Exploration of Medicine

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Open Access Original Article

Cognitive impairment in patients with acute myocardial infarction: an assessment of the role of arrhythmic factors

Natalya Akimova*, Ekaterina E. Kutorova, Larisa E. Konshina, Alexander A. Ryabov, Yury G. Shvarts

Federal State Budgetary Educational Institution of Higher Education V.I. Razumovsky Saratov State Medical University of the Ministry of Healthcare of the Russian Federation, 410012 Saratov, Russia

***Correspondence:** Natalya Akimova, Federal State Budgetary Educational Institution of Higher Education V.I. Razumovsky Saratov State Medical University of the Ministry of Healthcare of the Russian Federation, 112 Bolshaya Kazachya str., 410012 Saratov, Russia. astraveritas@yandex.ru

Academic Editor: Hua Su, University of California, USA

Received: November 20, 2024 **Accepted:** February 26, 2025 **Published:** March 14, 2025

Cite this article: Akimova N, Kutorova EE, Konshina LE, Ryabov AA, Shvarts YG. Cognitive impairment in patients with acute myocardial infarction: an assessment of the role of arrhythmic factors. Explor Med. 2025;6:1001295. https://doi.org/10.37349/emed.2025.1001295

Abstract

Aim: A growing body of research suggests that acute myocardial infarction (AMI) may be an independent risk factor for cognitive impairment in patients with cardiovascular disease. The role of premature ventricular contractions (PVCs) or premature atrial contractions (PACs) occurring during the day has not been fully explored in this patient population. The objective of the study was to investigate the clinical and functional relationships between cognitive functions and the severity of daytime premature cardiac contractions, as well as echocardiographic parameters in patients with either old myocardial infarction (OMI) or recent AMI.

Methods: The main group consisted of 32 patients who had experienced an AMI no more than seven days prior. The comparison group included 20 patients who had had one myocardial infarction more than one year earlier. All participants underwent a 24-hour Holter monitoring, Doppler echocardiography. Cognitive testing included the Mini-Mental State Examination, Wechsler Subtests 5 and 7, and the Bourdon Test. Statistical methods included multivariate analysis, univariate analysis of variance, canonical correlation analysis, nonparametric correlation analysis, and multivariate analysis was also performed using the generalized normalized log model.

Results: In the patients of the main group, the characteristics of mental functions were worse than in the control group. The cognitive test scores were significantly correlated with the presence of akinesia zones in the myocardium, as well as with a higher grade of PVCs and a large number of PVCs during the day in patients with AMI. No significant correlations were found between cognitive test results and echocardiographic findings in the comparison group, a weak correlation was only noted between the number of PACs and cognitive test results.

Conclusions: The presence of even non-life-threatening PVCs occurring within 24 hours may be a marker of significant cognitive deficit in the acute period of myocardial infarction.

Keywords

Myocardial infarction, ventricular extrasystole, cognitive disorders, cognitive tests, coronary heart disease

Introduction

The history of research into the issue of morphofunctional interrelationships between the cardiovascular and central nervous systems dates back to 1552 BCE, as evidenced by the Papyrus Ebers, an ancient Egyptian compilation of medical knowledge [1]. Over the past few decades, there has been a significant increase in the interest of researchers in this area, owing to the varied clinical manifestations of cardiovascular disorders, their primary contribution to the structure of morbidity and mortality in the population [2, 3]. The findings from several scientific studies indicate the occurrence and subsequent progression of cognitive impairment (CI) among patients with chronic heart failure (CHF), atrial fibrillation, and, of course, hypertension. Simultaneously, it has been established that these conditions can act as direct contributors to the development of morphological and functional alterations in the central nervous system [4, 5]. One of the primary pathogenic mechanisms underlying the development of CI following myocardial infarction (MI) appears to be a reduction in myocardial contractility, which leads to compromised systemic blood flow and cerebral hypoperfusion. In addition, impaired cerebral perfusion can occur due to myocardial dysfunction, leading to increased venous pressure, impaired cerebrospinal fluid absorption, and its accumulation in cerebrospinal fluid spaces. It is also important to consider other potential causes. Other mechanisms that may contribute to the development of CI in MI and CHF: are increased levels of components of the renin-angiotensin-aldosterone system and changes in the concentration of thrombin/antithrombin complex, which can lead to microembolization of cerebral vessels, as mentioned in scientific literature [6].

According to some research, MI has the potential to induce neuroinflammatory and neurodegenerative processes in the brain, probably through the activation of pro-inflammatory cytokines [7, 8]. However, the potential impact of varying degrees of arrhythmias, such as supraventricular and ventricular extrasystoles, on the development of CIs appears to have been understudied.

