Assessment of left ventricular arrhythmogenic substrate in patients with ischemic heart disease by cardiac magnetic resonance

Neuschl V[1], Berecova Z[2], Madaric J[3], Simkova J[1], Glezlova A[1], Hatala R[3]

[1]*Institute of Diagnostic Imaging, MRI s.r.o., Trnava, Slovakia*

Neuschl V, Berecova Z, Madaric J, Simkova J, Glezlova A, Hatala R. **Assessment of left ventricular arrhythmogenic substrate in patients with ischemic heart disease by cardiac magnetic resonance.** Cardiology Lett. 2018;27(1):20–26

Abstract. *Background:* The most common cause of sudden death is malignant ventricular tachyarrhythmia – ventricular tachycardia and ventricular fibrillation occurring based on the morphological substrate of the infarction scar.

Objectives: Results of qualitative and quantitative analysis of the scar and LV (left ventricular) function acquired by cardiac magnetic resonance (CMR) were correlated with the subsequent occurrence of malignant ventricular arrhythmias in patients with a high risk of sudden cardiac death (SCD).

Methods: We have prospectively followed 47 patients (mean age 60 ± 11 years) who were hospitalized for an implantable cardioverter-defibrillator (ICD) implantation to prevent SCD. All post-myocardial infarction (post-MI) patients had severe residual LV dysfunction (LVEF 33±14%). Patients were examined by CMR. In the CMR analysis, we evaluated the basic functional parameters of the LV as well as the mass, volume, transmurality and heterogeneity of the post-MI scar.

Results: The patients with malignant arrhythmias were characterized by smaller LV diameters in the end-diastole (LVED 192 ± 79 vs. 254 ± 47 mm, p = 0.003) and end-systole (LVES 131 ± 80 vs. 181 ± 45 mm, p = 0.01). As for the other observed functional and morphological CMR parameters, no significant differences between the two groups were detected.

Conclusion: These results indicate that post-MI patients with severe residual left ventricular dysfunction and dilatation are in the long-term characterized by a lower incidence of malignant arrhythmias compared to the patients with less dilated LV with a comparably severe LV dysfunction. Fig. 3, Tab. 2, Ref. 24, online full text (Free, PDF), www.cardiologyletters.sk

Key words: myocardial infarction – cardiac magnetic resonance imaging – ventricular tachyarrhythmias – sudden cardiac death – implantable cardioverter defibrillator

Sudden cardiac death (SCD) affects annually more than 1 million people in Europe and North America and it continues to be a serious medical and social problem of the developed world (1). In Slovakia, up to 8000 out-of-hospital cardiac arrests occur annually (2). The most common cause of sudden death is malignant ventricular tachyarrhythmia – ventricular tachycardia and/or ventricular fibrillation. The occurrence of malignant ventricular arrhythmias is closely linked to fibrotic morphological substrate, typically an infarction scar (3). Currently the only reliable strategy

From [1]Institute of Diagnostic Imaging, MRI s.r.o., Trnava, [2]Department of radiology, St. Michal Hospital, Bratislava, [3]Department of Arrhythmias and Cardiac Pacing, Academic Divsion of Cardiology and Angiology, Medical Faculty, Slovak Medical University and National Cardiovascular Institute – NUSCH Bratislava, Slovakia

Manuscript received March 7, 2018; accepted for publication March 9, 2018

Address for correspondence: Vladimir Neuschl, MD, Institute of diagnostic imaging, MRI s.r.o., Starohájska 2, SK-917 01 Trnava, Slovakia, e-mail: neuschl.vlado.vn@gmail.com

Primárna práca bola uverejnená v: Neuschl V, Berecova Z, Madaric J, Simkova J, Glezlova A, Hatala R. Structural assessment of myocardial infarction scars and left ventricular function wit cardiac magnetic resonance imaging in patients with high risk of sudden cardiac death. Bratisl Med J 2018;119(5), in press.

to prevent arrhythmic SCD is the implantation of a cardioverter-defibrillator (ICD). Most ICDs are implanted in patients with high risk of arrhythmic death as a primary preventative therapy. In the majority of patients the high risk of SCD is determined by the presence of chronic heart failure, both of ischemic and non-ischemic etiology. The typical malignant arrhythmogenic substrate is represented by an old myocardial infarction scar.

