

DOI: 10.5937/halo26-27832

UDC: 616.12-008.315-085

Zdravković M, i sar.
Kardiomagnetna
rezonanca. Halo 194.
2020; 26(2):75-81.

REVIEW ARTICLE

**CARDIAC MAGNETIC RESONANCE IN CARDIAC
RESYNCHRONIZATION THERAPY - HOW USEFUL IT CAN BE?**

Marija ZDRAVKOVIĆ^{1,2}, Višeslav POPADIĆ¹, Slobodan KLAŠNJA¹

¹CHC Bežanijska kosa, Belgrade, Serbia; ²Medical faculty, University of Belgrade, Belgrade, Serbia.

ABSTRACT

Patients with heart failure, reduced ejection fraction, and signs of myocardial dyssynchrony have a poor prognosis. Cardiac resynchronization therapy is a proven therapeutic modality that reduces symptoms of heart failure as well as morbidity and mortality in these patients. Better identification of patients who could benefit from cardiac resynchronization therapy is an important factor because a significant percentage of patients do not experience clinical improvement after CRT implantation. Cardiac magnetic resonance is a useful, non-invasive, sophisticated diagnostic tool that can provide useful information on the aetiology of heart failure and the severity of mechanical dyssynchrony of the left ventricle. It helps evaluate the myocardial scar burden, which can predict a possible unsatisfactory response to therapy and helps improve clinical outcomes by enabling optimal positioning of the LV lead. Cardiac magnetic resonance in patient follow up after CRT implantation is proven to have significant clinical value. Conclusion: Cardiac magnetic resonance is a non-invasive imaging modality that can provide better identification of the patients who could respond well to cardiac resynchronization therapy. By providing valuable information about the severity of mechanical dyssynchrony, the myocardial scar burden and optimal positioning of the LV lead, it is useful in improving clinical outcomes after CRT implantation.

Keywords: cardiac magnetic resonance, cardiac resynchronization therapy, heart failure, mechanical dyssynchrony, myocardial scar burden

Rad primljen: 06.08.2020.**Prihvaćen:** 12.08.2020.**Korespondencija:**

Višeslav Popadić

Bul.Nikole Tesle 36

11070 Beograd, Srbija

Tel: +38164102-66-42

E-mail:

viseslavpopadic@gmail.com

Introduction

Heart failure approximately affects 1-2% of the population in developed countries, with absolute numbers of 15 out of 900 million affected people in Europe and 5.7 out of 300 million in the United States [1]. Cardiac resynchronization therapy is a proven therapeutic modality in patients with heart failure, reduced ejection fraction and a wide QRS complex. It reduces morbidity and mortality and improves the quality of life by reducing symptoms of heart failure [2]. Current guidelines for the treatment of heart failure recommend cardiac resynchronization therapy in symptomatic patients with heart failure, in sinus rhythm, with ejection fraction less than or equal to 35%, QRS duration more than 150ms and left bundle branch QRS morphology despite optimal medical therapy. It is also recommended in patients with heart failure, with ejection fraction less than or equal to 35% and with an indication for ventricular pacing and high degree AV block. It should be considered in a variety of other clinical implications [3]. The CRT implantation rate differs widely across countries, ranging from 7 per million inhabitants in the Russian Federation to 221 per million inhabitants in Germany and 448 inhabitants in the USA [1].

Although patients with CRT implants could significantly benefit from it, approximately 30% of the patients do not respond to the therapy [4]. There are various tools and factors of prediction that can help identify the patients that would respond.

Cardiac magnetic resonance is a useful, non-invasive, sophisticated diagnostic tool that can be used in the evaluation of cardiac volumes and function, the etiology of heart failure through specific tissues characterization and in the estimation of severity of the mechanical dyssynchrony [5, 6]. It can also help provide optimal LV lead positioning and identify the myocardial scar burden, which does improve outcomes [7]. Despite of its numerous advantages compared to some other imaging modalities, cardiac magnetic resonance is still not a standard in evaluating the patients with heart failure and possible indication for the resynchronization therapy, but with tendency to be more represented in the upcoming years. According to the available data, the number of cardiac MRI scans for the last decade in United Kingdom is growing for about 15-20% per year, mainly for the evaluation of heart failure etiology and structural heart diseases [8].

