

CHAPTER 3

**Clinical Consequences of Cardiac
Magnetic Resonance Imaging
versus Echocardiography-Guided
Patient Selection for Primary
Prevention Implantable Cardioverter
Defibrillator Therapy**

AMERICAN JOURNAL OF CARDIOLOGY. 2015 AUG;116(3):406-12

Mischa T. Rijniere*
Anne-Lotte C.J. van der Lingen*
Marjolein T.D. Weiland
Stefan de Haan
Robin Nijveldt
Aernout M. Beek
Albert C. van Rossum
Cornelis P. Allaart

*: Both authors contributed equally to this work

ABSTRACT

Introduction: The main eligibility criterion for primary prevention implantable cardioverter-defibrillator (ICD) therapy, i.e. left ventricular ejection fraction (LVEF), is based on large clinical trials using primarily 2-dimensional echocardiography (2DE). Presently, cardiac magnetic resonance imaging (MRI) is considered the gold standard for LVEF assessment. It has been demonstrated that cardiac MRI assessment results in lower LVEFs compared with 2DE. Consequently, cardiac MRI-LVEF assessment may lead to more patients eligible for ICD implantation with potential clinical consequences. The aim of this study was to evaluate the clinical impact of cardiac MRI-LVEF versus 2DE-LVEF assessment for ICD eligibility.

Methods: A total of 149 patients with cardiac MRI-LVEF $\leq 35\%$ referred for primary prevention ICD implantation who underwent both 2DE- and cardiac MRI-LVEF assessment were retrospectively included. 2DE-LVEF was computed by Simpson's biplane method. Cardiac MRI-LVEF was computed after outlining the endocardial contours in short-axis cine-images. Appropriate device therapy (ADT) and all-cause mortality were evaluated during 2.9 ± 1.7 years follow-up.

Results: The current study found that cardiac MRI-LVEF was significantly lower compared with 2DE-LVEF ($23 \pm 8\%$ vs. $30 \pm 8\%$, respectively, $p < 0.001$), resulting in 29 (19%) more patients eligible for ICD implantation according to current guidelines (LVEF $\leq 35\%$). Patients with 2DE-LVEF $> 35\%$ but cardiac MRI-LVEF $\leq 35\%$ experienced a lower ADT rate compared with patients having 2DE-LVEF $\leq 35\%$ (2.1%/year vs. 10.4%/year, respectively, $p = 0.02$). Application of cardiac MRI-LVEF cut-off of 30% resulted in 119 eligible patients experiencing 9.9%/year ADT, comparable with 2DE-LVEF cut-off value of 35%.

Conclusion: Cardiac MRI-LVEF assessment resulted in more patients eligible for ICD implantation compared with 2DE who showed a relatively low event rate during follow-up. The event rate in patients with cardiac MRI-LVEF $\leq 30\%$ was comparable with patients having a 2DE-LVEF $\leq 35\%$. This study suggests the need for re-evaluation of cardiac MRI based LVEF cut-off values for ICD eligibility.

INTRODUCTION

The benefit of implantable cardioverter-defibrillator (ICD) therapy for primary prevention of sudden cardiac death in patients with an impaired left ventricular ejection fraction (LVEF) was demonstrated in several large randomized trials.^{1,2} In these trials two-dimensional echocardiography (2DE) is primarily used for LVEF assessment. Consequently, current guidelines recommend ICD therapy for primary prevention in patients on optimal medical therapy with a LVEF $\leq 35\%$ who are in New York Heart Association (NYHA) class II or III of heart failure or LVEF $\leq 30\%$ in case of ischemic cardiomyopathy (CMP) and NYHA class I.^{3,4} As the guidelines do not specify the preferred method to assess LVEF, similar LVEF cut-off values for ICD eligibility are used for different imaging modalities.³ Presently, cardiac magnetic resonance imaging (MRI) is becoming increasingly common in clinical practice and is considered the gold standard for LVEF assessment due to its high reproducibility and accuracy.⁵ Previous studies comparing LVEF assessment by 2DE and cardiac MRI showed that they are not interchangeable.⁶⁻¹³ Especially in patients with impaired LVEF, most studies demonstrate that LVEF values as assessed using cardiac MRI are 3-7% lower when compared with LVEF assessed by 2DE, resulting in a substantial reclassification of patients with regard to ICD eligibility.^{7,10,11} Consequently, cardiac MRI-based LVEF assessment might lead to an increase of patients eligible for ICD implantation, which may have important clinical consequences for the benefit of primary prevention ICD therapy. A cardiac MRI-specific LVEF cut-off value for eligibility of ICD therapy has been suggested^{7,11}, but follow-up data on the clinical consequences of cardiac MRI-based LVEF assessment for the eligibility of primary prevention ICD therapy are lacking. The aim of the present study was to determine the clinical consequences of LVEF assessment by cardiac MRI compared to 2DE with respect to device eligibility and outcome (appropriate device therapy and death).

