# EVALUATION OF CARDIAC MRI EFFICACY IN THE DIAGNOSIS OF HIBERNATING MYOCARDIUM

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The efficacy of cardiac MRI in the diagnosis of hibernating myocardium remains understudied. The existing body of evidence on this matter comes mainly from observational studies carried out in heterogenous (in terms of cardiac pathology) cohorts of patients, which complicates the interpretation of the results. The aim of our study was to evaluate the efficacy of cardiac imaging techniques in 144 patients with a history of myocardial infarction, multivessel coronary artery disease and a low ejection fraction of the left ventricle. All participants underwent stress echocardiography and cardiac MRI examinations. The following parameters were factored into: a) the number of identified segments with abnormal myocardial contractility; b) the transmurality index (scar thickness); c) the volume of the viable myocardium relative to its total mass. The study revealed that on average there were 2.72 ± 0.82 segments with contractile dysfunction per patient. Cardiac MRI was able to detect significantly more hibernating segments than stress echocardiography. On average, the difference in the number of detected segments was 36 (56; 86) at 95% CI and $p < 0.01$. We established that as the transmurality index increases, the number of hypokinetic segments decreases ($r = –0.78$; $p = 0.0314$) while the number of akinetic segments ($r = –0.84$; $p = 0.0282$) goes up. This needs to be accounted for when selecting a treatment strategy for such patients. We conclude that cardiac MRI is a more effective and sensitive diagnostic technique in patients with hibernating myocardium that allows detecting significantly more cardiac segments with contractile dysfunction than stress echocardiography. Delayed contrast enhancement is instrumental in estimating the thickness and extent of cardiac fibrosis, the parameters that should be accounted for when deciding on the treatment strategy in such patients.

**Keywords:** hibernating myocardium, cardiac MRI, dobutamine stress echocardiography

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# ОЦЕНКА ЭФФЕКТИВНОСТИ МЕТОДА МРТ СЕРДЦА В ДИАГНОСТИКЕ ДИСФУНКЦИОНАЛЬНОГО МИОКАРДА

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Эффективность метода МРТ сердца в диагностике дисфункционального миокарда в настоящее время до конца не изучена. Это обусловлено тем, что доказательная база основана преимущественно на обсервационных исследованиях, которые отличаются разнородностью изучаемых групп по нозологическим формам, что не позволяет убедительно интерпретировать полученные результаты. Целью исследования была оценка эффективности методов визуализации дисфункционального миокарда у 144 пациентов, перенесших инфаркт миокарда и имеющих многососудистое поражение коронарного русла и сниженную фракцию выброса левого желудочка (ФВ ЛЖ). Для визуальной оценки дисфункционального миокарда всем участникам исследования выполняли стресс-эхокардиографию и МРТ сердца. Критерии оценки эффективности диагностических методов включали: а) количество сегментов с нарушенной кинетикой; б) глубину поражения (индекс трансмуральности); в) объем контрастируемого миокарда в пределах сегмента. По результатам исследования, на одного пациента, в среднем, приходилось 2,72 ± 0,82 сегмента с нарушенной кинетикой. При выполнении МРТ сердца выявлялось достоверно большее количество сегментов с нарушенной сократимостью. Средняя разница по количеству сегментов составила 63 сегмента (56; 82) при 95% ДИ, $p < 0{,}01$. Выявлено, что с увеличением индекса трансмуральности по толщине уменьшается количество сегментов с гипокинезом ($r = –0{,}78$; $p = 0{,}0314$) и увеличивается количество сегментов с акинезом ($r = –0{,}84$; $p = 0{,}0282$), что особенно важно учитывать при выборе тактики лечения таких пациентов. Можно предположить, что МРТ сердца является более эффективным и чувствительным методом диагностики дисфункционального миокарда и позволяет определять достоверно большее количество сегментов с нарушенной сократимостью, по сравнению с методом стресс-эхокардиографии. Методика отсроченного контрастирования позволяет оценить глубину и распространенность кардиального фиброза, что особенно важно учитывать при выборе стратегии лечения больных с дисфункциональным миокардом.