Evaluation of mechanical dyssynchrony by cardiac magnetic resonance

Cardiac magnetic resonance provides high spatial resolution imaging and has less intraobserver and interobserver variability than echocardiography [9]. These characteristics provide almost perfect conditions to gain enough information of interest, compared to other imaging modalities [10]. Three main CMR methods to evaluate mechanical dyssynchrony are myocardial tagging, phase-contrast tissue velocity mapping and displacement encoding with stimulated echoes, better known as DENSE. All three methods assess strain as the main diagnostic algorithm [11]. Different diagnostic methods use specific strain and strain rate values by detecting deformation in various directions: longitudinal, circumferential or radial. Myocardial tagging is similar to echocardiographic speckle tracking, but it has less spatial resolution compared to other cardiac magnetic resonance modalities for evaluating mechanical dyssynchrony. Tissue velocity mapping, because of its higher spatial resolution provides more information by calculating the deformation and strain. The main disadvantages

include long acquisition and breath-hold times. DENSE is a highly sophisticated tool in assessing dyssynchrony by direct strain measurement with high spatial resolution and improved temporal resolution [12, 13].

Myocardial scar burden as a predictor of response

Approximately 30% of the patients are non-responders after receiving CRT [14]. One of the most important factors in predicting the response to cardiac resynchronization therapy is a percentage of myocardial scar burden verified by cardiac magnetic resonance with late gadolinium enhancement (LGE) [15]. Several studies have presented myocardial scar burden as a factor of response after CRT, but very few have shown the effect of myocardial scar burden with clinical implications regarding heart failure and death [16]. *Serge C. Harb et al.* have shown that non-responders have a higher level of myocardial scar burden. Also, myocardial scar burden is an independent factor in predicting heart failure and death, and also in predicting ejection fraction recovery after CRT implantation (**Figure 1**) [17].

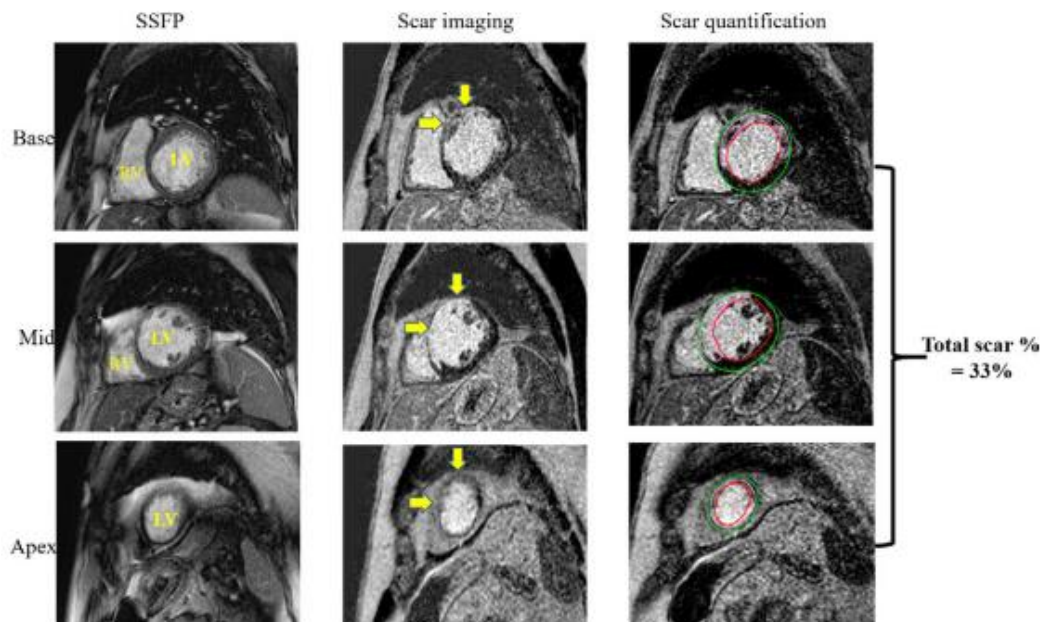


Figure 1. Myocardial scar quantification by cardiac magnetic resonance [17]