METHODS

Study population

In this retrospective observational cohort study, patients were included with a cardiac MRI assessed LVEF $\leq 35\%$ who received an ICD for primary prevention of sudden cardiac death from January 2005 to December 2012 in VU University Medical Center. Inclusion criteria were: (1) ischemic or dilated CMP, (2) assessment of LVEF using both 2DE and cardiac MRI within six months prior to ICD implantation, and (3) no reported clinical events between 2DE-LVEF and cardiac MRI-LVEF assessment. The local Ethics Committee of the VU University Medical Center approved the data collection and management of this study.

Patient characteristics prior to device implantation were collected from medical records: demographics, medical history of cardiovascular diseases, implantation indication, device type, medication, co-morbidities, NYHA class, QRS duration, and laboratory results.

Primary prevention was defined as no history of sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) (>48 hours after acute myocardial infarction). Ischemic CMP was defined as a history of (1) significant coronary artery disease, (2) myocardial infarction, (3) percutaneous coronary intervention, or (4) coronary artery bypass graft surgery.

Cardiac MRI and 2DE image acquisition and analysis

Cardiac MRI studies were performed on a 1.5-Tesla whole body scanner (Magnetom Sonata/Avanto, Siemens, Erlangen, Germany) using a dedicated phased-array body coil. After survey scans, cine imaging was performed using a retrospectively ECG-gated, steady-state free precession sequence during breath holds in mild expiration. Typical imaging parameters included slice thickness of 5 mm, slice gap 5 mm, temporal resolution <50 ms, repetition time 3.2 ms, echo time 1.54 ms, flip angle 60° and a typical image resolution of 1.3*1.6 mm. Stacks of 10 to 12 consecutive short-axis slices were acquired, fully covering the left ventricle. Subsequently, endocardial borders of the left ventricle were outlined manually in both end-diastolic and end-systolic phase. Papillary muscles were included in the left ventricular (LV) volume. LV volumes and LVEF were computed using these analyses. The cardiac MRI assessed LVEF data were extracted from clinical reports.

2DE was performed using commercially available ultrasound equipment and images were obtained in the standard parasternal long- and short-axis, and apical four- and two-chamber views. LV volumes and LVEF were calculated using the Simpson's biplane method after manual tracing of the endocardial borders from the four- and two-chamber images. Papillary muscles were included in the LV volumes. All measurements were performed according the American Society of Echocardiography standards.¹⁴ The 2DE-LVEF data were extracted from clinical reports.

Device programming and follow-up

All patients underwent ICD implantation or ICD combined with cardiac resynchronization therapy (CRT). The devices were typically programmed according to the PREPARE study with detection rates, depending on the device manufacturer, of > ~180 bpm (VT zone) and > ~250 bpm (VF zone), with extended detection intervals and appropriate utilization of antitachycardia pacing (ATP) therapy.^{15, 16} Clinical follow-up with device interrogation was routinely performed with regular intervals of six months. Event transmissions of patients connected with home-monitoring were reviewed instantly when they occurred. All recorded events and appropriate device therapy (ADT) were reviewed by specialized cardiac technicians or by electrophysiologists. ADT was defined as an episode of ATP and/or defibrillation shock to terminate VT or VF. The primary endpoint was defined as the occurrence of first ADT. The secondary endpoint was defined as the combined occurrence of ADT or all-cause mortality as first event.