**Ключевые слова:** дисфункциональный миокард, МРТ сердца, стресс-эхокардиография с добутамином

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The prognosis of postinfarction patients with hibernating myocardium largely depends on the timeliness and accuracy of the diagnostic evaluation. Among the diagnostic techniques used to predict the outcomes of this condition are dobutamine stress echocardiography, single-photon emission computed tomography (SPECT), positron emission tomography (PET), and magnetic resonance imaging (MRI) [1].

PET is a reliable prognostic tool in patients with marked heart failure symptoms and a low ejection fraction. Just like SPECT, PET images can be corrected for the attenuation of photons by soft tissues. With these techniques, the turnover of radiolabeled compounds can be easily quantified. In addition, high positron energies generate high-quality images even if patients are obese [2].

However, a wider clinical application of PET is constrained by its high costs and the ultrashort half-life of isotopes. The latter are normally fabricated either on site or close to the facilities where the scan is performed to ensure the quickest shipment possible.

Among the disadvantages of radionuclide-based techniques for the diagnostic evaluation of the myocardium, such as SPECT, is their inability to reliably identify patients with a poor prognosis. No SPECT or PET scanner has been designed yet to have a spatial resolution comparable to that of routinely used ultrasound, X-ray or magnetic resonance imaging machines. Indeed, the 6-mm-resolution scanners are able to identify clinically relevant perfusion and metabolism disturbances. But unlike computed tomography or MRI, these nuclear medicine techniques can "break" the myocardium only into segments but not layers [3]. Besides, currently available radiopharmaceuticals are nonspecific perfusion markers and do not allow discrimination between scars and viable myocardial tissue.

Dobutamine stress echocardiography is a relatively cheap and simple test in comparison with other cardiac imaging techniques. Dobutamine stress echo and SPECT performed after successful revascularization demonstrate similar sensitivity (74–100%); however, the specificity of radionuclide imaging is lower (40–55%) than that of stress echocardiography (77–95%). At the same time, stress echo tends to underestimate the viability of the myocardium, whereas nuclear medicine guarantees more accurate results [4–7].

Because stress echocardiography is used to evaluate myocardial viability while radionuclide cardiac imaging describes the state of cardiomyocyte membranes, these techniques should be regarded as complementary to each other and in some cases are recommended to be used in combination.

The key difference between modern magnetic resonance and radionuclide imaging modalities is that the former is totally safe and provides high spatial resolution [8].

There are two major types of MRI-ECG synchronization protocols; the first type allows visualization of myocardial contraction and relaxation, while the second produces detailed spatial images of myocardial anatomy, its structural layers and morphological components [9]. MRI-ECG synchronization also allows qualitative and quantitative assessment of left/right ventricular regional contractility, providing information on the volume of the intact portion of the cardiac muscle, which is an important factor predicting the course of coronary artery disease (CAD), especially in patients awaiting myocardial revascularization [10, 11].

Delayed contrast-enhanced cardiac MRI with paramagnetic contrast agents helps to identify fibrous tissue and postinfarction myocardial scarring caused by ischemia, inflammation or dystrophy. This technique is suitable for localizing acute myocardial infarction and estimating the size of the lesion; it is also exploited to assess the severity of the postinfarction myocardial fibrosis and to monitor scarring dynamics [12, 13].

Due to its good spatial and temporal resolution, cardiac MRI has become the gold standard in evaluating the global contractility of the left ventricle and detecting regional myocardial contractility abnormalities [14].

Yet the guidelines of the European Society of Cardiology on myocardial revascularization adopted in 2014 recommend high spatial resolution imaging modalities, such as cardiac MRI, only for the purpose of verification of ischemic damage in patients with moderate pretest probability of marked CAD (15–85%) or for the estimation of the volume of scar tissue and contractile reserve. It is emphasized that the diagnostic value of MRI is comparable to that of PET, SPECT and dobutamine stress echocardiography when it comes to estimating myocardial viability and predicting the degree of wall motion recovery [15].