The higher level of myocardial scar burden regardless of the scar location in terms of affected segments is marked as a predictor of adverse outcomes. Myocardial scar burden is not only important as a predictor of response to therapy but also as a predictor of future clinical events in terms of heart failure and death, keeping in mind a high mortality rate of non-responders in the follow-up [18]. The percentage of scar burden on cardiac magnetic resonance has also been evaluated as a predictor of response. Certain studies have shown

that patients with myocardial scar burden above 33% and transmural scarring have a greater chance of being non-responders [19]. Some studies marked septal scars, while others marked scars in lateral or posterolateral segments as predictors of bad response [20]. Keeping clinical outcomes in mind, myocardial scar tissue in any region will reflect on global left ventricle remodelling, therefore resulting in higher risk for future clinical events, regardless of the aetiology of heart failure (ischemic or non-ischemic) [21].

Cardiac magnetic resonance in LV lead positioning

The cardiac magnetic resonance study after CRT implantation, as well as multimodality imaging, usually with CT, is a reliable method and can reveal useful information about the LV lead position. Technical and software improvements in the last few years have enabled an easier and more expedient implementation of cardiac magnetic resonance in providing an optimal LV lead positioning. Although the LV lead position in the lateral wall segments area or other late activation areas of the myocardium is optimal, the presence of myocardial scarring in that area can be a predictor of future acute cardiac dysfunction or non-response [22]. Approximately

14% of the patients have had the LV lead positioned in the scar area [23]. Electrocardiographic evidence of QRS prolongation during LV pacing can indicate pacing in the myocardial scar [24]. The main aim is to position the LV lead in the segment with optimal viability and latest activation. Regarding the optimal LV positioning, CMR can also provide coronary venous anatomic images that can ease the process of preimplantation planning (Figure 2) [25].