Key in the identification of these high-risk patients is the presence of left ventricular systolic dysfunction expressed by the reduced left ventricular ejection fraction (LVEF). Thus there is, in a post-MI patient with a LVEF < 35% (in the absence of any other disease with a severe *quad vitam* prognosis), according to all major international guidelines, an indication in class I A for a primary preventative implantation of ICD (2015 ESC recommendation for the management of patients with ventricular arrhythmia and prevention of the sudden cardiac death) (4).

Albeit, such a simplified risk stratification for SCD has an acceptable negative predictive value but only a rather limited positive prediction value. Current research in this area of cardiology focuses new approaches on SCD risk stratification techniques in order to improve the accuracy of their predictive values (5). The new predictors can by classified into 3 categories:

- Complex computerized analysis of surface ECG signals with techniques for assessment of heart rate variability, Fourier spectral analysis in time and frequency domain, T-wave alternations, signal averaging and late ventricular potentials, etc.
- humoral biomarkers (e.g. natriuretic peptides, myocardial damage markers and others)
- imaging of proarrhythmogenic structural myocardial changes predisposing to malignant ventricular arrhythmias (echocardiography, magnetic resonance).

The aim of this study was the analysis of several MRI derived qualitative and quantitative parameters of LV myocardial structure and function in post-MI patients and to correlate CMR findings with the occurrence of death or malignant ventricular arrhythmias detected by ICD implanted shortly after the cardiac magnetic resonance (CMR) examination.

Patients and methods

The observed cohort consisted of patients hospitalized in our specialized tertiary care institution who presented as potential candidates for ICD implantation in both primary and secondary prevention. All patients had significant coronary heart disease with a history of myocardial infarction (MI) with residual severe LV dysfunction (EF ≤ 40%). The total number of analyzed patients was 47; their mean age was 60±11 years. The basic demographic characteristics of the cohort are listed in **Table 1**. During the observation period during the years 2010 – 2017 five patients died suddenly and 7 died of refractory congestive heart failure. Mortality data were obtained from the Statistical office of the Slovak Republic (Bratislava and Trnava offices).

Table 1 Basic demographic and clinical characteristics of the observed cohort

Total number of patients (n)	47
Age (years)	60 ± 11
Male : Female	41 : 6
LVEF (%)	33 ± 14
Number of primary preventative ICD implantations	26
Number of ICD implantations in secondary prevention	5
Patients without ICD with sudden cardiac death	5
Patients with ICD and heart failure death	7

All analyzed patients were divided into two groups:

Group A. Patients with malignant arrhythmias (n=17). This group comprised 3 subgroups:

1. patients after ICD implantation in primary prevention with appropriate shocks
2. patients after ICD implantation in secondary prevention (i.e. after spontaneous VT and/or aborted sudden death)
3. patients without ICD with a sudden cardiovascular (CV) death

Group B. patients without malignant arrhythmias (n=30). This group comprised 2 subgroups:

1. patients with implanted ICD in primary prevention but without appropriate shocks
2. surviving patients without ICD

Two patients underwent surgical revascularization during the follow-up period and one patient underwent successful heart transplantation.

MR screening. All investigations were performed at the magnetic resonance premises of a specialized imaging centre (IZD – Institute of Diagnostic Imaging – Inc., Trnava, Slovakia) equiped with the CMR 1,5 T Avanto MRI scanner by Siemens, Germany. Investigations were supervised by a trained radiologist and individually evaluated by a radiologist with CMR specialization.

