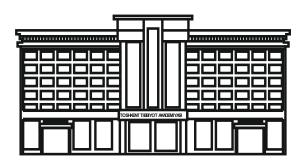
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ВЕСТНИК

ТАШКЕНТСКОЙ МЕДИЦИНСКОЙ АКАДЕМИИ

Тошкент





Выпуск набран и сверстан на компьютерном издательском комплексе

редакционно-издательского отдела Ташкентской медицинской академии

Начальник отдела: М. Н. Аслонов

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Компьютерная корректура: З.Т. Алюшева

Учредитель: Ташкентская медицинская академия

Издание зарегистрировано в Ташкентском Городском управлении печати и информации Регистрационное свидетельство 02-00128

Журнал внесен в список, утвержденный приказом № 201/3 от 30 декабря 2013года

реестром ВАК в раздел медицинских наук
Рукописи, оформленные в соответствии
с прилагаемыми правилами, просим направлять
по адресу: 100109, Ташкент, ул. Фароби, 2,
Главный учебный корпус ТМА,

4-й этаж, комната 444. Контактный телефон: 214 90 64 e-mail: rio-tma@mail.ru rio@tma.uz

Формат 60х84 1/8. Усл. печ. л. 9,75.

Гарнитура «Cambria». Тираж 150. Цена договорная.

Отпечатано на ризографе редакционно-издательского отдела ТМА. 100109, Ташкент, ул. Фароби, 2.

Вестник ТМА №4, 2024

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4 ISSN2181-7812 www.tma-journals.uz

MYOCARDITIS IMAGING IN PREGNANCY

Karimov Ah.Kh., Tukhtabaev A.A.

ВИЗУАЛИЗАЦИЯ МИОКАРДИТА ПРИ БЕРЕМЕННОСТИ

Каримов А.Х., Тухтабаев А.А.

ХОМИЛАРЛИКДА МИОКАРДИТНИ ТАСВИРЛАШ УСУЛЛАРИ

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Описаны особенности выполнения и интерпретации результатов методов лучевой диагностики при миокардите у беременных. Учитывая специфику контингента пациенток, в методических рекомендациях МРТ сердца рассматривается как основной метод визуализации. Представлены основные режимы МРТ, используемые при миокардите, и критерии диагностики. МРТ сердца можно назвать ключевым методом визуализации и диагностики в целом у беременных с миокардитом, поскольку разработанные критерии позволяют с достаточно высокой точностью подтвердить диагноз, не прибегая к биопсии.

Ключевые слова: миокардит, беременность, визуализация; MPT.

Мақолада хомиладор аёлларда миокардит учун рентгенологик диагностика усулларини бажариш ва натижаларини шархлаш хусусиятлари тасвирланган. Бемор контингентининг ўзига хос хусусиятларини хисобга олган холда, кўрсатмалар юрак магнит-резонанс томографиясини (МРТ) асосий тасвирлаш усули сифатида кўриб чиқади. Миокардит учун ишлатиладиган асосий МРТ усуллари ва диагностика мезонлари келтирилган. Миокардит билан оғриган хомиладор аёлларда юрак МРТни визуализация ва ташхиснинг асосий усули деб аташ мумкин, чунки ишлаб чиқилган мезонлар биопцияга мурожаат қилмасдан ташхисни жуда юқори аниқлик билан тасдиқлаш имконини беради.

Калит сўзлар: миокардит, хомиладорлик, визуализация, MPT.

Myocarditis is a significant cause of sudden cardiac death in young individuals, accounting for up to 12% of cases according to the findings of pathological studies. Timely identification of myocarditis can influence the choice of tactics and treatment methods for patients and the prognosis of the disease. Therefore, it is crucial for diagnostic imaging specialists to understand the role of cardiac imaging in diagnosis and treatment decision-making [1,3,5].

Taking into account the above, as well as data from various publications [8,12,17] dedicated to this issue, a conclusion can be drawn that the most optimal method of diagnostic imaging, allowing confirmation of myocarditis diagnosis in pregnant women and simultaneously not contraindicated, is magnetic resonance imaging (MRI).

The aim of this article is to justify and provide a detailed description of MRI diagnostic criteria for myocarditis that can be used to confirm the diagnosis in pregnant women.

General principles of diagnosing myocarditis in **pregnant women.** Endomyocardial biopsy is still considered the gold standard for establishing a definitive diagnosis of myocarditis. However, it is infrequently performed due to the invasive nature of the procedure, associated risks, and lower sensitivity compared to cardiac explantation at autopsy. Endomyocardial biopsy is usually indicated only when there is clinical evidence that the results will significantly impact the physician's decisions regarding the choice of tactics and treatment method. The Dallas criteria, requiring histological confirmation of inflammatory infiltrates in the myocardium associated with myocyte injury and/or non-ischemic necrosis, are typically used when performing endomyocardial biopsy for a conclusive diagnosis.