Statistical analysis

Continuous variables were expressed as mean \pm standard deviations (SD). Histograms were used to determine if continuous data was normally distributed. Dichotomous and categorical data were expressed as frequencies and percentages. Comparisons of baseline characteristics of patients with and without ADT were performed using the chi-square test or Fisher's exact test for categorical or dichotomous data. Continuous unpaired data were compared using the Student's t test or Mann-Whitney U test when appropriate. Levene's test for equality of variances was used to verify the equal variances assumption of the Student's t test. Furthermore, a one-way ANOVA was performed to compare unpaired data between all cardiac MRI-LVEF subgroups. The paired samples t test was used to compare imaging parameters of patients with both cardiac MRI and 2DE measurements. Occurrence of ADT and mortality during follow-up was presented as incidence density (% per person-year) and stratified according subgroups of cardiac MRI-LVEF and 2DE-LVEF. Furthermore, Kaplan-Meier curve survival analyses were performed comparing patients with 2DE-LVEF $\leq 35\%$ vs. $>35\%$, and cardiac MRI-LVEF $\leq 30\%$ vs. $>30\%$, and were tested for significance using the log-rank test. A p-value of 0.05 or less was considered statistically significant. All statistical analyses were performed using SPSS software package (version 20.0, IBM SPSS Statistics, Chicago, IL, USA).

RESULTS

Study population

During the study period, 1056 patients were referred to VU University Medical Center for ICD implantation. Figure 1 provides a consort diagram of the patient selection process for this study. In total, 149 patients were included in this study. The main reason for exclusion was no availability of both cardiac MRI and 2DE for LVEF assessment at our department. Cardiac MRI is generally performed at our department prior to device implantation irrespective of 2DE assessment to confirm LVEF impairment, detect LV thrombus, guide LV lead placement by scar assessment in CRT, or as part of other study protocols. Cardiac MRI was not performed in the majority of excluded patients due to patient related contra-indications for cardiac MRI (i.e. irregular heart rhythm, claustrophobia, or implanted devices) or logistical reasons. None of the patients underwent both 2DE and cardiac MRI because of inadequate LVEF assessments. Table 1 summarizes the baseline characteristics.

Table 1. Baseline patient characteristics

Variable	Study population (n=149)	Appropriate Device Therapy		P-value (ADT vs. without ADT)
		Yes (n=37)	No (n=112)	
Male gender	108 (73%)	32 (87%)	76 (68%)	0.03
Age (years)	68 ± 9	65 ± 11	69 ± 9	0.08
Resynchronization therapy	76 (51%)	20 (54%)	56 (50%)	0.67
Ischemic cardiomyopathy	92 (62%)	23 (62%)	69 (62%)	0.95
Chronic atrial fibrillation	7 (5%)	2 (5%)	5 (5%)	1.00
NYHA class†	2.5 ± 0.7	2.5 ± 0.7	2.4 ± 0.7	0.44*
Non-sustained ventricular tachycardia	11 (7%)	4 (11%)	7 (6%)	0.47
Medication:§				
β Blockers	118 (80%)	25 (68%)	93 (84%)	0.03
ACE/ARB	122 (82%)	28 (76%)	94 (85%)	0.21
Diuretics	107 (72%)	28 (76%)	79 (71%)	0.60
Digoxin	8 (5%)	3 (8%)	5 (5%)	0.41
Amiodarone	5 (3%)	3 (8%)	2 (2%)	0.10
Sotalol	4 (3%)	1 (3%)	3 (3%)	1.00
Statins	98 (66%)	24 (65%)	74 (67%)	0.84
Creatinine (umol/L)‡	103 ± 57	127 ± 88	95 ± 39	<0.01*
QRS-duration (ms)††	128 ± 32	127 ± 34	129 ± 32	0.69
Cardiac MRI-LVEF	23 ± 8	24 ± 6	23 ± 8	0.56
2DE-LVEF	30 ± 8	28 ± 7	30 ± 9	0.14

2DE, 2D-echocardiography; ACE, angiotensin-converting-enzyme inhibitors; ADT, appropriate device therapy; ARB, angiotensin receptor blockers; MRI, magnetic resonance imaging; LVEF, left ventricular ejection fraction; NYHA class, New York Heart Association class. † Based on n=110. § Based on n=148. ‡ Based on n=135. †† Based on n=146. * Compared using the Mann-Whitney U test.