After data acquisition following protocol for LV function evaluation and myocardial infarction scar detection was applied:

1. Morphological sequences to distinguish pathological infiltrates in the myocardium (adipose deposits and other)
2. Multi-segmental sequences (for evaluation of regional and global LV function)
3. Myocardium perfusion (rest)

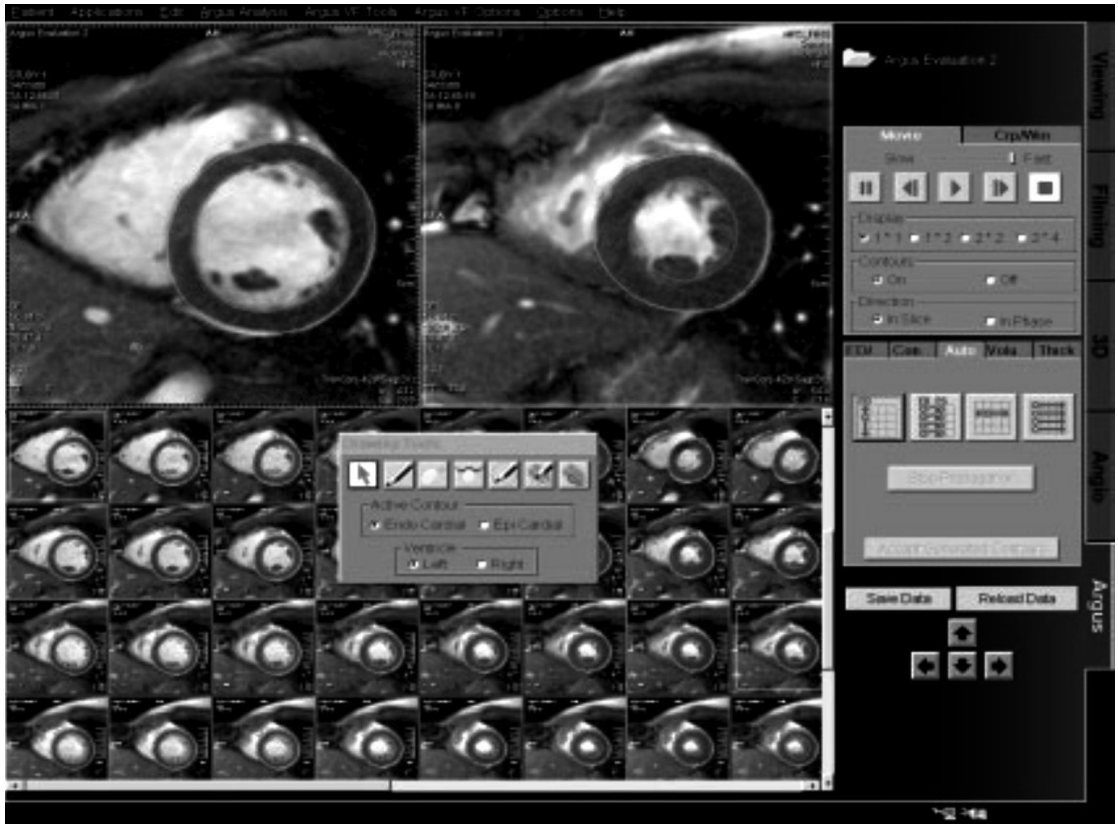

Figure 1 CMR diagnostic console with Siemens Argus software, to determine endo and epicardial contour left ventricular in enddiastolic and endsystolic phase in short axis. (Figure from the IZD archive in Trnava).

4. Aortic and pulmonary artery flow
5. Ischemic and non-ischemic LV myocardial scar detection in 2D and 3D IR sequences

Volumetric data were obtained in 2-chamber view by standard steady-state (TRUFI) sequences. The scans were 6 mm thick and covered the entire left ventricle from the base to the apex. The used settings were: PAT factor 2, FOV 340x340 mm, matrix 256x256, Flip angle 80`, TR 36 mm, TE 1,2 ms. Gadobutrol, an extracellular macrocyclic non-ionic gadolinium contrast agent, was administered to all patients (Gadovist 1 mmol/ml/ manufactured by Bayer AG, Germany).

