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Využití magnetické rezonance srdce pro posouzení patofyziologie dilatační kardiomyopatie.

Use of cardiovascular magnetic resonance for assessment of pathophysiology in dilated cardiomyopathy.

MUDr. Marek Šramko

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Předseda oborové rady: Prof. MUDr. Jaroslav Pokorný, DrSc.

Školicí pracoviště: Univerzita Karlova v Praze

Fyziologický ústav 1. LF UK

Albertov 5, 128 00 Praha 2

Autor: MUDr. Marek Šramko

Školitel: MUDr. Miloš Kubánek, Ph.D:

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Abstrakt

Dilatační kardiomyopatie (DCM) je druhou nejčastější příčinou srdečního selhání. Patofyziologie DCM není zcela objasněna. Jedním z důvodů jsou limitace současných klinických metod pro výzkum tohoto onemocnění. Cílem této práce bylo posudit schopnost magentické rezonance srdce (CMR), s využitím moderních zobrazovacích technik, pro in vivo vyšetření některých klíčových patofyziolgických mechanizmů, které mají s DCM přímou souvislost. Dalším cílem práce bylo pousoudit, zda patologické nálezy na CMR umožní předpovědět klinicky relevantní zlepšení morfologických a funkčních parametrů levé komory srdeční – reverzní remodelaci (LVRR).

U 44 pacientů s nově manifestovanou DCM (délka trvání <6 měsíců) byla provedena CMR, endomyokardiální biopsie, zátěžové vyšetření a vyšetření srdečních biomarkerů. CMR byla zopakována po 1 roce klinického sledování.

U 34 % pacientů byly pomocí biopsie zjištěny zánětlivé změny myokardu. LVRR byla po roce pozorována u 45 % pacientů. Přítomnost pozdního sycení gadolinia (LGE) v levé komoře byla senzitivním ale málo specifickým znakem zánětu myokardu, protože přítomnost LGE byla taktéž projevem hemodynamického zatížení při srdečním selhání. Rozsah LGE byl nezávislým prediktorem LVRR a taktéž prediktorem závažných klinických událostí. Přítomnost perikardiálního výpotku a zvýšené časné sycení gadolina byly specifickými ale málo častými známkami zánětu myokardu. Vyšetření edému myokardu pomocí T2-vážených sekvencí nebylo přínosné pro detekci zánětu myokardu, avšak ukázalo se užitečné pro predikci LVRR.

Lze tedy uzavřít, že CMR se jeví jako suboptimální metoda pro detekci zánětu myokardu u pacientů s nově manifestovanou DCM. Nicméně, u těchto pacientů může CMR odhalit poškození myokardu v souvislosti s hemodynamickým zatížením a navíc umožňuje spolehlivě predikovat LVRR.

Klíčová slova: patofyziologie, kardiomyopatie, zánět myokardu, reverzní remodelace, magnetická rezonance

Abstract

Dilated cardiomyopathy (DCM) is the second leading cause of heart failure. The pathophysiology in DCM is still poorly understood, partly because of currently limited research tools. We investigated whether cardiovascular magnetic resonance (CMR), using novel imaging techniques, could be used for in vivo assessment of some key pathophysiological mechanisms related to DCM. In addition, we evaluated whether the pathological findings on CMR would predict clinically relevant functional and morphological improvement of the left ventricular (LV) function – the LV reverse remodeling (LVRR).

CMR together with endomyocardial biopsy, echocardiography, cardiopulmonary exercise testing and a thorough assessment of cardiac biomarkers was performed in 44 patients with new-onset DCM (<6 months of duration). The imaging was repeated after 12 months of clinical follow-up.

Endomyocardial biopsy revealed myocardial inflammation in 34 % of the patients. LVRR at 12 months occurred in 45 % of the patients. Presence of late gadolinium enhancement (LGE) in the left ventricle was a sensitive but unspecific sign of myocardial inflammation because it was also a feature of hemodynamic stress related to the heart failure. The baseline extent of LGE was an independent predictor of future LVRR and also a predictor of adverse clinical events. Pericardial effusion and increased early gadolinium enhancement were specific but uncommon signs of myocardial inflammation. Assessment of myocardial edema by T2-weighted imaging did not add value to detection of myocarditis but it was valuable for predicting of LVRR.