New proposed criteria rely on immunohistochemical methods that may be more sensitive. In clinical practice, diagnostic criteria based on expert consensus are more commonly used to suspect myocarditis. Cases are considered suspicious of acute myocarditis when there is at least one clinical criterion and/or at least one diagnostic criterion. Clinical criteria include acute chest pain, shortness of breath, unexplained episodes of arrhythmia, syncope, and episodes of sudden cardiac death or non-ischemic cardiogenic shock. Diagnostic criteria include abnormalities on electrocardiography, Holter monitoring, or stress testing, elevated troponin levels, functional and structural anomalies detected by cardiac imaging methods, and characteristic signs of tissue edema and/or late gadolinium enhancement (LGE) on cardiac MRI [2,4,6,14].

Cardiac MRI can be used to confirm any of the latter two criteria, emphasizing the crucial role of visualization in the diagnosis of acute myocarditis. Radiological study results can also be helpful in determining or ruling out other potential diagnoses with a similar clinical presentation, including acute coronary syndrome or stress-induced cardiomyopathy. In some cases, visualization results may indicate a specific potential cause of myocardial damage, although there is significant overlap in imaging results between myocarditis with different etiologies [3,5,9,11].

The American College of Cardiology recommends conducting diagnostics in patients with signs typical of myocarditis using one or more imaging methods.

Echocardiography. Echocardiography is often the preferred method in the diagnostic process of myocarditis, as it is widely available and allows for a relatively quick assessment of heart size and function. These characteristics make echocardiography the most optimal method for use in pregnant women. Typical signs identified during echocardiography include increased myocardial thickness, changes in echogenicity, impairment of global systolic function, regional wall motion abnormalities, and ventricular dilation. Despite these relatively nonspecific features, echocardiography provides important prognostic information regarding left ventricular (LV) enlargement and deterioration of its function, serving as predictors of unfavorable outcomes in patients [10,11].

Computer Tomography (CT). The use of CT is limited in pregnant women due to radiation exposure. Coronary CT angiography is a non-invasive imaging method that can be useful for excluding coronary artery patency issues in patients with acute chest pain and elevated troponin levels, thanks to its high negative prognostic value. In later stages, contrast agents may be useful for assessing myocardial damage, especially in patients with contraindications to MRI, although data on its application in cases of acute myocarditis are limited [7,8,14].

Positron Emission Tomography (PET). PET using fluorodeoxyglucose has proven effective in evaluating active myocardial inflammation. Limited available data demonstrate that PET with fluorodeoxyglucose can also detect inflammation in the context of acute myocarditis. PET is usually performed in conjunction with CT for anatomical localization, although combined PET/MRI scanners have recently emerged, providing additional information from both modalities in patients with myocarditis. However, the use of PET in pregnant women is extremely limited due to radiation exposure [2,6,15].

MRI. In terms of diagnosis in pregnant women, cardiac MRI is the most important non-invasive imaging method for diagnosing, monitoring, and stratifying risk in patients with non-ischemic myocardial involvement, as it has extremely high potential for assessing myocardial tissue changes. According to the recommendations of the American Heart Association, the American College of Cardiology, the American Society of Echocardiography, the American College of Physicians, the Society of Academic Emergency Medicine, the Society of Cardiovascular Computed Tomography, and the Society of Cardiovascular Magnetic Resonance in the 2021 Chest Pain Evaluation and Diagnosis Guidelines, cardiac MRI is the most effective method for differentiating myocarditis from other pathologies causing acute chest pain in patients related to non-ischemic cardiac pathology [2-4,11]. Cardiac MRI is also useful in patients with suspected myocarditis or myopericarditis when there is diagnostic uncertainty or to determine the presence and extent of myocardial or pericardial inflammation and fibrosis [18,19].

Updated Lake Louise Criteria. MRI signs of myocardial inflammation are typically assessed using the guiding principles of expert consensus, the Lake Louise Criteria (LLC), first published in 2009. These criteria were widely used in clinical practice, although their evaluation was limited due to subjectivity in qualitative assessment and moderate diagnostic sensitivity. The LLC were revised in 2018 to incorporate parametric mapping, allowing for the quantitative assessment of regional and overall relaxation times on T1 and T2 of the myocardium and extracellular volume (ECV). Compared to the original LLC, the revised

criteria have significantly higher sensitivity while maintaining very high specificity [4,5,13,14,16].

According to the revised criteria, cardiac MRI provides compelling evidence of acute myocardial inflammation in patients with a high clinical probability of a preliminary diagnosis if at least one criterion in each of the following two categories is positive: a marker based on myocardial edema on T2 and a marker based on myocardial injury on T1. The presence of only one marker can still confirm the diagnosis of myocardial inflammation in the corresponding clinical context, albeit with lower specificity. It is important to note that these criteria are intended for use in patients with clinical suspicion of myocardial inflammation and should not be widely used as a screening test for detecting myocardial injury in asymptomatic patients [8,10,12,15] (Fig. 1).