Acquired MRI data analysis. LVEF, left ventricle volume and mass were examined by commercially available cardio software within the Siemens-Argus function **(Figure 1)**. LV segments were set automatically, according to the American Heart Association (AHA) model with 17 segments according to the main coronary artery supply. Key data such as LVEF, LVED and LVES volume and mass were calculated.

Scar analysis included three aspects of quantifying the percentage of LV myocardial scarring – the amount of MI, converted scar mass and transmurality and heterogeneity count. The evaluation was performed by the Medis QMass diagnostic software (QMassMR version 8.1; Medis, Leiden, Netherlands.) The scarring was assessed by the 2-SD technique (standard deviation) (6).

Percentage of the total scar size was calculated automatically with Q Mass program by summing all the hyperintense subendocardial to transmural myocardial zones of the left ventricle.

Scar heterogeneity was assessed visually when detecting intermediate scarring signal of the border zone.

Mass of the scar was calculated by multiplying the scar percentage with the total LV mass in the ED.

Electrophysiological monitoring. Thirty-one patients were implanted with an ICD, all as Class I indications according to the ESC recommendations for the prevention of SCD (4). Twenty-six patients were implanted in primary

prevention and 5 patients in secondary prevention (84% vs. 26%).

There was no change in the health status of patients in the period between MR examination and ICD implantation. Patients were followed every 6 months and relevant data were provided by the Department of Arrhythmias and Cardiac pacing of the National Cardiovascular Institute (NÚSCH a.s.) in Bratislava, Slovakia.

Statistical methods

All continuous variables are presented as mean ± SD. Normal distribution of the cohort division was tested by the Kolmogorov-Smirnov test. The Mann-Whitney test (t-test) for comparing continuous data was used and the e Fisher exact test was used for the categorical variables. For all analyses, the value of $p<0.05$ was considered statistically significant.

Results

Overall, 47 patients were prospectively followed after ICD implantation. All patients had coronary heart disease with a severe residual LV dysfunction (LVEF 33±14%). The mean observation period was 2.7 years. Nine patients experienced adequate shocks (28% of implanted patients). Seven ICD patients died non-suddenly.

When compared to patients from group B, patients with malignant arrhythmias (group A) were characterized by a lower LV diameter in end-diastole (LVED = 192±79 vs. 254±47 mm, p=0.003), as well as in end-systole (LVES = 131±80 vs. 181±45 mm, p=0.01). No other significant differences were found in the observed functional and morphological MR parameters between the two groups **(Table 2)**.

We compared the LVEF assessed by MR to echocardiographic assessment performed at the same time as the MR examinations. Based on echocardiographic assessment mean LVEF in group A was LVEF 35±11%, and in the group B32±6%. There were no significant differences between LVEF assessed by MR and by echocardiography (ECHO LVEF of group A+B p=0.11 vs. CMR LFEF of group A+B p=0.13).

Furthermore, smaller post-MI scarring (7-12% of LV mass) was detected in 3 patients, who clinically did not have MI.

Small **LV mural thrombi** (not identified by echocardiography) were detected in 4 out of 47 patients. The thrombus size in the long axis ranged from 7 mm to 12 mm. All thrombi were localized apically, at the site of post-MI scarring **(Figure 2)**.