Certainly, severe disturbances in cardiac rhythm and conduction of the heart, such as paroxysmal ventricular tachycardia or complete atrioventricular block, often result in acute disturbances of the central nervous system. These disturbances can manifest clinically as Morgagni-Adams-Stokes attacks. However, the issue of whether extrasystole, frequently occurring in individuals with diverse cardiac conditions, may contribute to the progression of pathological neurological alterations remains a subject of exploration within the contemporary medical field. In this context, it appears particularly pertinent to investigate the potential interconnections between brain function and cardiac activity in individuals experiencing acute MI (AMI). As is well-documented, a wide range of cardiac rhythm and conduction abnormalities are frequently observed among this patient population.

To investigate the clinical and functional relationships between cognitive function, the severity of daytime premature contractions, and echocardiographic parameters in patients with a history of single old MI (OMI) and recent AMI.

Materials and methods

The study was conducted in accordance with the requirements of the Helsinki Declaration of the World Medical Association (2013) and the provisions of biomedical ethics, according to the Geneva Convention on Human Rights (1997), approved by the local ethics committee at the Federal State Budgetary Educational Institution of Higher Education "Saratov State Medical University named after V.I. Razumovsky" of the Ministry of Health of Russia.

A total of 52 patients with coronary heart disease were included in the study. These patients were divided into two groups: the main group and the comparison group. All participants had controlled arterial hypertension and compensated CHF II-III functional class (FC) according to the New York Heart Association

(NYHA) functional classification. The main group consisted of 32 patients who had experienced an AMI within the past 7 days. The patients in this group were aged between 42 and 65 years, with an average age of 64 years. Of these, 20 were men and 12 were women. The exclusion criteria for the study were: age over 65, diabetes mellitus, any history of cancer, stroke or transient ischemic attack (TIA), dementia [Mini-Mental State Examination (MMSE) score less than 24], Alzheimer's disease, hemodynamically significant stenosis of the arteries in the head and neck, sick sinus syndrome, the use of psychoactive substances or alcohol, and any other conditions that the opinion of the researcher, can independently influence the development and/or progression of CI. In this study, patients with atrial fibrillation of any type were excluded (the results of Holter monitoring and all patients' historical data were carefully analyzed to detect atrial fibrillation) as it is one of the factors contributing to the development/prognosis of cognitive disorders [9]. Additionally, the study did not include patients with MI complicated by cardiogenic shock, acute heart failure, or life-threatening arrhythmias. The comparison group consisted of 20 patients who had suffered a single MI suffered more than one year ago and were aged between 48 and 65 years (with an average age of 57). Of these, 12 were male and 8 were female. The exclusion criteria for this group were similar to those for the main patient group.

In addition to a general clinical examination, all patients underwent echocardiography (ECHO-CG), which assessed the parameters of the right and left heart chambers. These included the left ventricular end-diastolic dimension (LVEDD), the left atrial end-systolic dimension (LAESD), the left ventricular ejection fraction (LVEF), the local myocardial contractility, and the presence of hypokinetic and akinetic zones. The left ventricular mass index (LVMI) and systolic pulmonary artery pressure (sPAP) were also determined.

Electrocardiography (ECG) and 24-hour Holter monitoring were performed to count the total number of premature atrial contractions (PACs) and premature ventricular contractions (PVCs) per day. The daily distribution of these complexes, as well as the number of right- and left-sided PVCs, was recorded. The gradation of PVCs according to the Lown-Wolff classification, the duration of compensatory pauses, and the coupling intervals of PACs and PVCs were also assessed. Finally, the corrected QT interval was measured.

Neuropsychological research methods were used to evaluate cognitive functions. The cognitive functions were assessed via Wechsler Verbal and Nonverbal Scale of Ability (V and VII subtests) and Bourdon test (Dot Cancellation Test). To exclude dementia, the MMSE scale—a brief scale assessing mental status, was used. Holter monitoring and assessment of the patient's cognitive function were conducted three to four days following the onset of AMI. For the control group of patients, these assessments were also carried out within one day.

Statistical analysis

The statistical analysis was conducted using Statistica 10.0 software. The following statistical techniques were employed: multivariate analysis, univariate analysis of variance (ANOVA), canonical correlation analysis, and non-parametric correlation analysis. Depending on the data type, either the Kendall's Tau or Gamma coefficient was used for non-parametric correlations. Due to the large amount of data analyzed, a multivariate approach using the generalized normalized log model was also utilized, taking into account the Wald criterion.