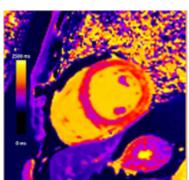
Criteria based on myocardial edema features on T2 images. Myocardial edema is a characteristic sign of inflammation, often identified in cases of myocarditis, although diffuse edema can also be determined. T2-based criteria for myocardial edema include regional high signal intensity ratio on T2-weighted images, global signal intensity ratio on T2-weighted images equal to or greater than 2.0, or regional or global increase in T2 myocardial relaxation time. The assessment of myocardial edema in cardiac MRI was previously based on T2-weighted images, which have high diagnostic accuracy for local edema, although image quality may be compromised by artifacts and signal inhomogeneity, limiting reproducibility. T2 mapping allows for the direct quantitative assessment of relaxation time on T2 and is particularly useful for ruling out active inflammation due to its very high sensitivity (89%). High signal intensity on T2 is specific to increased water content in tissues, thus contributing to the differentiation of the active phase and resolution phase in myocarditis [9,10,14,15].

Criteria based on myocardial injury on T1. If myocardial inflammation is severe enough, it can lead to myocardial injury and necrosis, ultimately resulting in fibrosis. T1-based criteria for myocardial injury include the presence of late gadolinium enhancement (LGE) - signal enha-cement in the late phase after gadolinium administration, regional or global increase in native T1 values, or myocardial extracellular volume (ECV) [17,19].

The depiction of LGE remains one of the most crucial MRI methods in cases of suspected myocarditis since the presence of myocardial injury is a characteristic feature of myocarditis. Gadolinium-based contrast agents are retained in damaged and necrotic tissue, leading to hyperintensity on T1-weighted inversion-recovery images. The LGE pattern in myocarditis patients typically has a subepicardial or midmyocardial nature and often exhibits a linear configuration. In contrast, the LGE pattern in ischemic myocardial injury is subendocardial or transmural, corresponding to the territory of a coronary artery. The most common location of LGE in viral myocarditis is the basal inferolateral wall. Other segments frequently involved include the basal anterior septum, mid posterior wall, and basal to mid inferior wall. Transmural enhancement and more diffuse LGE have been described, especially in severe cases of fulminant and giant-cell myocarditis [2,5,18].

Main criteria

Signs of edema on T2, high signal intensity on T2 images



Signs of myocardial damage on T1. Increased ECV (extracellular volume)

Widening of the pericardial shadow, a sign of pericarditis.

Additional criteria

Local or global hypokinesia. Signs of

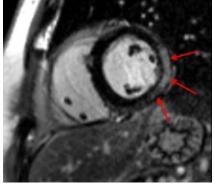
systolic dysfunction.

If patients are likely to have a diagnosis based on clinic: The presence of one of the main T1 and T2 criteria - a high level of evidence; The presence of one of T1 or T2 criteria - medium level of evidence; Additional criteria are not mandatory, but increase the likelihood of diagnosis.

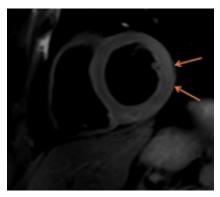
Fig. 1. Lake Louise criteria.

The specific LGE pattern is present in both acute inflammation (with myocyte necrosis and hyperemia) and fibrosis (due to the expansion of interstitial space) and, therefore, cannot serve as a reliable criterion for differentiation between the acute process and convalescence in myocarditis. Over time, the degree of LGE usually decreases as inflammation resolves and scar tissue contracts. T1 ECV is increased in cases of interstitial and replacement myocardial fibrosis. T1 is a composite measurement reflecting signals from both cellular (mainly myocytes) and extracellular (mainly interstitial) myocardial compartments, while ECV is an assessment of the fraction of extracellular space. These parametric mapping techniques may have additional diagnostic and prognostic value beyond LGE, especially in cases of diffuse inflammation, thanks to the ability to directly quantitatively measure changes in myocardial tissue. T1 ECV is also increased in myocardial edema; however, unlike the elevation on T2, these changes are not specific to acute inflammation.

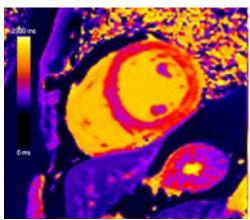
Considering the additional information provided by T1 and T2 mapping, it is useful to interpret these values together. For example, in a patient with suspected myocarditis, corresponding elevated ECV values on both T2 and T1 indicate a high likelihood of myocardial edema, while increased ECV values on T1 with normal T2 conditions suggest the presence of fibrosis or infiltration without acute inflammation [4,8,12-14] (Fig. 2).