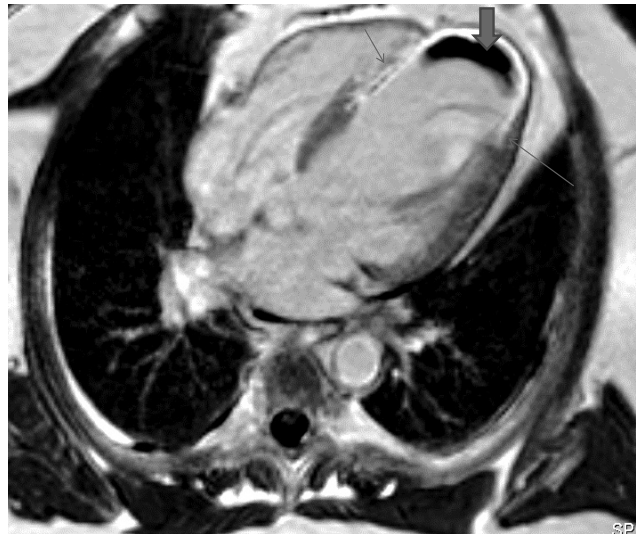

Figure 2 4-chamber LGE sequence projection in an individual patient. Non-viable myocardium and wall apex thrombus – thick arrow, viable myocardium apico-lateral wall (scar size is 50% of the wall) – long arrow, heterogenuos enhancement of the medial septum – short arrow. (Figure from the IZD archive in Trnava).

Discussion

In recent years, CMR research has upgraded this investigative method to a reference method of assessing left ventricular structure and function. Myocardial infarction lesions can be precisely visualized in all stages of its development. The basis of CMR infarction lesion analysis is the technique of late enhancement of saturation after administering the contrast agent gadolinium (LGE – late gadolinium enhancement). Fibrous tissue absorbs gadolinium, resulting in higher signal strength. Bello et al. (7) hypothesized for the first time that the LGE-CMR determined size and morphology of the infarction deposit, and might be a better predictor of ventricular tachycardia inducibility than traditional LVEF<35%. Patients with monomorphic ventricular tachycardia had greater infarction lesions compared to patients without inducible arrhythmia.

Table 2 MR parameters of the scar and left ventricular function

CMR parameters of LV scar and function	A n = 17	B n = 30	p – value
Scar volume (%)	23 ± 9	25 ± 8	0.19
LV mass (g)	176 ± 39	185 ± 38	0.25
Scar mass (g)	41 ± 16	47 ± 18	0.15
Scar transmurality (n)	14	26	0.69
Scar heterogeneity (n)	12	24	0.49
LVEF (%)	35 ± 16	30 ± 8	0.13
EDV (ml)	192 ± 79	254 ± 47	0.003
ESV (ml)	131 ± 80	181 ± 45	0.01

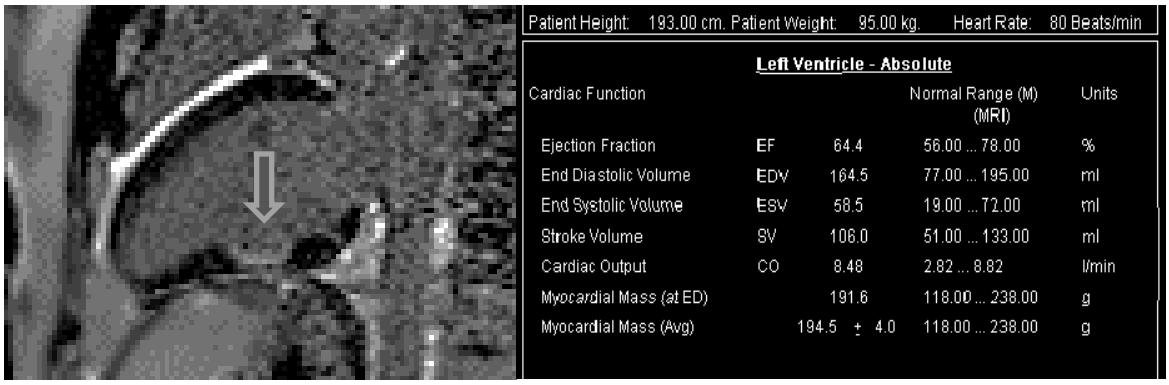

Figure 3 MR scan of the left ventricle in long axis – patient with atypical chest pain, with nonspecific ECG and negative cardiac biomarkers. CMR finding of a small transmural scar of the lower wall. The scar volume of 5%, scar mass 9 g and the EF LV 65% (patient not included in the study).

CMR has a unique ability to visualize the character of peri--infarct zone, which, due to its heterogeneity, is considered to be the part of the infarction deposit with the greatest arrhythmogenic potential (8, 9).

