MI (R=0.29, p=0.0002 against previous R – 0.25 and 0.24, respectively).

Table 2.

Endpoints taken for further multiple linear regression analysis of NSTEMI patients' quality of life

Total score on the MIDAS-35	Spearman R	P-value
The presence of ventricular arrhythmias (frequent VE, episodes or paroxysms of VT) on the 1st day of MI	0,29	0,0005
History of smoking (yes - 1, no - 0)	0,29	0,0002
Degree of stenosis of LCx > 70% (yes -1, no - 0)	0,38	<0,0001
LA, mm	0,32	<0,0001
Ve/Va < 1,4 (yes - 1, no - 0)	0,33	<0,0001
ST2 level > 50 ng/ml (yes - 1, no - 0)	0,40	<0,0001

The indicator that characterized the severity of diastolic disturbances (binary indicator) was replaced by a more specific parameter – Ve/Va < 1.4 [15]. The latter was obtained using a serial analysis of the strength of the rank correlation of various values of Ve/Va with the original parameter with the selection of those that had the largest R. The use of the parameter made it possible to increase the strength of the

connection with the original parameter (increase the value of R) and change its sign to +, which simplified data interpretation (R=0.33, p<0.0001 vs. R=-0.22). Similarly, the indicator ST2 > 50 ng/ml in plasma was derived, which replaced such parameters as the quantitative level of ST2 in plasma in ng/ml and the presence of an association ST2 < 36 ng/ml + Tp I > 6 ng/ml with feedback (R=0.40, p<0.0001 vs. R=0.18 and -0.23, respectively) and the CAG indicator of the degree of stenosis of the LCx > 70% instead of the indicator of the quantitative assessment of the degree of stenosis of the LCx in % (R=0.38, p<0.0001 against R=0.31).

The results of the conducted multiple linear regression analysis (Table 3) made it possible to identify informative independent predictors of the QL of NSTEMI patients and calculate the contribution of each predictor (performed by the value of beta) in predicting its level. It should be noted that only those variables that revealed a reliable (p<0.05) linear regression relationship with the original parameter were included in the resulting model.

Table 3.

Results of multiple linear regression of the level of quality of life in NSTEMI patients

Independent predictors	Beta	Std. Error of beta	Koef.	Std. Error of koef	p-value
Intercept	-	-	24,11	2,76	<0,0001
Ve/Va ratio < 1.4 (yes -1, no - 0) (A)	0,22	0,07	6,61	2,43	0,0003
Degree of stenosis of LCx > 70% (B)	0,30	0,06	6,89	2,18	<0,0001
Smoking history (yes -1, no - 0) (C)	0,18	0,07	6,13	2,32	0,009
ST2 level > 50 ng/ml (yes - 1, no - 0) (D)	0,29	0,06	4,53	2,05	<0,0001

Note: Informativeness of the model: multiple R = 0.678; F=6.21; p=0.0001, standard error of estimate = 10.22.

The informativeness of the obtained model was sufficiently high – multiple R = 0.678; Fisher's test (F) = 6.21 and model p = 0.0001, the standard error of the estimate was 10.22. Shown in the table. 3 coef made it possible to create a regression equation, with the help of which it was possible to determine the value of the total score on the MIDAS-35 in NSTEMI patients. The latter looked as follows:

The value of the total score = 24.11 + 6.61A + 6.89B + 6.13C + 4.53D

The obtained regression model showed that the QL of NSTEMI patients depends on the nature of the LV diastolic dysfunction, which is characterized by the ratio Ve/Va < 1.4 (A) (beta = 0.26, p=0.0002). At the same time, the nature of the relationship demonstrates that the level of QL life will depend, first of all, on the severity of the violation of the myocardial relaxation process, which is characterized by the degree of decrease in the value of Ve/Va. It is logical to assume that the more severe the decrease in Ve/Va ratio will be, the more significant the decrease in QL of NSTEMI patients will be.

In addition, the results of the analysis showed that as a predictor of QL one should also consider lesions of LCx > 70% according to CAG data (B) (beta = 0.30, p<0.0001), smoking history (C) (beta = 0.18, p=0.009) and ST2 level in plasma > 50 ng/ml (D) (beta = 0.29, p<0.0001). Analysis data show that a decrease in the QL of NSTEMI patients (characterized by an increase in the score on the MIDAS-35) should be expected in the presence of hemodynamically significant stenoses or occlusion of the LCx, in the case of such a risk factor as smoking and the level of ST in the plasma > 50 ng/ml.

The analysis of the informativeness of independent predictors in predicting a decrease in the QL of NSTEMI patients was carried out using the calculation of the event odds ratio (OR) and confidence interval (CI 95%) (Table 4) and the informativeness of the predictors, which characterized the proportion of positive prediction results using this predictor.

Table 4.