In conclusion, CMR seems a suboptimal method for detection of myocardial inflammation in new-onset DCM. However, in these patients CMR may reveal myocardial injury related to hemodynamic stress and it may predict future LVRR.

Key words: pathophysiology, cardiomyopathy, myocardial inflammation, reverse remodeling, cardiovascular magnetic resonance

Introduction

Dilated cardiomyopathy (DCM) is a heart disease in which the left ventricle (LV) becomes dilated, thin-walled and dysfunctional. DCM is after the coronary artery disease the second leading cause of chronic heart failure in adults (Mosterd et al. 2007). Although the LV function may improve or even fully recover in some individuals, the overall prognosis of the patients with DCM remains poor (Merlo et al. 2014).

Pathophysiology in DCM is still unresolved (Elliott et al. 2008). However, a better recognition of the underlying pathophysiology is a critical prerequisite for development of new, more specific, therapeutic approaches and also for individualization of the management of the DCM patients (Frustaci et al 2009).

The lack of understanding of the pathophysiology in DCM may be largely explained by the limitations of the currently available methods for investigating pathological processes in vivo. In this regard, cardiovascular magnetic resonance (CMR) using novel imaging techniques emerges as a promising diagnostic tool.

Besides accurate quantification of cardiac morphology and function, CMR enables direct visualization of important pathophysiological tissue processes, such as myocardial edema, hyperperfusion, capillary leakage and replacement fibrosis (Friedrich et al 2009). A comprehensive evaluation of the CMR tissue characteristics can be used to detect myocardial inflammation or to assess the extent of myocardial injury.

Thus, CMR has the potential not only to provide new insights into the etiology and patophysiollogy of DCM, but the pathological CMR findings could be used also to predict clinical course of the disease – particularly occurrence of the LVRR. However, even though CMR proved a valuable method in various clinical scenarios, there is a lack of experience with its use in the setting of new-onset DCM.

Aims and hypotheses

Aims:

1. To evaluate performance of CMR in detection of myocardial inflammation in patients with new-onset DCM, using endomyocardial biopsy (EMB) as a reference standard.
2. To clarify pathological and pathophysiological background of the CMR findings in these patients.
3. To evaluate value of the CMR findings for prediction of LVRR

Hypotheses:

1. We expect that myocardial inflammation will be a common finding in the patients with new-onset DCM. Multisequential CMR imaging could detect the myocardial inflammation with an acceptable accuracy, provided that the inflammation would have certain minimal level of activity.
2. Pathophysiology of the CMR findings could be clarified by a simultaneous assessment by CMR, EMB and specific cardiac biomarkers that reflect ongoing myocyte necrosis (high-sensitivity troponin T [hs-TnT]) and hemodynamic stress (B-type natriuretic peptide [BNP]).
3. Some CMR findings might reflect myocardial inflammation but they could also reflect pathophysiological processes related to the heart failure itself, such as myocardial injury due to hemodynamic stress.
4. LVRR could be a common phenomena in our patients. A greater extent of myocardial damage at baseline, as assessed by CMR, could predict a worse chance for the LVRR.

Methods

We investigated 44 consecutive patients with new-onset DCM (symptoms of heart failure <6 months). We excluded individuals with a history of excessive alcohol consumption, individuals presenting with persistent tachy-arrhythmias and individuals with clinically suspected acute myocarditis.

At baseline, all patients underwent CMR, EMB, cardiopulmonary exercise testing and assessment of hs-cTNT and BNP. The patients were followed during regular clinical visits for a minimum of 12 months (mean, 25 ± 9 months). The follow-up visits included echocardiography, exercise testing and assessment of BNP. CMR was repeated after 12 months.