The main finding of our analysis is that post-MI patients with severe residual LV dysfunction and significantly dilated LV have lower incidence of malignant arrhythmias compared to patients with a comparable LV dysfunction but less LV dilatation. This observation offers a plausible support of the hypothesis that dysfunctional and massively dilated LVs are prone to intractable pump failure and have lower arrhythmogenic potential compared to the less dilated, but dysfunctional ventricles. This finding might be the starting point of the hypothesis that the risk of sudden arrhythmic death is determined not only by the degree of LV dysfunction. LV mass and LVEF were similar in both groups as well as the other scar parameters.

Our study did not confirm the expected differences of post-infarction scar parameters when comparing patients with malignant ventricular arrhythmias and sudden cardiac death to those without them. The reasons for not revealing differences in scar architecture between individual groups are likely to be complex, both biologically and methodologically. As for the latter, a relatively small population with mixed ICD indications together with semi-automatic assessment of the scar may have contributed to our observations.

Statistically significant differences between the groups have been found in the exact volumetric sizes of end-diastolic and end-systolic LV volume. We consider this data to be very reliable as the CMR is a gold standard of non-invasive quantification of these measurements (10). Considerable changes in the remodeling and left ventricular wall hypertrophy in the group A may be expected. Additional parameters, such as relative myocardial thickness, hypertrophy distribution and segmental kinetic evaluation of the wall were not evaluated in more detail which might have increased the accuracy of the observed findings.

Interestingly, there were some patients with no relevant clinical and/or ECG evidence of MI but with clear presence of smaller ischemic scars (4 – 12%) **(Figure 3)**. According to some authors, they have prognostic significance in CV mortality (11, 12). Compared autopsy findings of MI is considered to be one of the most frequently overlooked clinical diagnoses (13, 14). These non-identified MIs may be too small for the ECG detection and MI is without typical chest pain symptoms (11). Non-identified MIs detected by MR occurred in the group of patients older >70 year with a significant risk for adverse CV events (15). Similar findings were observed also in a sub-study of the ICELAND-MI trial of the AGES Reykjavik study (16) comparing patients with MI not reflected in the ECG but clearly visualized by MR. Mortality in the latter group was similar to patients with clinically diagnosed MI.

More recent data (17) point out the predictive significance of the size of LV myocardium scar of non-coronary etiology, such as in hypertrophic cardiomyopathy. Scar exceeding >15% of LV is associated with an increased risk of sudden cardiac death. These patients might benefit from primary preventative ICD therapy.

Thrombus in the heart chambers has a predominantly hypointense signal in LGE sequences and is well-discrimmated from the perifocal hyperintense myocardial scar. Four patients in our cohort had apical thrombi not detected echocardiographically at the LV wall. For detecting endocavitary thrombi, contrast CMR examination has the highest sensitivity and specificity (88±9% and 99±2%) compared to TTE (23±12% and 96±3.6%) and TEE (40±14% and 96±3.6%) (18). Low LVEF and transmural myocardial scar were independent risk factors in the development of intracardiac thrombus (19). During the 6-month follow-up in the study, the incidence of cerebrovascular accident was 5.6% in thrombus patients and 2.1% without thrombus.

The use of different types of gadolinium contrast agent also affects the technique of measuring the post-MI scar (20, 21). Macrocyclic non-ionic gadolinium contrast agent – gadobutrol was used in our study, which is recommended by some researchers to improve contrast between LV cavity and myocardial scar (22).

Study limitations

Limitations of the submitted study can be divided into two primary groups; limitations of the study design and limitations of the CMR examination. The particular limiting factor of the study design is the low number of patients from both groups with a relatively short follow-up (2.7 years). Analyzing a patient with both primary and secondary preventative ICD indications is also a limiting factor, but was also used in most similarly focused studies. Furthermore, several possible parameters of LV geometry were not studied (e.g. RWT – relative wall thickness, etc.)