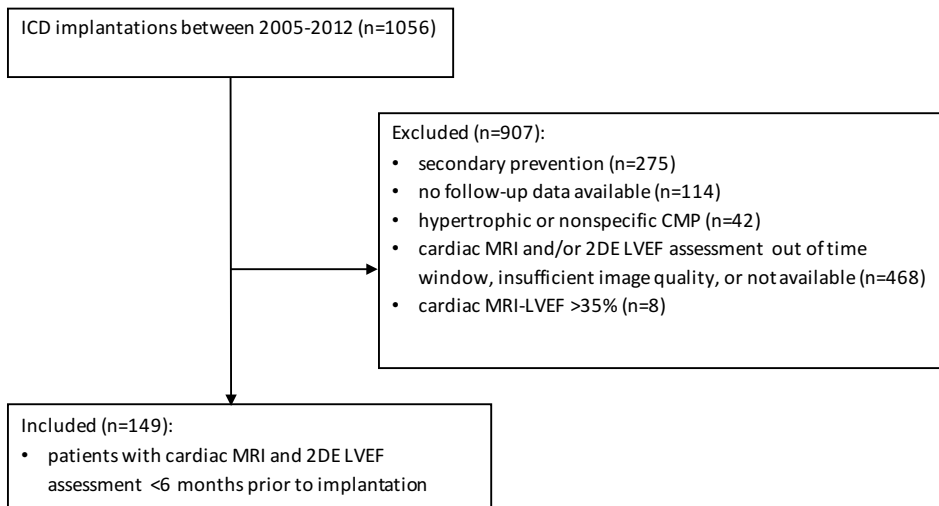


Figure 1. Consort diagram of the study inclusion process. 2DE, 2D-echocardiography; CMP, cardiomyopathy; MRI, magnetic resonance imaging; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction.

Cardiac MRI versus 2DE for LVEF assessment

Median time between cardiac MRI and 2DE LVEF assessments was 5 days (IQR 0 - 42 days). The LVEF assessed with 2DE was found to be significantly higher compared with the LVEF quantified by cardiac MRI ($30 \pm 8\%$ vs. $23 \pm 8\%$, $p < 0.001$), resulting in an overestimation of $6 \pm 7\%$ by 2DE when taking cardiac MRI as the reference (Table 2). Comparable results were obtained in patients with ischemic and dilated CMP. Furthermore, no differences were observed in LVEF discrepancy between patients who received CRT and patients who received an ICD alone (mean difference $6 \pm 6\%$ vs. $7 \pm 7\%$, respectively, $p = 0.24$). As demonstrated in figure 2, 2DE-LVEF assessment resulted in a higher LVEF compared with cardiac MRI in all LVEF subcategories and the difference was found to increase with decreasing LVEF (ANOVA $p < 0.01$). In total, 29 of 149 (19%) patients showed a 2DE-LVEF $> 35\%$ (but cardiac MRI-LVEF $\leq 35\%$), and would not have been eligible for ICD implantation based on 2DE-LVEF assessment using the eligibility threshold of 35% (figure 3). These 29 reclassified patients showed a mean 2DE-LVEF of $41 \pm 3\%$.

Follow-up

In total, 37 of 149 (25%) patients received ADT during a mean follow-up of 2.9 ± 1.7 years (8.5% per person-year) and another 16 patients died (3.7% per person-year). In most ADT cases, VT was the initial detected arrhythmia (32 of 37 cases, 81%) and VF was detected in another 5 patients (19%). A successful shock was delivered in 16 of 37 (43%) patients, whereas 21 (57%) patients received ATP. Patients who experienced ADT were significantly more often male ($p = 0.03$), used less frequently beta-blocking therapy ($p = 0.03$), and displayed a higher creatinine ($p < 0.01$) (table 1).