Interestingly, the existing body of evidence on this matter comes from observational studies and meta analyses: randomized trials have solely addressed the efficacy of PET. Besides, clinical trials of MRI efficacy recruit heterogenous (in terms of cardiac pathology) groups of patients, which means that their findings cannot be reliably interpreted.

Considering the abovesaid, there is a need for new research studies aimed to investigate the efficacy of existing techniques for the visualization of hibernating myocardium and to assess their impact on the choice of treatment strategies in a homogenous cohort of patients.

## METHODS

The study was conducted at the facilities of the Second Department of Internal Diseases (Azerbaijan Medical University, Baku) and the Department of Hospital Surgery with a course in Pediatric Surgery (Peoples' Friendship University of Russia, Moscow).

The inclusion criteria were as follows: a history of myocardial infarction; class II–III angina (Canadian Cardiovascular Society grading scale); multivessel coronary artery disease concluded from digital angiography (SYNTAX score of < 32 points); the presence of segments with impaired regional left ventricular contractile function; class I–III heart failure (NYHA classification); the left ventricular ejection fraction (LVEF) < 50%.

Patients with acute coronary syndrome, claustrophobia, implantable cardiac pacemakers or cardioverter defibrillators and those in whom an endovascular intervention was technically impossible were excluded from the study.

Based on the findings of coronary angiography ordered for all the participants, a standard dobutamine stress echo test was recommended to assess myocardial viability in the zones of coronary occlusion.

Regional myocardial contractile function was assessed using a cardiac segmentation model of 17 segments and a 4-point scale; the regional contractility index was calculated as a ratio of the sum scored by each segment of the left ventricle to the total number of analyzed segments. Normal segments scored 1 point; hypokinetic segments, 2 points; akinetic segments, 3 points; dyskinetic ones, 4 points.

The segments were considered viable if their regional contractility improved by 1 or more points. The test was considered negative if no systolic wall thickening was observed following administration of a low dobutamine dose (5–10 mg/kg/min) or if myocardial contractility decreased following administration of a high dobutamine dose (20–40 mg/kg/min).

To visualize myocardial defects, all patients underwent stress echo and cardiac MRI examinations. The obtained images were subsequently analyzed to assess the efficacy of the applied diagnostic techniques.

The following parameters were factored into: a) the number of identified segments with abnormal myocardial contractility; b) the transmurality index (scar thickness); c) the volume of the viable myocardium relative to its total mass.

Cardiac MRI scans were performed on the 1.5 T Magnetom Essenza scanner (Siemens; Germany) synchronized with ECG.

During the scan, the patients were asked to hold their breath on exhale for 6 to 12 s depending on the type of a pulse sequence applied. The contrast agent was injected after precontrast mapping was done and a series of cine, T1- and T2-weighted images was obtained for further cardiac morphology analysis.

Postinfarction fibrosis was estimated by delayed contrast-enhanced MRI using a gadolinium-based paramagnetic agent injected manually.

Ten to fifteen minutes after the contrast agent was injected (2 ml of 0.5 M solution per 10 kg body weight), its accumulation was assessed in a left ventricular segment (corresponding to an ECG segment) with regard to its thickness and volume. The inversion time increment for each successive frame was 10 msec.

The images obtained in the inversion-recovery mode were scrutinized to localize postinfarction fibrosis and gauge its size. Those scars were visualized as hyperintense homogenous areas of delayed washout of the contrast agent, had clear outlines and a typical subendocardial localization.

Using CVI 42 (Circle) and CAAS MRV, the myocardial volume and LF mass were quantified semiautomatically from the short-axis slices of the left ventricle. LF contractility, the amount of scar tissue and the volume of viable myocardial tissue that was not accumulating the contrast agent were also evaluated.

Transmurality of the left ventricle was calculated as a ratio of the maximum wall thickness accumulating the paramagnetic agent to the myocardial thickness in a given segment; we also calculated the volume of the myocardium within the segment (%) accumulating the contrast agent.