Basic CMR limitations include the impossibility of examining patients with ferromagnetic implants, including impulse generators of the pre-MRI compatible era. Furthermore, there are limiting CMR data in some patients with irregular heart beat.

Non-standard scar definition in a semi-automatic 2SD measurement methodology is the reason for a potential overestimation of the signal intensity of the entire scar (23). Finally, the reference methods of non-invasive evaluation of the total amount of myocardial scarring are inaccessible. Experimental studies using histopathological techniques of scarring measurement from biopsy did not determine the total amount and scar distribution (24).

Conclusion

CMR represents a new dimension in the quality of heart imaging. In the conditions of the health-care system in the Slovak Republic it is still a heavily underused method. This paper has the ambition of pointing out clinically useful applications of CMR imaging for the practising cardiologist. Thanks to its accuracy, non-invasiveness and radiation safety, CMR is undoubtedly the imaging method of the future. In contrast to the severe risks linked to any X-ray imaging method, no adverse effects of CMR, with or without contrast agents, have been reported.

Study results acquired mainly in the last decade form a solid basis for the hypothesis that the quantitative and qualitative analysis of morphological aspects of the infarction scar may become a highly desirable complementary parameter in identifying patients with a high risk of SCD. Scar detection in CMR imaging has a unique spatial resolution with the ability to capture not only the overall scar architecture but also to characterize the fine tissue structure. Thus, we believe that CMR is not only a precise tool for evaluating regional and global LV function, but has also an important potential to refine risk stratification of malignant ventricular arrhythmias in post-MI patients.

Our findings summarized in the presented study are only a very modest contribution to this topic, mainly due to the fundamental limitation of a relatively small number of patients (even though the majority of publications also refer to less than 100 patients). In the structural parameters of infarction scar-extent and transmurality no differences were found between groups with and without malignant arrhythmias. However, the finding that patients with severe left ventricular dysfunction and concomitant significant dilatation profit less from the ICD implantation may be very useful complementary information for a clinically meaningful decision in primary SCD prevention using ICD.

Literature

1. Mozaffarian D, Benjamin EJ, Go AS, et al. 2015 Heart disease and stroke statistics-2015 update: a report from the American Heart Association. Circulation. 2015;131:e29-322. doi: 10.1161/CIR.00000000000001
2. Gräsner JT, Lefering R, Koster RW, et al. EuReCa ONE-27 Nations, ONE Europe, ONE Registry: A prospective one month analysis of out-of-hospital cardiac arrest outcomes in 27 countries in Europe. Resuscitation. 2016 Aug;105:188-195. doi: 10.1016/j.resuscitation.2016.06.004
3. Bayés De Luna A, Coumel P, Leclercq JF. 1989. Ambulatory sudden cardiac death: mechanisms of production of fatal arrhythmia on the basis of data from 157 cases. Am Heart J. 1989;117:151-159.
4. Priori SD, Blomström-Lundquist C, Mazzanti A, et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Eur Heart J. 2015;1;36(41):2793-2867. doi: 10.1093/eurheartj/ehv316.
5. Dagres N, Hindricks G. 2013 Risk stratification after myocardial infarction: is left ventricular ejection fraction enough to prevent sudden cardiac death? Eur Heart J. 2013;34:1964-1971.
6. Fernández-Armenta J, Berruezo A, Mont L, et al. 2012. Use of myocardial scar characterization to predict ventricular arrhythmia in cardiac resynchronization therapy. Europace. 2012;14:1578-1586. doi:10.1093/europace/eus104
7. Bello D, Fieno D., Kim RJ, et. al. 2005 Infarct morphology identifies patients with substrate for sustained ventricular tachycardia. J Am Coll Cardiol. 2005;45:1104-1108.
8. Schmidt A, Azevedo CF, Cheng A, et al. 2007 Infarct tissue heterogeneity by magnetic resonance imaging identifies enhanced cardiac arrhythmia susceptibility in patients with left ventricular dysfunction. Circulation. 2007;115:2006-2014.