Results

The main clinical characteristics of the patient groups are presented in Table 1.

There were no significant differences in the clinical, demographic, physical, or gender characteristics of the patients included in the study (Table 1).

The results of the tests evaluating cognitive functions and the main echocardiographic parameters in patients with AMI and those with a single MI more than one year ago (control group) are presented in Table 2. Analysis of variance revealed a number of significant differences in cognitive test parameters between the patients in the main group and the comparison group. Patients with AMI performed worse on Wechsler Subtests 5 and 7 ($p < 0.05$). The Bourdon Correction Test showed that the speed and accuracy of

Table 1. Main clinical characteristics among the examined patient groups

Parameter	Main group (*n* = 32)	Comparison group (*n* = 20)	Significance of differences, *p*
Age (years), Me (25%; 75%)	64 (42; 65)	57 (48; 65)	0.31
Males, *n* (%)	62.5%	60.0%	0.56
Females, *n* (%)	37.5%	40.0%	0.52
Height (cm), Me (25%; 75%)	170 (164; 176)	170 (166; 172)	0.83
Body weight (kg), Me (25%; 75%)	83 (75; 93)	87 (80; 95)	0.59
BMI (kg/m^2), Me (25%; 75%)	28.4 (25.20; 32.39)	30.1 (27.68; 33.25)	0.59
CHF, II FC according to NYHA, *n* (%)	80.6%	78.3%	0.83
CHF, III FC according to NYHA, *n* (%)	19.4%	21.7%	0.83

BMI: body mass index; CHF: chronic heart failure; FC: functional class; NYHA: New York Heart Association; *n*: number; Me (LQ; UQ): data presented as median with low and upper quartiles

their performance, as well as their level of concentration, were lower in patients of the AMI group ($p < 0.05$). No significant differences were found between the quantitative echocardiographic indicators of the two groups during analysis of variance.

Table 2. Indicators of cognitive tests and echocardiographic parameters in the groups of patients examined

Parameter	Main group (*n* = 32)	Comparison group (*n* = 20)	Significance of differences, *p*
Wexler 5, medians and quartiles	7.5 (6.5; 9.0)	10.5 (9.0; 11.5)	0.01
Wexler 7, medians and quartiles	26.5 (23.0; 35.5)	45 (30; 53)	0.01
Bourdon's test (level of attention concentration), medians and quartiles	0.56 (0.22; 0.74)	0.83 (0.093; 0.900)	0.01
Bourdon's test (speed of execution), medians and quartiles	94.21 (80.78; 111.42)	114.65 (89.35; 142.83)	0.03
Bourdon's test (switching of attention), medians and quartiles	41.37 (29.11; 58.33)	30.5 (19.35; 47.22)	0.46
Bourdon's test (accuracy index), medians and quartiles	1.28 (0.83; 2.80)	2 (1.16; 4.28)	0.70
LVMI (g/m^2), medians and quartiles	114 (100; 128)	103.5 (93.5; 121.0)	0.56
LVEF (%), medians and quartiles	58.5 (45; 60)	55 (48; 67)	0.21
LVEDD (cm), medians and quartiles	5 (4.65; 5.45)	5.2 (4.7; 5.5)	0.72
LAESD (cm), medians and quartiles	3.95 (3.65; 4.55)	4.2 (3.85; 4.70)	0.90
sPAP (mmHg), medians and quartiles	32 (27.5; 36.5)	30 (26; 34)	0.25

LVMI: left ventricular mass index; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic dimension; LAESD: left atrial end-systolic dimension; sPAP: systolic pulmonary artery pressure

When conducting a canonical correlation analysis on the main group of patients, a statistically significant and sufficiently strong relationship was identified between the indicators of cognitive tests (results of the Wechsler subtests 5 and 7 and the Bourdon correction test) and ECHO-CG parameters (LVMI, LAESD, LVEDD, sPAP) (R = 0.62; $p = 0.04$). Regarding the comparison group, a similar statistical analysis did not reveal any statistically significant associations between the groups of cognitive test scores and the aforementioned echocardiographic parameters (R = 0.73; $p = 0.40$). Additionally, through paired correlation analysis using the Gamma coefficient, statistically significant relationships between ECHO-CG features and cognitive test results among patients in the main group were identified. Specifically, LVEF was associated with poorer performance on Wechsler subtests 5 and 7 (R = 0.35 and R = 0.30 respectively), as well as lower concentration, attention switching index, and accuracy index in the Bourdon test (R = 0.20; R = 0.27; R = 0.23, respectively).