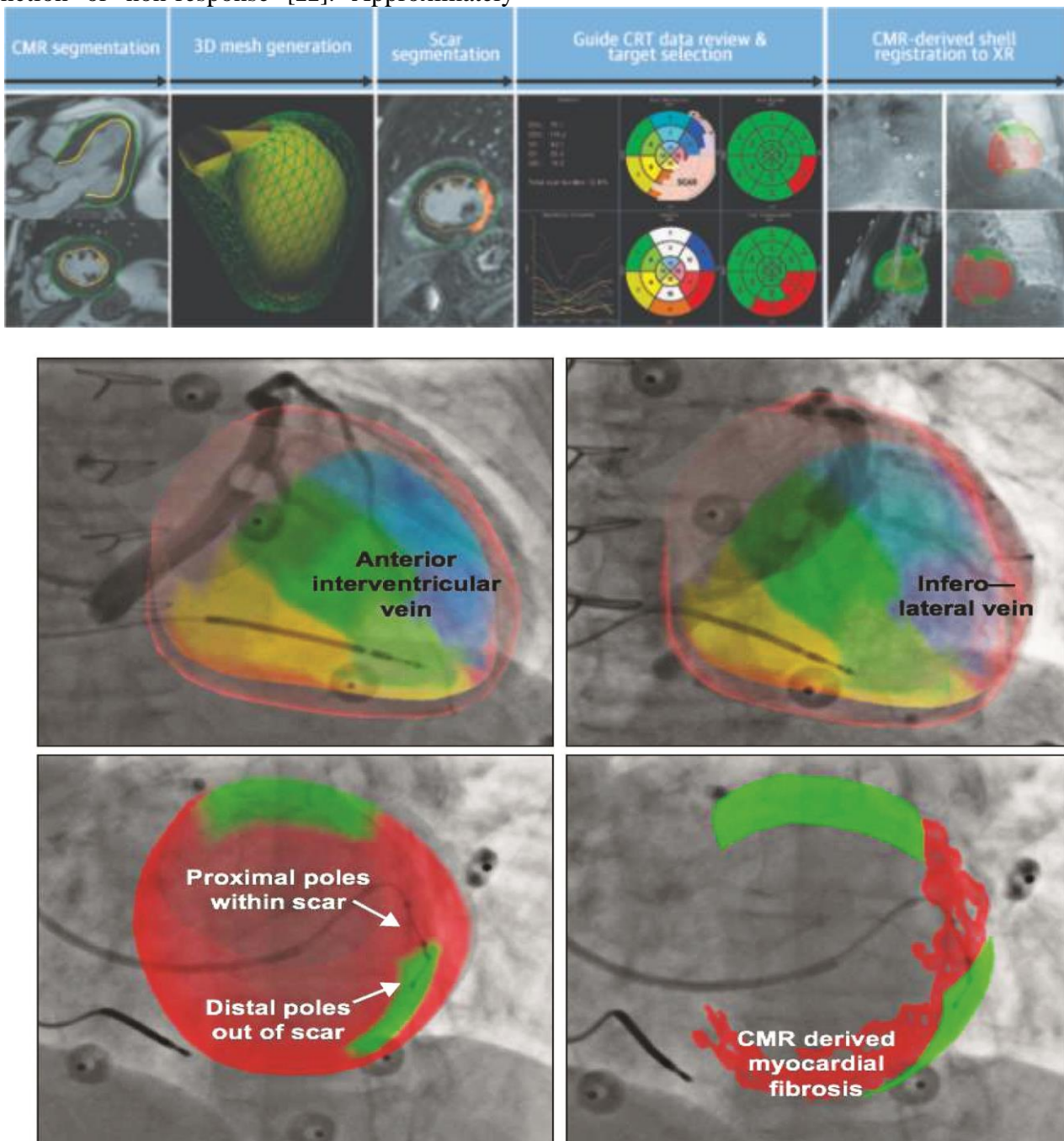


Figure 2. Optimal LV lead position guided by multiple imaging technics [25]

The role of cardiac magnetic resonance after CRT implantation

Recent volumetric and functional assessment studies with cardiac magnetic resonance undoubtedly revealed the potential of CMR for meticulous patient follow-up in terms of response after CRT implantation. By recording the cardiac output with CRT turned off or on, it is possible to get useful information about improved left ventricular function after the implantation [26]. Technical aspects of patient follow-up for patients with cardiac resynchronization therapy turned on have improved over the years (**Figure 3**), expanding the opportunities cardiac magnetic resonance has to improve outcomes. Multiple studies and a number of more than 10.000 MRI scans have proven the safety of MRI-conditional devices [8].

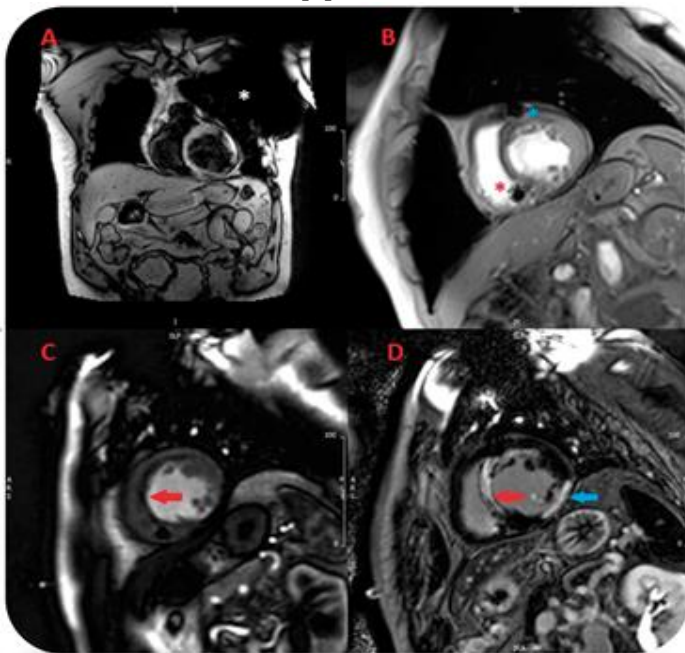


Figure 3. Different approaches of scanning patients with cardiac resynchronization turned on [26]

To improve the usefulness of cardiac magnetic resonance before and after cardiac resynchronization therapy, a multidisciplinary approach is required with cardiologists, MRI radiologists, clinical experts, and electrophysiologists.