Evaluation of the informativeness of independent predictors in predicting poor quality of life in NSTEMI patients

Independent predictors	QL according to MIDAS-35 > 40 points (n=79)	OR (CI 95%)	Informativeness (%)
A. Ve/Va ratio < 1.4	52	1,93 (1,62; 2,21)	65,8
B. Degree of stenosis LCx > 70%	58	2,76 (2,44; 3,14)	73,4
C. Smoking history	44	1,26 (1,08; 1,50)	55,7
D. ST2 level > 50 ng/ml	60	3,16 (2,92; 3,34)	75,9
Combinations of two predictors			
A or/and B	72	10,3 (8,8; 12,5)	91,1
A or/and C	60	3,16 (2,85; 3,39)	75,9
A or/and D	76	25,3 (23,4; 27,1)	96,2
B or/and C	65	5,42 (5,11; 5,87)	82,3
B or/and D	75	18,8 (15,7; 20,9)	94,9
C or/and D	69	6,9 (4,9; 8,5)	87,3
Combinations of three predictors			
A or B or C	77	38,5 (36,8; 40,7)	97,5
A or B or D	79	-	100
A or C or D	77	38,5 (36,8; 40,7)	97,5
B or C or D	77	38,5 (36,8; 40,7)	97,5

Thus, > 40 points on the MIDAS-35 score were taken as a conditionally low QL criterion. The taken conditional score essentially represented the rounded value of the median of the indicator (37.9 points) calculated for the general group of NSTEMI

patients. At the same time, the number of patients with a total score > 40 points according to MIDAS-35 in our study was 79.

From the data in the table 4, it can be seen that the level of ST2 in plasma > 50 ng/ml should be considered as the most informative independent predictors of low QL of patients (informativeness – 75.9%, OR – 3.16, CI 95% 2.92 - 3.34) and lesions of LCx > 70% according to CAG data (73.8%, OR – 2.76, CI 95% 2.44 - 3.14). The obtained data showed that the use of these predictors in 75.9% and 73.8% of cases, respectively, provides an opportunity to predict the low QL of NSTEMI patients (> 40 points on the MIDAS-35). On the other hand, the obtained data showed that in the presence of the ST2 level in plasma > 50 ng/ml by 3.16 times and the damage of LCx > 70% according to CAG data by 2.76 times, respectively, the chances of low QL in these patients increase.

In turn, taking into account indicators such as the Ve/Va ratio < 1.4 by 1.93 times and such a risk factor as smoking by 1.26 times increases the chances of low QL. Of great interest was the fact that the biochemical marker ST2 allowed predicting low QL in NSTEMI patients with a slightly higher probability than the invasive indicator – LCx lesions.

On the other hand, the data in the table demonstrate that the use of 2 independent predictors (in the or/and format) significantly increases the informativeness of predicting low quality of life in NSTEMI patients. It was established that the highest informativeness of forecasting according to 2 predictors occurred when using the combination of A or/and D – Ve/Va ratio < 1.4 + ST2 level > 50 ng/ml (informativeness – 96.2%, OR – 25.3, CI 95% 23.4 - 27.1), B or/and D – the degree of stenosis of the LCx > 70% + ST2 level > 50 ng/ml (94.9%, OR – 18.8, CI 95 % 15.7-20.9) and A or/and B – ratio Ve/Va < 1.4 + degree of stenosis of LCx > 70% (91.1%, OR – 10.3, CI 95% 8.8 - 12.5). In turn, the least informative was the combination of A or/and C – ratio Ve/Va < 1.4 + history of smoking (75.9%, OR - 3.16, CI 95% 2.85 - 3.39). Thus, the presence of such 2 predictors as the Ve/Va ratio < 1.4 + ST2 level > 50 ng/ml in 25.3 times, the degree of stenosis of LCx > 70% + ST2 level > 50 ng/ml – in 18 .8 times and the ratio Ve/Va < 1.4 + the degree of stenosis of LCx > 70% increase the

risk of low QL in patients with NSTEMI by 10.3 times. It was observed that the combination of two independent predictors, which did not take into account the results of invasive research methods, showed the highest informativeness.

In addition, as evidenced by the obtained data, the inclusion of any three independent predictors in terms of informativeness approached 100%, and in the case of considering such a combination as A or B or D – Ve/Va ratio < 1.4 + LCx stenosis > 70% + ST2 level > 50 ng/ml was effective in all cases without exception (informativeness of the combination 100%).

Thus, the results of the conducted study are convincing that as predictors of reduced QL in patients with NSTEMI, one should consider impaired relaxation of the LV myocardium, which is determined by the value of the Ve/Va ratio < 1.4 according to Doppler-EchoCG data, the nature of the anatomical damage of the CAs, namely stenosis LCx > 70%, according to invasive CAG, the level of biochemical marker ST2 in plasma > 50 ng/ml and the presence of such a risk factor for cardiovascular diseases/complications as smoking.