Value of Cine-MRI sequences before and after injection in the diagnosis of acute myocarditis

Apport diagnostique des séquences Ciné-IRM avant et après injection dans la myocardite aigue

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RÉSUMÉ

Introduction: L'IRM cardiaque est devenue l'examen de choix en cas de suspicion de myocardite aigue. La séquence du rehaussement tardif est une séquence clé pour établir ce diagnostic. Les séquences Ciné-IRM sont utiles pour l'étude de la contractilité myocardique.
But: Evaluer l'intérêt des séquences ciné-IRM avant et après injection pour le diagnostic de myocardite aiguë comparativement à la séquence du rehaussement tardif.
Méthodes: 40 patients ayant une forte suspicion de myocardite aiguë ont été explorés par une IRM cardiaque 1.5 Tesla. Des séquences Ciné-IRM avant et après injection ont été réalisées. Le protocole comportait également des séquences "triple-inversion-récupération" T2 et du rehaussement tardif (RT) huit minutes après injection avec ajustement visuel du temps d'inversion (Ti).
Résultats: le rehaussement tardif était trouvé chez 23 patients. Quinze patients (65%) présentaient un hypersignal spontané détecté visuellement sur les séquences Ciné-IRM avant injection et 11 patients (48%) sur la séquence " triple-inversion-récupération" T2.
L'hypersignal sur les séquences Ciné-IRM après injection précoce de gadolinium était de même topographie que le RT chez les 23 patients. Nous avons mis en évidence une relation statistiquement significative entre cet hypersignal avant injection et la fraction d'éjection du ventricule gauche ainsi qu'avec le volume télésystolique du ventricule gauche indexé à la surface corporelle (p=0,039).
Conclusion: La séquence Ciné-IRM avant injection est de performance égale à la séquence du RT pour établir le diagnostic de myocardite aiguë. Son apport est important pour raccourcir la durée de l'examen ou en cas de Ti non optimal.

Mots-clés

SUMMARY

Background :Cardiovascular magnetic resonance (CMR) has become the examination of choice in case of suspicion of acute myocarditis. Late gadolinium enhancement (LGE) imaging is very important to establish this diagnosis. Cine MRI sequences are useful for the study of the myocardial contractility.
Aims: The purpose is to estimate the value of cine MRI sequences before and after injection for the diagnosis of acute myocarditis compared with late gadolinium enhanced sequences.
Methods: We prospectively included 40 patients having a high suspicion of acute myocarditis and examined using a 1.5 Tesla CMR. Cine MRI sequences before and after injection were performed. The protocol also include T2-weighted short- tau-inversion-recovery (STIR T2) fast spin echo MRI and LGE imaging eight minutes after injection with visual adjustment of inversion time.
Results: Delayed enhancement was found among 23 patients. Fifteen patients (65 %) presented a spontaneous hyper signal detected visually on Cine MRI sequences before injection and 11 patients (48 %) on STIR T2.
The hyper signal on Cine MRI sequences after injection of gadolinium was the same topography that the late raising at 23 patients. In addition, we highlighted a significant difference between this hyper signal before injection and the left ventricle ejection fraction (p=0.022) as well as with the telesystolic volume of the left ventricle (LV) indexed by the body mass (p=0.039).
Conclusion: Our study suggests that Cine MRI sequences after injection are of equal performance in the diagnosis of acute myocarditis as the LGE sequences and its contibution is important when we want to shorten the examination or when inversion time isn't optimal.

Key-words
Myocarditis, cine MRI, late gadolinium enhancement

Cardiovascular magnetic resonance (CMR) has become the primary tool to highlight signs of myocardial inflammation in patients with suspicion of acute myocarditis (1). Late gadolinium enhancement imaging (LGE) is a key sequence for the diagnosis by highlighting enhancement of the subepicardium and/or midwall sparing endocardium. Cine MRI sequences are used to study the myocardial contractility. Besides theses sequences benefit from an excellent signal to noise ratio, they allow a good study of the contrast between the healthy and the pathological myocardium.
The purpose of our study is to compare the efficiency of these sequences with the late gadolinium enhancement imaging.