Conclusions

Better identification of patients who could respond to cardiac resynchronization therapy is an important aspect of treating patients with heart failure. Cardiac magnetic resonance is a useful tool before CRT implantation in terms of evaluating the aetiology of heart failure and the degree of mechanical dyssynchrony. It helps evaluate the myocardial scar burden and the optimal positioning of the LV lead to improve clinical outcomes. Also, the effects of cardiac resynchronization therapy

could be evaluated after implantation by the synergistic effects of cardiac magnetic resonance and other imaging tools. Future large clinical trials will provide even more insights into the usefulness of this sophisticated imaging modality.

Conflict of interest: The authors declare that they have no conflict of interest.

References:

1. Boriani G, Diemberger I. Cardiac resynchroni-zation therapy in the real world: need to focus on implant rates, patient selection, co-morbidities, type of devices, and complications. *Eur Heart J.* 2017; 38(27): 2129-2131. PMID: 28430905. doi: 10.1093/eurheartj/ehx137.
2. Charron P, Elliott PM, Gimeno JR, Caforio ALP, Kaski JP, Tavazzi L, et al. The Cardiomyopathy Registry of the EURObservational Research Programme of the European Society of Cardiology: baseline data and contemporary management. *Eur Heart J.* 2018; 39(20): 1784-1793. PMID: 29378019. doi: 10.1093/eurheartj/ehx819.
3. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail.* 2016; 18(8): 891-975. PMID: 27207191. doi: 10.1002/ejhf.592.
4. Gorcsan J. Finding pieces of the puzzle of nonresponse to cardiac resynchronization therapy. *Circulation.* 2011;123(1):10-12. PMID: 21173347. doi: 10.1161/CIRCULATIONAHA.110.001297.
5. Popadic V, Zdravkovic M, Hinic S. Correlation between optimal coronary functional assessment results and cardiac magnetic resonance in patients after primary PCI. PCR 2020 Abstract Book.2020.
6. Klasnja S. Correlation between the usage of anabolic steroids and ST-elevation myocardial infarction in young adults. KBC Bezanijska kosa: Odeljenje kardiologije - Odsek za interventnu kardiologiju i pejsmejker. 2016.
7. Thomas G, Kim J, Lerman BB. Improving Cardiac Resynchronisation Therapy. *Arrhythm Electrophysiol Rev.* 2019; 8(3): 220-227. PMID: 31463060. doi: 10.15420/aer.2018.62.3.