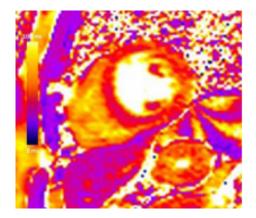
On LGE signs of subepicardial and transmural edema (shown by red arrows)



Enhanced T2 signal in areas of tissue edema (orange arrows)



Increased focal signal at T1 (1480 msec)



Increased focal signal on native T2 mode (56 msec)

Fig. 2. Clinical examples of cardiac damage due to myocarditis according to MRI.

Left ventricular dysfunction. In more severe cases of myocarditis, MRI can reveal regional wall motion abnormalities and signs of left ventricular (LV) systolic dysfunction. LV systolic dysfunction, both regional and global, is a confirming criterion for myocarditis but is not mandatory for diagnosis according to the revised Lake Louise Criteria (LLC). After an acute myocarditis episode, global systolic function often rapidly resolves, and in most cases, indicators return to normal. Systolic dysfunction is typically more severe in cases of fulminant myocarditis, and despite frequent improvement in the acute period, LV function remains lower on average compared to non-fulminant cases in the long term. Quantitative measurement of myocardial deformation may increase sensitivity in assessing subtle wall motion abnormalities, but such studies have not been routine in clinical practice to date [18,19].

Pericardial Inflammation. Signs of pericardial inflammation are also considered confirmatory for the diagnosis of myocarditis and include pericardial signal enhancement, high values on T1 or T2 mapping, or the presence of fluid in the pericardial cavity. Pericardial involvement is most often observed in areas adjacent to inflamed myocardial regions, although it can also be diffuse [6,8,11].

MRI markers of adverse outcomes. The presence of late gadolinium enhancement (LGE) is a robust, independent predictor of cardiac and overall mortality in myocarditis patients. The risk of severe cardiovascular complications increases by approximately 80% with a 10% increase in the quantitative extent of LGE. It is noteworthy that the presence of LGE in combination with hyperintensity on T2 is associated with a more favorable prognosis compared to isolated LGE without T2 hyperintensity. This is likely because LGE without accompanying edema typically reflects fibrosis, which is irreversible, whereas LGE in the context of T2 hyperintensity suggests the possibility of at least partial recovery, as edema may decrease over time. Other important adverse prognostic markers on MRI include global systolic dysfunction (left ventricular ejection fraction less than 40%) and higher signal intensity on T1, as well as ECV [3,7,11,12].

MRI follow-up protocol. For patients with acute myocarditis showing signs of myocardial edema and/ or LV dysfunction in the initial examination, a follow-up cardiac MRI may be considered at 3-6 months to assess the degree of functional recovery and the potential formation of residual scar tissue [7,8].

Cardiac MRI protocol for pregnant women with myocarditis. When myocarditis is suspected, the MRI protocol should include short- and long-axis cine sequences to assess ventricular volumes and function, T2based imaging (T2-weighted black and white images and/or T2 mapping), and T1-based imaging (LGE and/ or T1 mapping before and after contrast enhancement). An important consideration for the evaluation of parametric maps is that values significantly vary depending on technical factors and certain patient characteristics, including field strength. T2 values are higher when using 1.5 T systems compared to 3 T, while T1 values are significantly higher at 3 T compared to 1.5 T. Therefore, mapping values should be compared with normative ranges. Maps should be evaluated both visually and quantitatively, including a global assessment of diffuse tissue changes along with a focal assessment of myocardial segments that appear visually abnormal or demonstrate regional wall motion abnormalities. For optimal diagnostic efficiency, MRI should be performed during the active phase. MRI findings in myocarditis typically demonstrate rapid and continuous improvement in the first few weeks after the onset of symptoms. Sensitivity for detecting myocardial edema significantly decreases if patients undergo examination several weeks after the initial clinical manifestation of the disease. Establishing a diagnosis of myocarditis in the non-acute phase is particularly challenging, as findings are often nonspecific [10,11,17,19].

Thus, cardiac MRI can be considered a key method for diagnostic visualization and overall diagnosis in pregnant women with myocarditis, as the developed criteria allow for confirming the diagnosis with relatively high accuracy without resorting to biopsy.

MYOCARDITIS IMAGING IN PREGNANCY

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This article describes the specifics of performing and interpreting results in diagnostic imaging of myocarditis in pregnant women. Taking into account the specifics of the patient population, the methodological recommendations consider cardiac MRI as the main imaging method.

The main MRI modalities used for myocarditis and diagnostic criteria are presented. Cardiac MRI can be called a key method of diagnostic imaging and diagnosis in general for pregnant women with myocarditis, since the developed criteria allow us to confirm the diagnosis with fairly high accuracy without resorting to a biopsy.

Key words: myocarditis, pregnancy, visualization; MRI.