METHODS

Study design: This was a prospective observational study.

Study Population: The study prospectively recruited 40 patients (28 males) aged 35.75 +/- 13.31 years, who were prospectively enrolled between January 2013 and January 2016 referred to our department for the realization of a CMR with presumptive diagnosis of acute myocarditis. All studies were performed according to the guidelines of the hospital on medical ethics and clinical investigation. All patients gave written consent for the study. The criteria of inclusion were symptoms and clinical signs suggesting an acute myocarditis (chest pain, dyspnea, palpitations) with revealing of a myocardial suffering on the data of the electrocardiogram (modification of the ST segment) and/or rise of the blood rate of troponin and normal coronary angiography. The average duration between symptom onset and MRI exam was of 7.4 days±4.3 (extremes varying between 1 and 14 days).

CMR: All CMR studies were performed on a 1.5 Tesla unit General Electric Medical Healthcare using an eight-element phased array cardiac coil and electrocardiogram was triggered during all the examination. After sequences of localization in echo of gradient, we performed Cine SSFP (Steady State Free Precession) in short axis, long axis two and four chamber views, and morphological sequences “dark blood” in T2-weighted short–tau-inversion-recovery in short-axis view. After intravenous injection of 0.2 mmol/kg body weight of gadolinium (gadoteric acid, Dotarem, Guerbet, France) injected into a flow of 4 ml/second pulsed by the same quantity of salt solution, we made Cine sequences MRI in long axis two and four chamber views as well as sequences of late gadolinium enhancement. For the study of delayed enhancement we performed an acquisition T1 Fast Gradient Echo (FRGE) in 2 D in inversion-recovery with saturation of the signal of the fat to delete (eliminate) the signal of the healthy myocardium and highlight zones with late uptaking of contrast. A preparation of the magnetization was performed by means of an impulse of inversion-recovery followed by a deadline of time inversion. The inversion time was adjusted for each patient visually by the radiologist for optimal suppression of normal myocardial signal. Inversion time varied between 200 and 400 ms. These sequences were performed 8 minutes after injection in short-axis, and long axis four chamber views of the left ventricle. The average duration of the examination was of 45 minutes. The parameters of acquisition were summarized in Table 1.

Table 1 : CMR sequences

Sequences	TE (ms)	TR (ms)	Matrix	Slice thickness/ gap (mm)	Flip angle
T2 STIR	80	1100	256*256	8/1	90°
SSFP	1.7	3.9	224*224	8/1	45°
SSFP +gado	1.9	4.2	224*224	8/1	75°
LGE	2.5	5.6	192*160	8/1	20°

For the assessment of LV function, Simpson technique was used. The endocardial contours of all short-axis Cine MRI images encompassing the left ventricle were delineated at end diastole and end systole enabling calculation of ejection fractions, end-diastolic ,end-systolic volumes and myocardial mass.

CMR analysis: All MRI exams were reviewed by one experienced radiologist. We proceeded to a triple analysis. At first, a morphological analysis realized on the morphological sequences T2-weighted short–tau-inversion-recovery and on cine MRI sequences. Then an analysis of late gadolinium enhancement was made by specifying for every patient the topography of the DE according to the cardiac segmentation established by the American Heart Association (AHA) and its topography exclusively subepicardial or at the same time subepicardial and midwall Finally we studied the correlations between the presence of an increased signal on Cine MRI sequence before injection and the clinic and biologic data.

Statistical methods: Quantitative variables were expressed as means and standard deviations (SD), and qualitative variables were expressed as frequencies and percentages. Student’s t test was used to compare the means of quantitative variables (or when appropriate, nonparametric tests) were used for comparisons. A two-tailed *P*-value<0.05 was considered significant.