8. Bhuvana AN, Moralee R, Moon JC, Manisty CH. Making MRI available for patients with cardiac implantable electronic devices: growing need and barriers to change. *Eur Radiol.* 2020; 30(3): 1378-1384. PMID: 31776746. doi: 10.1007/s00330-019-06449-5.
9. Vasiljevic Z, Krljanac G, Zdravkovic M, Lasica R, Trifunovic D, Asanin M. Coronary Microcirculation in Heart Failure with Preserved Systolic Function. *Curr Pharm Des.* 2018; 24(25): 2960-2966. PMID: 29992878. doi: 10.2174/1381612824666180711124131.
10. Chavanon ML, Inkrot S, Zelenak C, Tahirovic E, Stanojevic D, Apostolovic S, et al. Regional differences in health-related quality of life in elderly heart failure patients: results from the CIBIS-ELD trial. *Clin Res Cardiol.* 2017; 106(8): 645-655. PMID: 28361371. doi: 10.1007/s00392-017-1101-6.
11. Tee M, Noble JA, Bluemke DA. Imaging techniques for cardiac strain and deformation: comparison of echocardiography, cardiac magnetic resonance and cardiac computed tomography. *Expert Rev Cardiovasc Ther.* 2013; 11(2): 221-231. PMID: 23405842. doi: 10.1586/erc.12.182.
12. Cao JJ, Ngai N, Duncanson L, Cheng J, Gliganic K, Chen Q. A comparison of both DENSE and feature tracking techniques with tagging for the cardiovascular magnetic resonance assessment of myocardial strain. *J Cardiovasc Magn Reson.* 2018; 20(1): 26. PMID: 29669563. doi: 10.1186/s12968-018-0448-9.
13. Obeng-Gyimah E, Nazarian S. Cardiac Magnetic Resonance as a Tool to Assess Dyssynchrony. *Card Electrophysiol Clin.* 2019; 11(1): 49-53. PMID: 30717852. doi: 10.1016/j.ccep.2018.11.007.
14. Thomas G, Kim J, Lerman BB. Improving Cardiac Resynchronisation Therapy. *Arrhythm Electrophysiol Rev.* 2019; 8(3): 220-227. PMID: 31463060. doi: 10.15420/aer.2018.62.3.
15. Zdravkovic M, Tschope C, Pieske B, Kelle S. Myocardial Fibrosis Due to Exorbitant Exercise or Just Undetected Post-Inflammatory Stages? *JACC Cardiovasc Imaging.* 2019; 12(2): 381-382. PMID: 30732724. doi: 10.1016/j.jcmg.2018.12.008
16. Ypenburg C, Roes SD, Bleeker GB, Kaandorp TAM, de Roos A, Schalij MJ, et al. Effect of total scar burden on contrast-enhanced magnetic resonance imaging on response to cardiac resynchronization therapy. *Am J Cardiol.* 2007; 99(5): 657-660. PMID: 17317367. doi: 10.1016/j.amjcard.2006.09.115.
17. Harb SC, Toro S, Bullen JA, Obuchowski NA, Xu B, Trulock KM, et al. Scar burden is an independent and incremental predictor of cardiac resynchronization therapy response. *Open Heart.* 2019; 6(2): e001067. PMID: 31354957. doi: 10.1136/openhrt-2019-001067.
18. Ahmed W, Samy W, Tayeh O, Behairy N, El Fattah AA. Left ventricular scar impact on left ventricular synchronization parameters and outcomes of cardiac resynchronization therapy. *Int J Cardiol.* 2016; 222:665-670. PMID: 27517660. doi: 10.1016/j.ijcard.2016.07.158.
19. Chalil S, Foley PWX, Muyhaldeen SA, Patel CRK, Yousef ZR, Smith EAR, et al. Late gadolinium enhancement-cardiovascular magnetic resonance as a predictor of response to cardiac resynchronization therapy in patients with ischaemic cardiomyopathy. *Europace.* 2007; 9(11): 1031-1037. PMID: 17933857. doi: 10.1093/europace/eum133.
20. Chalil S, Stegemann B, Muhyaldeen SA, Khadjooi K, Foley PW, Smith REA, et al. Effect of posterolateral left ventricular scar on mortality and morbidity following cardiac resynchronization therapy. *Pacing Clin Electrophysiol.* 2007; 30(10): 1201-1209. PMID: 17897122. doi: 10.1111/j.1540-8159.2007.00841.x.
21. Rickard J, Jackson G, Spragg DD, Cronin EM, Baranowski B, Wilson Tang WH, et al. QRS prolongation induced by cardiac resynchronization therapy correlates with deterioration in left ventricular function. *Heart Rhythm.* 2012; 9(10): 1674-8167. PMID: 22583844. doi: 10.1016/j.hrthm.2012.05.013.
22. Zdravkovic M, Tschope C, Pieske B, Kelle S. Myocardial Fibrosis Due to Exorbitant Exercise or Just Undetected Post-Inflammatory Stages? *JACC Cardiovasc Imaging.* 2019; 12(2): 381-382. PMID: 30732724. doi: 10.1016/j.jcmg.2018.12.008.
23. Bisson A, Pucheux J, Andre C, Bernard A, Pierre B, Babuty D. Localization of Left Ventricular Lead Electrodes in Relation to Myocardial Scar in Patients Undergoing Cardiac Resynchronization Therapy. *Heart Rhythm.* 2016; 13(2): 481-489. PMID: 26498258. doi: 10.1016/j.hrthm.2015.10.024.
24. Taylor RJ, Umar F, Panting JR, Stegemann B, Leyva F. Left ventricular lead position, mechanical activation, and myocardial scar in relation to left ventricular reverse remodeling and clinical outcomes after cardiac resynchronization therapy: a feature-tracking and contrast-enhanced cardiovascular magnetic resonance study. *Heart Rhythm.* 2016; 13(2): 481-489. PMID: 26498258. doi: 10.1016/j.hrthm.2015.10.024.