The EMB specimens were obtained from the right ventricular side of the interventricular septum by the jugular venous approach. The specimens were assessed for the presence of inflammation (by histopathology and by immunohistochemistry with CD3- and CD68-targeted antibodies), for the extent of interstitial fibrosis and for the presence of cardiotropic viruses.

CMR imaging and image analyses followed previously described methods (Friedrich et al. 2009). The analysis included quantification of ventricular volumes and function; quantification of pericardial effusion; assessment of myocardial edema by T2-weighted imaging; evaluation of hyperemia and capillary leakage by the early gadolinium enhancement (EGE) technique; and assessment of myocardial necrosis and replacement fibrosis by the late gadolinium enhancement (LGE) technique.

The CMR findings were compared with the EMB and biomarker results. Prognostic value of the CMR findings was analyzed with regard to prediction of LVRR at 12 months of follow-up (defined as an absolute increase in LV ejection fraction ≥10 % to a final value of >35%, and at the same time a decrease in LV end diastolic diameter ≥10%).

Results

Baseline characteristics of the study population

Baseline clinical characteristic of the study population are summarized in Tables 1 and 2. None of the patients had a history of a cardiovascular disease. Moreover, none of the patients presented with a clinical picture suggestive of acute myocarditis. In contrast, every forth patient reported typical symptoms of a viral respiratory disease occurring a few weeks before onset of the symptoms of heart failure. Also, interestingly, every fourth patient reported a family history of a cardiomyopathy in a first-degree relative.

Besides the default LV dilatation and systolic dysfunction, 39 % of the patients had also severely impaired LV diastolic function. The LV systolic dysfunction was usually paralleled by the right ventricular systolic dysfunction. Furthermore, more than a half of the patients had at least moderate functional mitral regurgitation. The impairment of the ventricular function was translated to the markedly reduced exercise tolerance.

Immunohistochemical analysis of the EMB revealed myocardial inflammation in 15 individuals (34 %). However, the activity of the inflammation was generally low: classical histological (Dallas) criteria of myocarditis were met only in 3 cases (7 %), but even in these 3 individuals the inflammation was classified as borderline (Figure 1). Genome of at least one virus was found in the EMB in 66 % of the patients. The most common found virus was parvovirus B19, followed by human cytomegalovirus and one case of enterovirus.

Figure 1 – Findings in EMB

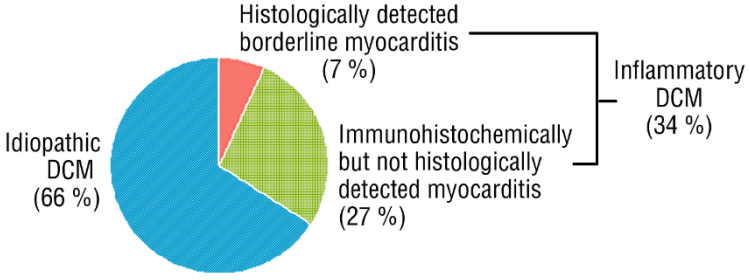


Table 1: Baseline characteristics of the study population - Part I

Variable	n = 44
Clinical variables	
Age (years)	43 ± 11
Males	31 (71 %)
Family history of dilated cardiomyopathy	11 (25 %)
Diabetes mellitus	2 (4 %)
Systemic hypertension	3 (7 %)
Viral prodromes during preceeding month	12 (27 %)
Duration of symptoms of heart failure (months)	2.0 [1.0–3.4]
Hospitalisation for heart failure in previous 6 months	29 (66 %)
Decompensated heart failure at admission	14 (32 %)
NYHA class	
I	1 (2 %)
II	23 (52 %)
III	14 (32 %)
IV	6 (14 %)
Body mass index (kg/m^2)	25 ± 4
Systolic blood pressure (mm Hg)	112 ± 17
Diastolic blood pressure (mm Hg)	69 ± 7
Heart rate (beats/min)	84 ± 18
Sinus rhythm	43 (98 %)
QRS duration (ms)	106 ± 21
Complete left bundle branch block	5 (11 %)
Exercise capacity	
Peak exercise heart rate (beats/min)	142 ± 17
Peak exercise systolic BP (mm Hg)	135 ± 22
Peak oxygen consumption (ml kg/min)	19.4 ± 0.5
Peak oxygen consumption (% of predicted value)	57 ± 16
VE/VCO2 slope	28.8 ± 0.9
Biomarker testing	
Sodium (mmol/l)	141 ± 2
Creatinine (µmol/l)	95 ± 4
Estimated glomerular filtration rate (ml/min)	79 ± 23
B-type natriuretic peptide (ng/l)	635 [276–1081]
High-sensitivity troponin T (ng/l)	14.5 (5.0–30.0)
High-sensitivity troponin T positive	23 (52 %)
Conventional troponin I positive	13 (29 %)
Galectin-3 (µg/l)	3.0 [0.2–4.6]
C-reactive protein (mg/l)	3.0 [1.0–8.2]