RESULTS

After CMR analysis, we retained the diagnosis of acute myocarditis in 23 patients (57.5% of the population). It is

about 20 men and 3 women (sex ratio=6.66), the average age was 32.19±12.54 years old with extremes from 17 to 67 years old. Acute chest pain was the most common symptom. The clinical and biological characteristics were summarized in Table 2.

Table 2 : Patient characteristics

Patient	Sex	Age	Symptoms	Troponin (ng/ml)
1	M	28	viral syndrome, ACP,fever	22
2	M	38	ACP	11,08
3	M	23	viral syndrome, ACP,fever	3.86
4	F	51	viral syndrome, ACP, Dyspnea	0
5	M	21	ACP, fever, diarrheal	100
6	M	27	ACP,viral syndrome	3.71
7	M	25	ACP	22
8	M	27	ACP	3.31
9	F	46	ACP, Dyspnea	0.04
10	M	27	ACP, viral syndrome	14.37
11	M	17	ACP, viral syndrome, fever	11.5
12	M	27	ACP, viral syndrome, fever	7
13	M	49	ACP	11.45
14	M	20	ACP, viral syndrome, fever	4.42
15	M	28	ACP, viral syndrome	1.82
16	M	34	ACP	0
17	M	17	ACP	6
18	F	67	Dyspnea	0.04
19	M	48	ACP	67
20	M	22	ACP,viral syndrome	28.52
21	M	44	ACP,viral syndrome, fever	2.8
22	M	39	ACP,viral syndrome	9.44
23	M	32	ACP,viral syndrome, fever	30
Average		32.9		15.66

ACP= acute chest pain

Analysis of delayed enhancement: Delayed enhancement was objectified in 23 patients. All the segments were affected with predominance of the lateral wall of the left ventricle. Delayed enhancement was distributed as follows: lateral wall (44,37 %), septal wall (23.07 %), inferior wall (15.97 %) and finally anterior wall (14.79 %). The different types of DE were specified with regard to the thickness of the myocardium of the left ventricle. DE was exclusively subepicardial in 19 patients (83 %) (Figure 1 A) and at the same time subepicardial and midwall in 4 patients (17 %) (Figure 1 B). DE spared subendocardium in these 23 patients.

Analysis of cine MRI sequences before injection: The study of the signal on the cine MRI sequence before injection showed a spontaneous hypersignal at 15 patients (65 %) of the same topography as on delayed enhancement imaging while it was found only at 11 patients on T2-weighted short–tau-inversion-recovery (48 %) (Figure 2 A and 2 B).

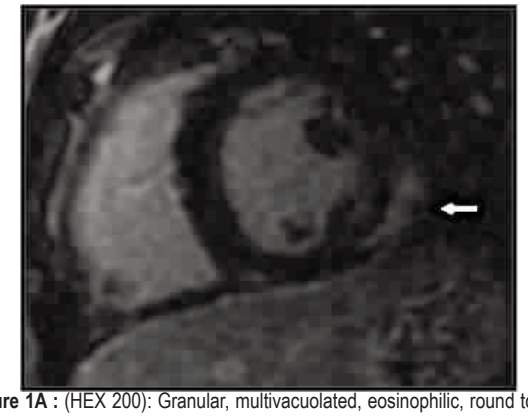

Figure 1A : (HEX 200): Granular, multivacuolated, eosinophilic, round to oval cells with centrally placed nuclei and multiple small lipid droplets. Figure 1A: Acute myocarditis in a 17–year-old male presenting with acute chest pain. short axis view showing delayed enhancement (white arrow) of the lateral wall exclusively subepicardial.

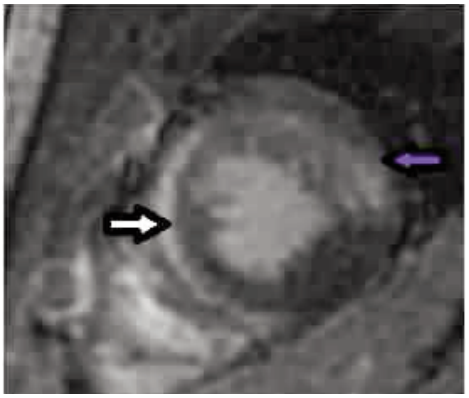

Figure 1B: Acute myocarditis in another 17-year-old male presenting with acute chest pain, fever and viral syndrome. Short axis views showing delayed enhancement of the lateral wall subepicardial(white arrow) and midwall (blue arrow).