25. Behar JM, Mountney P, Toth D, Reiml S, Panayiotou M, Brost A, et al. Real-Time X-MRI-guided left ventricular lead implantation for targeted delivery of cardiac resynchronization therapy. *JACC Clin Electrophysiol.* 2017; 3(8): 803-814. PMID: 29759775. doi: 10.1016/j.jacep.2017.01.018.
26. Thomas G, Kim J, Lerman BB. Improving Cardiac Resynchronisation Therapy. *Arrhythm Electrophysiol Rev.* 2019; 8(3): 220–227. PMID: 31463060. doi: 10.15420/aer.2018.62.3.

PREGLEDNI RAD

ULOGA KARDIOMAGNETNE REZONANCE U RESINHRONIZACIONOJ TERAPIJI SRČANE SLABOSTI - KOLIKO KORISNA MOŽE BITI?*Marija ZDRAVKOVIĆ^{1,2}, Višeslav POPADIĆ¹, Slobodan KLAŠNJA¹*¹ KBC Bežanijska kosa, Beograd, Srbija; ² Medicinski fakultet, Univerzitet u Beogradu, Beograd, Srbija**SAŽETAK**

Pacijenti sa srčanom slabošću, redukovanom ejectionom frakcijom, i znacima mehaničke i električne asinhronije, imaju lošu prognozu. Resinhronizaciona terapija srčane slabosti je dokazan terapijski modalitet, koji redukuje simptome srčane slabosti, mortalitet i morbiditet kod ovih pacijenata. Dobra identifikacija pacijenata, koji bi mogli da imaju koristi od resinhronizacione terapije je od ključnog značaja, s obzirom na procenat pacijenata kod kojih ne postoji kliničko poboljšanje nakon implantacije CRT. Kardiomagneta rezonanca je korisno, neinvazivno, sofisticirano dijagnostičko sredstvo koje može pružiti značajne informacije o etiologiji srčane slabosti, stepenu mehaničke asinhronije leve komore, te u boljoj identifikaciji pacijenata koji bi mogli optimalno da odgovore na resinhronizacionu terapiju. Takođe je od izuzetnog značaja u evaluaciji miokardnog ožiljka, kao jednog od pokazatelja mogućeg nezadovoljavajućeg odgovora na terapiju, a od koristi je i u optimalnom pozicioniranju LV elektrode u cilju poboljšanja kliničkih ishoda. Uloga kardiomagnetne rezonance u praćenju pacijenata, a u cilju procene optimalnog odgovora na resinhronizacionu terapiju srčane slabosti sve više dobija na značaju. Pružajući korisne informacije o etiologiji srčane slabosti, anatomiji koronarnog venskog sistema, stepenu mehaničke asinhronije leve komore, opterećenju miokardnim ožiljkom i pozicioniranju LV elektrode, kardiomagnetna rezonanca može biti od esencijalnog značaja u poboljšanju kliničkih ishoda kod ovih pacijenata. Dalji razvoj metode omogućiće bolju selekciju pacijenata, bolju optimizaciju samog uređaja, kao i razumevanje mehanizama neadekvatne resinhronizacije.

Ključne reči: kardiomagnetna rezonanca, srčana slabost, resinhronizaciona terapija, mehanička asinhronija, miokardni ožiljak