Table 2: Baseline characteristics of the study population - Part II

Variable	n = 44
Echocardiography	
LV enddiastolic diameter (mm)	69 ± 6
LV enddiatstolic diameter index (mm/m)	39 ± 3
Interventricular septum thickness (mm)	9 ± 1
Posterior wall thickness (mm)	8 ± 1
LV ejection fraction (%)	23 ± 7
Restrictive pattern of mitral inflow	17 (39 %)
E/E' ratio	13.2 ± 0.5
Left atrial short axis diameter index (mm/m)	26 ± 4
Left atrial volume index (ml/m^2)	49 ± 19
Mitral regurgitation mdrate or severe	25 (57 %)
RV enddiastolic diameter (mm)	29 ± 6
TAPSE (mm)	17 ± 5
Magnetic resonance imaging	
LV enddiastolic volume (ml)	280 ± 85
LV enddiastolic volume index (ml/m^2)	140 ± 40
LV ejection fraction (%)	21 ± 10
LV ejection fraction category	
< 20 %	15 (34 %)
20–24 %	16 (36 %)
25–29 %	7 (16 %)
30–34 %	3 (7 %)
35–45 %	3 (7 %)
LV mass (g/m^2)	105 ± 26
RV enddiastolic volume index (mL/m^2)	77 ± 30
RV ejection fraction (%)	24 ± 8
Endomyocardial biopsy	
Area of available biopsy specimen (mm^2)	6 ± 2
Myocardial inflammation	15 (34 %)
Myocardial inflammation by immunohistochemistry	12 (27 %)
Borderline myocarditis by histological criteria	3 (7 %)
CD3+ T lymphocytes (n/mm2)	4 [2–9]
CD68+ macrophages (n/mm2)	2 [0–5]
Presence of virus genome	29 (66 %)
Parvovirus B19 positive	27 (61 %)
Parvovirus B19 in EMB (copies/µg/DNA)	120 [0–622]
Human cytomegalovirus	4 (9 %)
Enterovirus	1 (2 %)
Human herpes virus 6	0 (0 %)
Adenoviruses	0 (0 %)
Extent of myocardial fibrosis (%)	15 ± 5
Degree of myocyte vacuolization (grades 1–3)	2 [2–3]

Accuracy of CMR for detection of myocardial inflammation

The diagnostic performance of CMR for detection of myocardial inflammation was suboptimal for clinical application (Table 3). Assessment of myocardial edema by T2-weighted imaging did not add any diagnostic value. LGE was sensitive but less specific sign, while abnormal pericardial effusion and increased EGE ratio turned to be specific but uncommon signs.