A negative correlation was observed between the results of the MMSE test and certain ECHO-CG parameters, such as LVEF, LAESD, sPAP, and the presence of areas of local myocardial contractile dysfunction (R = 0.53; R = –0.22; R = –0.27; R = –0.62, respectively). Additionally, paired correlation analysis revealed weak but statistically significant associations: patients with myocardial akinesia areas performed significantly worse on Wechsler Subtests 5 and 7 than patients with hypokinetic zones of the myocardium (R Gamma = 0.31; –0.34). A negative correlation was also found between the Wechsler subtest 5 score and the LAESD score (R Gamma = –0.34).

In the comparison group, weak statistical associations were identified using paired correlation analysis (using the Gamma coefficient). Patients with lower LVEF demonstrated worse results in attention switching and the accuracy index when performing the Bourdon correction test (R = –0.29; R = 0.27, respectively). The results of the MMSE were worse in patients with areas of impaired local myocardial contractility (R = –0.60).

In addition, within the main group of subjects, statistically significant correlations were identified using paired correlation analysis between higher levels of FC CHF and poorer results on cognitive tests, specifically: lower scores on Wechsler Subtests 5 and 7 (R Gamma = –0.56; –0.45, respectively), lower speed on the Bourdon Correction Test (R Gamma = –0.70), and a lower MMSE score (R = –0.68). It should be noted that among patients in the comparison group, only a single correlation was identified between FC CHF and MMSE scores using this analysis (R = –0.60).

When conducting a multivariate analysis including body mass index (BMI), LVEF, LAESD, LVEDD in the model for the main group of patients, we found the following statistically significant relationships: the worst score on the Wechsler subtest 7 was associated with lower LVEF and larger LAESD (p = 0.0008 and p = 0.034, respectively). However, in the comparison group, the multivariate analysis did not reveal any statistically significant relationships between cognitive test scores and echocardiographic parameters.

Thus, patients with AMI have more severe CI than those with single MI that occurred more than one year ago.

The findings from 24-hour Holter ECG monitoring in patients with AMI did not significantly differ from those of the comparison group. This lack of difference may be attributed to the specific selection criteria for the study, including the exclusion of patients with complicated MI [10]. Additionally, patients with arrhythmias (for example, ventricular tachycardia, atrial fibrillation, and others) were also excluded, as these conditions, according to the literature, can significantly affect the clinical condition and hemodynamics of patients [11].

When conducting a paired correlation analysis in the main group of patients several statistically significant relationships were revealed. Specifically, it was found that the higher the total number of PVCs, both during the day and at night, the lower the MMSE score and the lower the concentration of attention when performing the Bourdon correction test at the 6th minute (R Kendall Tau = –0.42; –0.44; –0.41, respectively; R Kendall Tau = –0.25; –0.33, respectively). The higher the gradation of PVCs according to Lown-Wolf, the lower the MMSE and Wechsler subtest 5 (R = –0.34; R = –0.33, respectively). A greater number of PACs, both during the day and at night, was associated with lower results of the Wechsler subtest 5 (R Gamma = 0.41; 0.35; 0.38). A longer corrected QT interval was associated with the lower MMSE score (R = –0.33).

A multivariate analysis with the inclusion of BMI, LVEF, LAESD, and LVEDD in the model among the main group of patients revealed a statistically significant independent association between the number of PVCs, both during the day and night, and the results of the Wechsler Subtest 7 (p = 0.028). In the comparison group, statistically significant weak correlations were revealed during paired correlation analysis: a greater number of PACs was associated with lower scores on the Wechsler 5 and Wechsler 7 subtests (R Kendall Tau = –0.35; –0.24, respectively). Additionally, the higher number of PACs was correlated with the lower MMSE score (R Gamma = –0.33).

When conducting a multivariate analysis, it was determined that the studied parameters of Holter monitoring, ECHO-CG, and cognitive testing in patients with AMI and single OMI did not significantly depend on the patient's age, gender, body weight, or height. Therefore, the findings of the study indicate a negative, moderate although statistically significant correlation between the rate of extrasystolic cardiac arrhythmias and cognitive function in patients with AMI.

Discussion

The findings of the study indicate that MI is an independent risk factor for the development and progression of CI, which is in line with previous literature [12, 13]. It has been demonstrated that the severity of cognitive decline depends on the age of MI (acute or old). Specifically, patients who experience acute phase of AMI have a greater degree of cognitive deficit compared to those with the single MI that is more than one year old. Among other factors, extrasystolic heart arrhythmias (PVCs and PACs) may contribute directly to the formation of cognitive dysfunction in patients after AMI. These arrhythmias are typically considered clinically insignificant, but their severity and frequency throughout the day have been linked to the severity of CI. Conversely, in patients with a history of single OMI, premature cardiac contractions are significantly less linked to CI. Therefore, given the lack of substantial differences between the parameters of 24-hour ECG monitoring in both groups of patients, it becomes evident that extrasystoles, which are clinically insignificant in the context of chronic coronary heart disease, in the acute phase of MI can contribute to the development or progression of cognitive deficit.