9. Zeidan-Shwiri T, Yang Y, Lashevsky I, et al. 2015 Magnetic resonance estimates of the extent and heterogeneity of scar tissue in ICD patients with ischemic cardiomyopathy predict ventricular arrhythmia. Heart Rhythm. 2015;12:802-808. doi: 10.1016/j.hrthm.2015.01.007.
10. Alfakih K, Reid S, Jones T, et al. Assessment of ventricular function and mass by cardiac magnetic resonance imaging. Eur Radiol. 2004;14:1813-1822.
11. Brieger D, Eagle KA, Goodman SG, et al. 2004 Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events. Chest. 2004;126:461-469.
12. Schelbert EB, Cao JJ, Sigurdsson S, et al. 2012 Prevalence and prognosis of unrecognized myocardial infarction determined by cardiac magnetic resonance in older adults. JAMA. 2012;308:890-896. doi: 10.1001/2012.jama.11089.
13. Perkins GD, Mcauley DF, Davies S, et al. 2003 Discrepancies between clinical and postmortem diagnoses in critically ill patients: an observational study. Crit Care. 2003;7: R129-132.
14. Spiliopoulou C, Papadodima S, Kotakidis N, et al. 2005. Clinical diagnoses and autopsy findings: a retrospective analysis of 252 cases in Greece. Arch Pathol Lab Med. 2005;129:210-214.
15. Barbier CHE, Bjerner T, Johansson L, et al. 2006. Myocardial scars more frequent than expected: magnetic resonance imaging detects potential risk group. J Am Coll Cardiol. 2006;48:765-771.
16. Schelbert EB, Cao JJ, Sigurdsson S, et al. 2012 Prevalence and prognosis of unrecognized myocardial infarction determined by cardiac magnetic resonance in older adults. JAMA. 2012;308:890-896. doi: 10.1001/2012.jama.11089
17. Rowin EJ, Maron MS. 2016 The role of cardiac MRI in the diagnosis and risk stratification of hypertrophic cardiomyopathy. Arrhythmia & Electrophysiology Review. 2016;5:197-202. DOI: 10.15420/aer.2016:13:3
18. Srichai MB, Junor C, Rodriguez LL, et al. Clinical imaging, and pathological characteristics of left ventricular thrombus: a comparison of contrast-enhanced magnetic resonance imaging, transthoracic echocardiography, and transesophageal echocardiography with surgical or pathological validation. Am heart J. 2006 Jul 152(1):75-84.
19. Weinsaft JW, Kim HW, Shah DJ, et al. 2008 Detection of left ventricular thrombus by delayed enhancement cardiovascular magnetic resonance prevalence and markers in patients with systolic dysfunction. J Am Coll Cardiol. 2008;52:148-157.
20. Durmus T, Schilling R, Doeblin P, et al. 2012 Gadobutrol for magnetic resonance imaging of chronic myocardial infarction: intraindividual comparison with gadopentetate dimeglumine. Invest Radiol. 2012;47:183-188.
21. Wildgruber M, Stadlbauer T, Rasper M, et al. 2014 Single-dose gadobutrol in comparison with single-dose gadobenate dimeglumine for magnetic resonance imaging of chronic myocardial infarction at 3 T. Invest Radiol. 2014;49:728-734.
22. Wagner M, Schilling R, Doeblin P, et al. 2013 Macrocyclic contrast agents for magnetic resonance imaging of chronic myocardial infarction: intraindividual comparison of gadobutrol and gadoterate meglumine. Eur Radiol. 2013;23:108-114.
23. Flett AS, Hasleton J, Cook C, et al. 2011 Evaluation of techniques for the quantification of myocardial scar of differing etiology using cardiac magnetic resonance. JACC Cardiovasc Imaging. 2011;4:150-156.
24. de Jong S, van Veen TAB, de Bakker JMT, van Rijen HVM. 2012 Monitoring cardiac fibrosis: a technical challenge. Neth Heart J. 2012 Jan; 20(1):44-48.