Table 3: Performance of CMR in detection of myocardial inflammation

Variable	SN	SP	ACC	OR [95% CI]
Myocardial edema*	13 %	93 %	64 %	NS
Increased EGE†	40 %	96 %	76 %	17 [2–164]
LGE present	87 %	44 %	60 %	5 [1–28]
Pericardial effusion‡	47 %	89 %	74 %	7 [1.5–34]
Any two criteria simultaneously	67 %	85 %	79 %	12 [3–52]
LGE + increased EGE	86 %	74 %	76 %	17 [2–164]
LGE + pericardial effusion	70 %	75 %	74 %	7 [1.5–37]

ACC = accuracy; CI = confidence interval; NS signifies statistically not significant by logistic regression; OR = odds ratio; SN = sensitivity; SP = specificity; * Edema ratio >1.9; † EGE > 45 %; ‡ Pericardial effusion > 50 ml

CMR finding after 12 months of follow-up

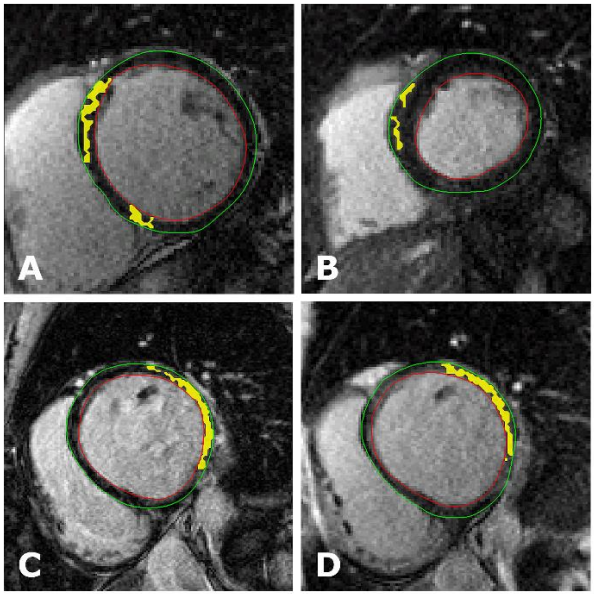
A follow-up CMR was available in 30 non-transplanted patients who did not have implanted a metallic cardiac device; LGE was present at baseline in 20 of them (67 %). Of the 20 patients with LGE at baseline 13 (43 %) had LGE also after one year but in 7 (23 %) the LGE disappeared. Of 10 patients who did not have LGE at baseline 8 (27 %) remained without LGE but 2 (7 %) developed a new LGE lesion. Overall, the LGE extent and also the myocardial edema ratio decreased significantly during the follow-up (from 5.5 [0-12] g to 1.3 [0-6] g; and from 1.53 ± 0.37 to 1.29 ± 0.25, $p = 0.001$ and 0.002; respectively). The decrease in the extent of LGE was more pronounced in the patients with LVRR (Figure 2).

Figure 2 –
Change in the extent of LGE after 1 year

Top row: Patient #1 at baseline (A) and after 1 year (B)

Bottom row: Patient #2 at baseline (C) and after 1 year (D)

LGE receded in the Pateint #1, who had LVRR, but not in the patient #2 without LVRR



Pathophysiology of LGE

LGE occurred at baseline in 28 (67 %) individuals. Figure 3 presents several typical patterns of LGE that were observed in the patients. The presence of LGE was associated with myocardial inflammation (detected by immunohistochemistry in EMB), with an ongoing myocyte necrosis (represented by increased hs-TnT) and with hemodynamic stress (reflected by increased BNP concentrations and a higher NYHA class, Table 4). No pattern or localization of the LGE seemed to be specific for myocardial inflammation.

LVRR and its relationship to the patient's clinical status

Follow-up for evaluation of LVRR was available in 39 patients (89 %) that did not receive a heart transplant or a ventricular assist device. LVRR at 12 months was observed in 20 of them (45 %), but only in 3 cases (7 %) the LV ejection fraction increased above 50 %.