Statistical data processing was done in MS Statistica 10.0. We performed dispersion, correlation, regression, discriminant and contingency analyses applying parametric and nonparametric tests. Contingency tables were analyzed using Pearson's $\chi^2$; multiple comparisons were done using the F-test and the Newman–Keuls test. Qualitative parameters were compared by the Mann–Whitney U-test.

## RESULTS

Our study recruited a total of 144 patients. The time between infarction and the study was 3 to 18 months (7.7 ± 3.3 months on average).

Clinical, demographic and angiographic characteristics of the patients are presented in Tables 1 and 2.

Table 3 features diagnostic tools used in the study and the number of hibernating segments detected by each tool.

On average, there were 2.72 ± 0.82 hibernating segments per patient. Cardiac MRI was able to detect significantly more segments with contractile dysfunction than stress echocardiography. Specifically, cardiac MRI was more successful in detecting hypo- and akinetic segments than stress echo. On average, the difference in the number of detected segments was 36 (56; 86) at 95% CI and $p < 0.01$.

Images obtained from cardiac MRI with delayed enhancement were analyzed and the transmurality index was calculated, as well as the volume of the myocardial segment accumulating the paramagnetic agent. Based on the transmurality index value, the patients were distributed into a few subgroups: 0.3–0.4, subendocardial accumulation of the paramagnetic agent ($n$ = 25); 0.4–0.5, intramural accumulation (postinfarction fibrosis) ($n$ = 107); over 0.5, transmural accumulation ($n$ = 12). The myocardial volume that actively accumulated the contrast agent in a given segment indicated myocardial fibrosis. Its extent is expressed below as percentage: 20–30% in 54 patients; 30–40% in 52 patients; 40–50% in 23 patients, and over 50% in 12 patients.

We established a negative correlation between the thickness of myocardial scarring and the type of regional contractility dysfunction (Table 4). As the transmurality index increases, the number of hypokinetic segments decreases ($r$ = –0.78; $p$ = 0.0314) while the number of akinetic segments ($r$ = –0.84; $p$ = 0.0282) goes up. This needs to be accounted for when selecting a treatment strategy for such patients.

Interestingly, we did not reveal a correlation between the severity of myocardial fibrosis (the myocardial volume accumulating the contrast agent in a given segment) and global myocardial contractility (Table 5), which leads us to conclude that the severity of myocardial fibrosis has no effect on the global contractility of the myocardium.

**Table 1.** Clinical and demographic characteristics of patients

| Parameter | *n* = 144 | |
|---|---|---|
| | Abs. | % |
| Number of men | 96 | 66.7 |
| Number of women | 48 | 33.3 |
| Mean age | 58.4 ± 9.8 | |
| Mean interval post-myocardial infarction | 7.7 ± 3.3 | |
| FC 2 angina | 52 | 36.1 |
| FC 3 angina | 60 | 41.7 |
| FC 4 angina | 32 | 22.2 |
| Hypertensive disease | 108 | 75 |
| Type 2 diabetes mellitus | 32 | 22.2 |
| Heart failure (NYHA)<br>FC I<br>FC II<br>FC III | <br>19<br>90<br>35 | <br>13.2<br>62.5<br>24.3 |
| Smoking | 76 | 52.8 |
| High cholesterol | 98 | 68.1 |
| History of ACVE | 12 | 8.3 |
| Arrhythmias and conduction disturbances | 78 | 54.2 |

**Note:** FC — functional class, ACVE — acute cerebrovascular event.

**Table 2.** Angiographic characteristics of patients

| Type of vascular disorder | *n* = 144 | |
|---|---|---|
| | Abs. | % |
| Double vessel disease | 48 | 33.3 |
| Triple vessel disease | 56 | 38.9 |
| Bifurcation stenosis | 28 | 19.4 |
| Ostial stenosis | 12 | 8.3 |
| Arteries involved | | |
| ADA stenosis | 70 | 48.6 |
| CA stenosis | 32 | 22.2 |
| RCA stenosis | 42 | 29.2 |