Figure 2 A : Acute myocarditis in 38 -year-old male presenting with acute chest pain.SSFP-Cine MRI before injection and T2-weighted STIR. (spontaneous hypersignal= white arrow)

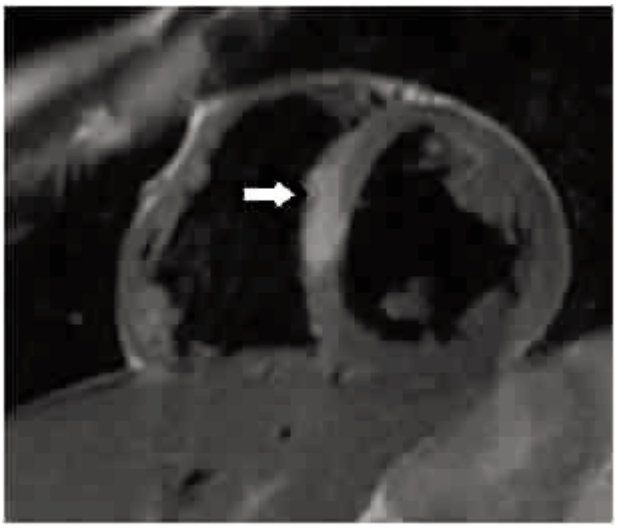

Figure 2 B : Images showing spontaneous hypersignal (white arrow) in the septal wall of the left ventricle.

Cine MRI after injection-sequences analyzing: The dynamic cine MRI sequences performed immediately after injection revealed an increased signal in the subepicardium layer in 23 patients having an acute myocarditis the location of which corresponded in every case to the zones of delayed enhancement (Figure 3 A, 3 B and 3 C).

Analysis: There were a significant difference between the presence of increased signal found in SSFP Cine MRI before injection and:
- the LVEF (p=0,022): that means the ejection fraction of the left ventricle is raised.
-the telesystolic volume of the left ventricle indexed on the physical surface: (p=0,039) that means the indexed TSVLV is lower when an increased signal intensity before injection is present.

DISCUSSION

Our study suggests that Cine MRI sequences after injection are of equal performance in the diagnosis of acute myocarditis as the late gadolinium enhanced sequences. Their contribution is important when we want to shorten the examination or when we do not obtain an optimal inversion time.

The acute myocarditis is an inflammation of the myocardium mostly consecutive to a viral infection (1). Its diagnosis is one of the most difficult to put with certainty in cardiology, because of the absence of specificity of the clinical presentation, electric and ultrasound modifications, and the restrictive appeal to the endomyocardial biopsy. For these reasons, the prevalence of the acute myocarditis is not known with accuracy and its incidence is probably underestimated (2). Cardiac MRI allows the direct characterization of the myocardium injuries; various diagnostic sequences allow visualizing myocardial tissue injuries consisting in inflammation, edema and necrosis (3). The realization of a CMR if presumptive diagnosis of acute myocarditis is a recommendation of class I of the European Society of cardiology since 2004 (4).

In 2009 an international group of expert, leaning on a meta analysis has defined the indications, the procedure