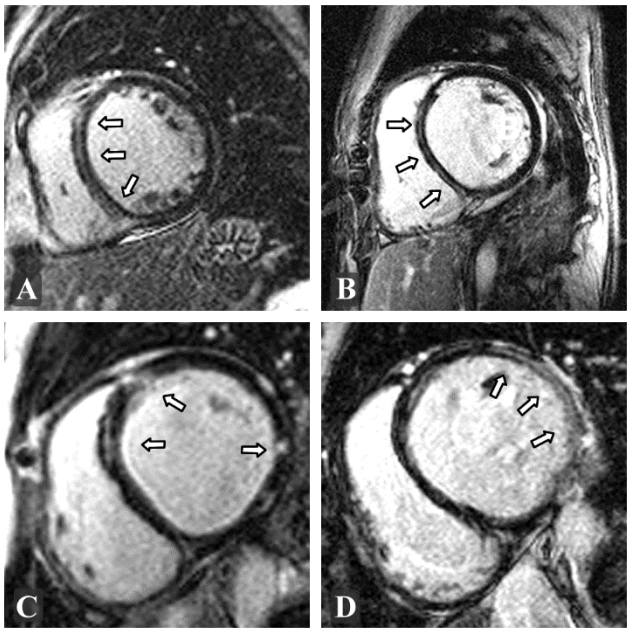


Figure 3 – Typical patterns of LGE

A and B: thin stripe intramurally in the LV septum

C: multifocal patches

D: transmural lesion in the LV free wall

Table 4: Variables associated with occurrence of LGE in the left ventricle.

Variable	LGE- n = 14	LGE+ n = 28	p-Val
NYHA class	2.2 ± 0.7	3.0 ± 0.8	0.006*
LV ejection fraction (%)	23 ± 11	21 ± 9	0.44
LVEDV (ml/m^2)	128 ± 38	147 ± 42	0.19
LVEDD (mm)	67 ± 9	69 ± 7	0.47
LV mass (g/m^2)	108 ± 28	123 ± 23	0.59
BNP (ng/L)	283 [113–812]	1031 [592–1469]	0.003*
Hs-TnT (ng/L)	6 [4–16]	18 [9–54]	0.02*
Hs-TnT > 13.5 ng/L	4 (28 %)	19 (68 %)	0.02*
Troponin I > 0.03 µg/L	3 (21 %)	10 (36 %)	0.35
Inflammation in EMB	2 (14 %)	13 (46 %)	0.04*
Fibrosis extent in EMB (%)	12 ± 5	16 ± 9	0.18

The patients with future LVRR had already after three months significantly lower BNP, smaller indexed (but not absolute) LV enddiastolic diameter (LVEDD), improved LV diastolic function, less prevalent mitral regurgitation, smaller left atrium, lower resting heart rate, improved NYHA functional class and also improved all measures of functional exercise testing.

At 6 months, the patients with future LVRR differed even more significantly in the indexed LVEDD, prevalence of LV diastolic function, levels of BNP, prevalence of mitral regurgitation and in the left atrial dimensions. In addition, at 6 months the patients with future LVRR had already significantly higher LV ejection fraction and smaller absolute LVEDD.

After one year, the LVRR was furthermore accompanied (besides the default improvement of the LV dimensions and ejection fraction) with markedly improved exercise capacity, a shorter QRS complex duration, and also with improved right ventricular ejection fraction.

Prediction of LVRR

LVRR at 12 months was associated with baseline lower concentration of hs-TnT, higher concentration of sodium, finding of myocardial inflammation in biopsy and with two CMR variables - a smaller extent of LGE and a higher myocardial edema ratio. However, at baseline only the extent of LGE and myocardial edema ratio were independent predictors of LVRR. Pattern or localization of the LGE did not predict the LVRR.

Baseline BNP level did not predict LVRR but lower BNP at 3 months was the only independent predictor of LVRR out of 60 follow-up variables. BNP at 3 months <344 ng/L predicted LVRR with a 95 % sensitivity and 50 % specificity. Conventional methods of follow-up (LVEDD index and E/E' ratio) became independent predictors of LVRR only after 6 months of follow-up. Importantly, LGE extent and the myocardial edema ratio remained independent predictors of LVRR even when combined with the BNP at 3 months or with the LVEDD index and E/E' ratio at 6 months (Table 5).

Table 5: Results of multivariate analysis showing independent predictors of LVRR at baseline, 3 and 6 months of follow-up.