**Note:** ADA — anterior descending artery; CA — circumflex artery; RCA — right coronary artery.

**Table 3.** The number of cardiac segments with impaired regional contractility

| Contractile dysfunction | Number of segments | | Number of discrepancies | *p* |
|---|---|---|---|---|
| | Cardiac MRI | Stress echocardiography | | |
| Hypokinesis | 224 | 186 | 38 | 0.002 |
| Akinesis | 175 | 154 | 21 | 0.024 |
| Dyskinesis | 6 | 8 | 2 | 0.322 |
| Total | 405 | 348 | 61 | 0.017 |

**Note:** $p < 0.05$ indicates statistical significance of differences.

**Table 4.** The correlation analysis of scar thickness and regional contractility

| Contractile dysfunction | Transmurality index (scar thickness) | | | *p* |
|---|---|---|---|---|
| | 0.3–0.4 ($n = 25$) | 0.4–0.5 ($n = 107$) | over 0.5 ($n = 12$) | |
| Hypokinesis[1] | 65 | 142 | 17 | 0.0314 |
| Akinesis[2] | 8 | 169 | 28 | 0.0282 |

**Note:** $r^1 = -0.78$; $r^2 = -0.84$.

**Table 5.** The correlation analysis of fibrosis extent (%) and global myocardial contractility parameters

| Global myocardial contractility parameters | Volume of the myocardial segment accumulating the contrast agent (%) | | | | *p* |
|---|---|---|---|---|---|
| | 20–30 ($n = 54$) | 30–40 ($n = 52$) | 40–50 ($n = 23$) | over 50 ($n = 12$) | |
| EDV (ml) | 149.2 ± 3.7 | 146.4 ± 3.2 | 150.8 ± 3.3 | 154.2 ± 3.8 | 0.632 |
| ESV (ml) | 71.4 ± 0.9 | 68.2 ± 0.7 | 68.8 ± 0.8 | 64.8 ± 0.8 | 0.824 |

**Note:** for EVD $r = 0.01$; for ESV $r = 0.01$.

## DISCUSSION

The extent of myocardial fibrosis in patients with a history of myocardial infarction is an objective prognostic criterion in patients awaiting surgical revascularization that can predict its outcome [10].

The technique planned for surgical revascularization should account for post-infarction structural changes in the myocardium such as ventricular aneurisms or mural thrombi. These sequelae of infarction determine the necessity of surgery on the coronary arteries or the lack of thereof. There is no point in recovering the blood flow in the area of extensive unviable postinfarction fibrosis. But it is necessary to measure the volume of the myocardium that has a potential to restore its contractility after revascularization [13, 15].

Despite relative safety and high informative value of cardiac MRI performed to assess heart morphology, function and structural changes, this modality does not enjoy wide application and is considered an ancillary technique that helps to decide on the strategy of revascularization in difficult cases.

In the course of our study we analyzed the findings of stress echocardiography and MRI in a cohort of postinfarction patients with hibernating myocardium who had not received a timely revascularization surgery on the involved artery and developed multivessel coronary artery disease in the background of reduced global myocardial contractility.

The obtained data were analyzed in an attempt to find correlations between the depth and extent of postinfarction fibrosis and the types of contractility defects, as well as global contractility of the myocardium. These parameters are crucial and should be estimated prior to surgical revascularization as they help to optimize the treatment strategy in patients with hibernating myocardium.

## CONCLUSIONS

Cardiac MRI is an effective and sensitive diagnostic technique in patients with hibernating myocardium that reliably detects more segments with contractile dysfunction that stress echocardiography. Delayed contrast enhancement allows assessment of scar thickness and is instrumental in visualizing subendocardial nontransmural myocardial lesions as small as 2–3 mm in size, which is an impossible ask for echocardiography. The established negative correlation between the thickness of myocardial scarring and the type of regional contractility dysfunction demonstrates that as the transmural index grows, the number of hypokinetic segments goes up, while the number of akinetic segments decreases. No correlation was found between the severity of myocardial fibrosis (the myocardial volume accumulating the contrast agent in a given segment) and global myocardial contractility (end-diastolic and end-systolic volumes).

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