One of the possible explanations for this phenomenon may be changes in hemodynamics, both intracardiac and systemic, that occur with premature contraction's heart rhythm disorders. As mentioned above, there is practically no information on studies in the literature of a similar focus. There is only a mention in a few works whose results allow us to assume the nature of pathogenetic interactions between the brain and premature contractions of the heart. In 1999, a research group led by G. Schmidt conducted a study to assess turbulence of heart rhythm, reflecting fluctuations in sinus cycle following PVC (acceleration of sinus rhythm following PVC with subsequent deceleration back to initial values) [14].

Two parameters are proposed: the onset of turbulence (magnitude of sinus rhythm acceleration) and slope of turbulence (intensity of sinus rhythm deceleration). The onset index of turbulence is associated with unrecoverable ion channels in cardiomyocytes at the time of premature ectopic contraction, leading to shortening of an action potential. As a result, it has been established that premature cardiac contractions are associated with incomplete diastolic filling of heart chambers, which leads to a decrease in stroke volume and myocardial contractility according to the Frank-Starling mechanism, causing activation of aortic and carotid baroreceptors and subsequent increase in heart rate. In addition, PVCs are known to be accompanied by a disruption of the synchronous functioning of the ventricles, depending on the location of the PVCs (in the right or left ventricle). Desynchronization of the ventricles contributes to a change in the pressure gradient between them.

Furthermore, intraventricular asynchronism results in a reduction in cardiac output due to the asynchronous contraction of ventricular walls.

Study limitations

It should be noted that in this work we have analyzed data from a relatively small number of patients, and therefore it is necessary to perform a larger study. It is evident that the interactions between local myocardial contractile disorders resulting from MI, arrhythmias, and cognitive dysfunction are more complex than what our study was able to establish using the statistical techniques employed. The causal relationships between these conditions remain unclear. It is possible that the use of artificial intelligence may provide a more accurate understanding of these interactions [15], but a significantly larger volume of data would be required for analysis.

Conclusions

Patients with AMI have more severe CI compared to those with a history of single OMI of more than one year. The severity of CI is associated with the presence and severity of local myocardial contractile dysfunction. The findings of the study suggest that the occurrence of even non-life-threatening PVCs within 24 hours may be an indicator of significant cognitive deficit in acute phase of AMI.

Abbreviations

AMI: acute myocardial infarction

BMI: body mass index

CHF: chronic heart failure

CI: cognitive impairment

ECG: electrocardiography

ECHO-CG: echocardiography

FC: functional class

LAESD: left atrial end-systolic dimension

LVEDD: left ventricular end-diastolic dimension

LVEF: left ventricular ejection fraction

LVMI: left ventricular mass index

MI: myocardial infarction

MMSE: Mini-Mental State Examination

OMI: old myocardial infarction

PACs: premature atrial contractions

PVCs: premature ventricular contractions

sPAP: systolic pulmonary artery pressure

Declarations

Author contributions

NA: Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing—original draft, Writing—review & editing. EEK: Methodology, Investigation, Resources, Writing—original draft. LEK: Visualization, Writing—review & editing. AAR: Data curation, Investigation. YGS: Formal analysis. All authors read and approved the submitted version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 2013 Helsinki Declaration and the 1997 Geneva Convention on Human Rights. The conduct of this study was approved by the local Ethics Committee of the Federal State Budgetary Educational Institution of Higher Education "Saratov State Medical University named after V.I. Razumovsky" of the Ministry of Health of Russia on November 07, 2023, Protocol #7.

Consent to participate

Informed consent to participate in the study was obtained from all participants.

Consent to publication

Not applicable.

Availability of data and materials

The datasets that support the findings of this study are available from the corresponding author on reasonable request. If someone wants to request the data you should contact Natalya Akimova, astraveritas@yandex.ru.

Funding

The work was carried out within the scope of the government commission of the Ministry of Health of the Russian Federation titled "Development of a portable software and hardware complex for remote monitoring of the function of the cardiovascular system, as well as automation of the 6-minute walking test for patients suffering from chronic non-infectious diseases", [No. 056-03-2024-071] dated January 24th, 2024. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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