Multivariate model	Odds ratio [95% CI]	p Value
(1) Baseline		
Indexed LGE extent†	0.67 [0.50–0.90]	0.008**
Myocardial edema ratio‡	1.45 [1.04–2.02]	0.027*
(2) 3 months		
B-type natriuretic peptide§	0.14 [0.02–0.94]	0.042*
(3) 6 months		
LVEDD index¶	0.73 [0.56–0.96]	0.014*
E/E' ratio	0.56 [0.33–0.94]	0.019*
(4) Baseline + 3 months		
B-type natriuretic peptide at 3 months§	0.13 [0.01;0.96]	0.001**
Myocardial edema ratio at baseline‡	1.37 [1.18–1.93]	0.048*
Indexed LGE extent at baseline†	0.75 [0.55–0.93]	0.028*
(5) Baseline + 3 months + 6 months		
E/E' ratio at 6 months	0.45 [0.20–0.98]	<0.001***
LVEDD index at 6 months¶	0.78 [0.59–0.95]	0.005**
Indexed LGE extent at baseline†	0.69 [0.45–0.96]	0.047*
Myocardial edema ratio at baseline‡	1.57 [1.12–2.7]	0.027*

† denotes odds ratio per % of LV mass; ‡, per 0.1 unit; §, per log(µg/l); ¶, per mm/m, respectively.

Model 1 (baseline data): decompensated heart failure at admission, sodium plasma level, estimated glomerular filtration rate, high-sensitivity cardiac troponin T, LGE extent, myocardial edema ratio, presence of myocardial inflammation in biopsy

Model 2 (3-month data) : NYHA functional class, heart rate, LVEDD index, restrictive mitral pattern, severity of mitral regurgitation, left atrial volume index, peak exercise systolic blood pressure, peak oxygen consumption, VE/VCO2 slope, Log BNP.

Model 3 (6-month data): NYHA functional class, LVEDD index, LV ejection fraction, E/Em, left atrial volume index, peak exercise systolic blood pressure, peak oxygen consumption, VE/VCO2 slope, Log BNP.

Model 4 (independent predictors from model 1 and 2): indexed LGE extent, myocardial edema ratio, Log BNP (3 months).

Model 5 (independent predictors from models 1 to 3): indexed LGE extent, myocardial edema ratio, Log BNP (3 months), LVEDD index (6 months), E/Em (6 months).

Discussion

Major findings

This is the first study that systematically evaluated use of a novel multisequential CMR protocol for assessment of pathophysiological processes in the individuals with new-onset DCM. One of the main strengths of the study was the complexity of the collected data: besides the CMR scans, we had available histopathological and immunohistochemical assessment of the myocardial tissue; biomarker data reflecting hemodynamic status and activity of myocardial necrosis; and a rigorous mid-term clinical follow-up. In addition, serial CMR scans enabled to intercept evolution of the myocardial pathological processes and its relationship to the LVRR. Finally, in this study we introduced novel CMR-derived predictors of LVRR that are much more robust than those previously reported. We showed that CMR provides an earlier prediction of LVRR than the conventional methods.

Among the extensive data obtained in the study there are several findings that should be pointed out: (1) Myocardial inflammation was common in the individuals with new-onset DCM (one third of the patients), though the inflammation had overall low activity. (2) Consequently, the performance of CMR for detection of myocardial inflammation was suboptimal for clinical use. (3) LGE was a sensitive sign for myocardial inflammation, however it was also a hallmark of hemodynamic stress related to the advanced heart failure. (4) In some patients the LGE had receded or even disappeared over one year and the reduction of the LGE extent was more pronounced in the patients with LVRR. (5) Lower extent of LGE and a higher myocardial edema ratio were the strongest baseline predictors of LVRR. In fact, at baseline CMR outperformed in the prediction of LVRR conventional methods of follow-up, BNP and EMB.

Comparison with previously published data

The evidence on the use of CMR for detection of myocardial inflammation comes mostly from studies in patients with acute myocarditis and preserved LV systolic function (Friedrich et al. 2009). The only somewhat comparable study—which evaluated diagnostic performance of CMR in 23 DCM patients—reported similar accuracy of CMR than we found in our study (75 % vs. 79%, respectively).