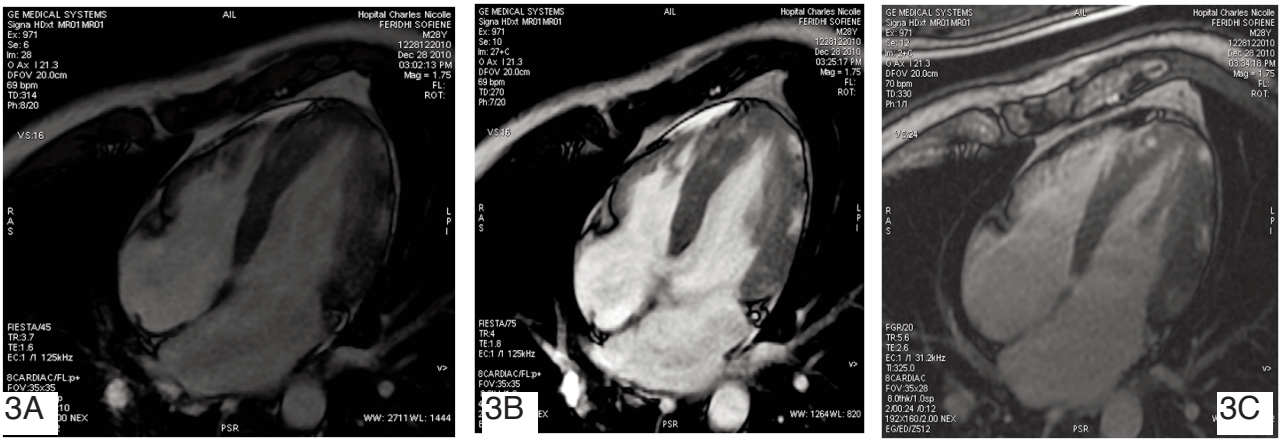

Figure 3 : Acute myocarditis in a 28 year-old-male presenting with acute chest pain, fever and viral syndrome. Long axis views showing a close matching between the abnormalities on Cine MRI before injection (Figure 3 A), after injection (Figure 3 B) and on late Gadolinium enhancement sequence (Figure 3 C).Delayed enhancement is exclusively subepicardial, linear and patchy and predominates in the lateral wall of the left ventricle.

and the protocol of MRI as well as the diagnostic criteria of myocarditis under the name of LAKE Louise CRITERIA (1). However MRI can be negative during acute myocarditis. Late gadolinium enhancement imaging is a key sequence for the diagnosis of acute myocarditis (5). In our study we found the same diagnostic performance of this sequence as SSFPcine MRI after injection. Indeed cine MRI sequences realized immediately after injection of Gadolinium allowed us to highlight an increased signal found in 23 patients with acute myocarditis confirmed in the MRI. These zones of increased signal corresponded to the zones of DE with a 100 % concordance. In the series of Deux and al (6) the sensibility of SSFP cine sequence after injection was 96 % while the sensibility of the sequence of LGE sequence was 89 %. For Cine MRI sequences, Steady State Free Precession (SSFP) was used. These dynamic sequences before and after injection are usually used to estimate the global cardiac function and regional (7).

Cine MRI sequences benefit from an excellent signal to noise ratio (8,9) and allow to study at the same time the cardiac morphology and the myocardial contractility. The myocardium has the same signal as the skeletal muscle, the liquid and fat are have an increased signal. There is an excellent contrast between the myocardium and blood. Even if it is hyper weighted T2, SSFP sequence preserves a T1 sensibility. It means that after injection of Gadolinium the myocardium presents a signal more important than that before contrast. These Cine MRI sequences thus allow detecting the myocardial increased signal to consolidate the diagnosis of acute myocarditis when an inversion time is difficult to obtain or when it is necessary to shorten the duration of the exam for example particular in patients of resuscitation units. They also find all their interest when the late gadolinium enhancement is absent or not detected.

In our study we also noted a good sensitivity of the Cine MRI sequence before injection (65%) compared the morphological sequence T2-weighted STIR or “dark blood” which is able to highlight the zones of myocardial edema in the form of spontaneous high signal intensity. This is in disagreement with published data (10, 11).

CONCLUSION

Cine MRI sequences after injection is of equal performance than late gadolinium enhancement sequence in the diagnosis of acute myocarditis. Its contribution is important when we wish to shorten the examination or when we do not obtain an optimal inversion time.

Acknowledgments and Disclosures

All authors disclose any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations that could inappropriately influence their work.

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