In patients with clinically suspected myocarditis, but who have preserved LV function, the LGE is highly specific for the inflammation. In contrast, in our study LGE had only 44% specificity for myocarditis. The lower specificity of LGE in our study may reflect fact that the LGE in DCM represents also pathophysiological processes that are related to the heart failure itself. In fact, the increased levels of BNP and cardiac troponin in our patients with LGE support a previously proposed hypothesis, according to which increased wall stress in the overloaded LV may lead to relative myocardial ischemia, which in turn may result to myocyte necrosis (Alter et al. 2007). Furthermore, in DCM patients the LGE seems to be more common in an earlier stage of the disease than at a chronic stage (67% in our study vs. 31% in Lehrke et al. 2011). It can be explained by a natural or pharmacotherapy-induced resolution of either the myocarditis or the stress-related myocardial injury. Thus, LGE in DCM must be interpreted in the context of the disease duration and the hemodynamic status.

Although the prognostic value of CMR (specifically the LGE) has been established in the patients with chronic DCM, our study was the first to confirm the prognostic value of LGE also in new-onset DCM.

Clinical implications

Determining the etiology of DCM in an affected individual may be clinically relevant. The patients with inflammatory DCM seem to have

somewhat better prognosis than the patients with idiopathic DCM, though our study was unable to confirm similar observations (Givertz et al. 2013). Furthermore, besides naturally more favorable course of the disease, the patients with inflammatory DCM may receive a specific therapy targeting inflammation on top of the standard management of heart failure (Kindermann et al. 2012). In this context, CMR may probably not replace EMB in establishing the diagnosis before initiation of a specific treatment; however, the LGE could serve as a screening tool for referring patients with new-onset DCM for EMB. Such approach could prevent many unnecessary biopsies.

Improved prediction of clinical outcome of individuals with new-onset DCM might be helpful for the cost-effective use of implantable cardioverter-defibrillators in the primary prevention of sudden cardiac death and it could also be used for optimal timing of referral to heart transplantation. Therefore, based on our data we propose to include CMR into the routine baseline assessment of all patients with new-onset DCM.

Conclusions

In patients with new-onset DCM, CMR has suboptimal accuracy for detection of myocardial inflammation - mainly because the activity of the inflammation is generally low. On the other hand, CMR can be used for noninvasive evaluation of hemodynamic stress and extent of myocardial damage. LVRR is relatively common, but complete recovery of the left ventricular dysfunction is rare. The pathological CMR findings, specifically the extent of LGE and the myocardial edema ratio provide at baseline a better prediction of the LVRR than endomyocardial biopsy, BNP and conventional methods of cardiologic follow-up.

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2. Novel predictors of left ventricular reverse remodeling in individuals with recent-onset dilated cardiomyopathy. Kubanek M, **Sramko M**, Maluskova J, et al., J Am Coll Cardiol. 2013;61(1):54-63. **(IF 15.3)**

Publikace *in extenso*, bez vztahu k tématu disertace:

1. Isolated X-linked hypertrophic cardiomyopathy caused by a novel mutation of the four-and-a-half LIM domain 1 gene. Hartmanova H, Kubanek M, **Sramko M,** et al., Circ Cardiovasc Genet. 2013;6(6):543-541**(IF 6.7)**
2. A novel biomarker-based approach for detection of asymptomatic brain injury during catheter ablation of atrial fibrillation. **Sramko M**, Peichl P, Wichterle D, et al., J Cardiovasc Electrophysiol. 2014;25(4):349-54 **(IF 3.5)**
3. Detection of Borrelia burgdorferi sensu lato in endomyocardial biopsy specimens in individuals with recent-onset dilated cardiomyopathy. Kubanek M, **Sramko M**, Berenova D, et al. Eur J Heart Fail. 2012; 14(6):588-96. **(IF 4.9)**
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