Table 2. Cardiac MRI versus 2D-echocardiography for left ventricular ejection fraction assessment

Imaging parameter (mean ± SD)	Cardiac MRI	2DE	Difference 2DE – cardiac MRI	P – value (cardiac MRI vs. 2DE)
LVEF (%):				
Total	23 ± 8	30 ± 8	6 ± 7	<0.001
Ischemic CMP	24 ± 7	30 ± 8	6 ± 6	<0.001
Dilated CMP	22 ± 9	29 ± 9	7 ± 7	<0.001
P-value (between CMP groups)	0.07	0.74	0.10	

2DE, 2D-echocardiography; CMP, cardiomyopathy; MRI, magnetic resonance imaging; LVEF, left ventricular ejection fraction.

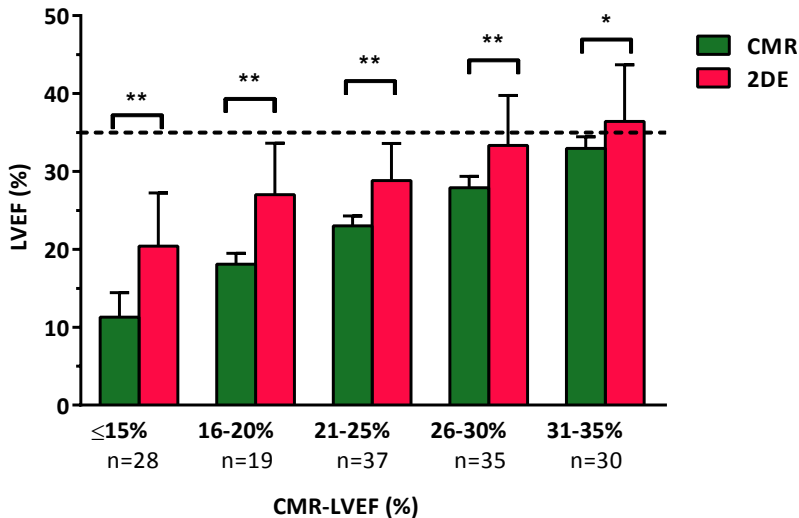


Figure 2. Comparison of mean 2DE-LVEF and cardiac MRI-LVEF stratified according cardiac MRI-LVEF subgroups. The dotted line represents the LVEF cut-off point for ICD eligibility. Cardiac MRI assessed LVEF was significantly lower compared with 2DE-LVEF in all LVEF subgroups. * p=0.01, ** p<0.001. 2DE, 2D-echocardiography; CMR, cardiac magnetic resonance imaging ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction.

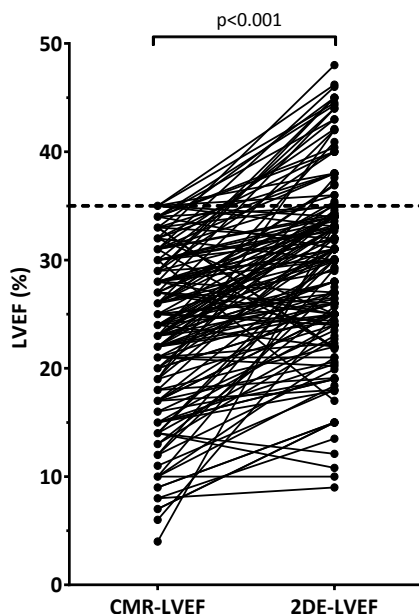


Figure 3. Aligned dot plot demonstrating the LVEF of each patient when assessed by cardiac MRI and 2DE with connecting lines. The dotted line represents the LVEF cut-off point for ICD eligibility ($LVEF \leq 35\%$). Mean LVEF was significantly lower when assessed using cardiac MRI as compared with 2DE. According to a 2DE based LVEF cut-off of 35%, 29 patients (19%) would not have been eligible for ICD implantation. 2DE, 2D echocardiography; CMR, cardiac magnetic resonance imaging; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction.

During follow-up, the incidence of ADT was significantly higher in patients with cardiac MRI-LVEF 21-25% ($n=15$, 14.4% per person-year) and 26-30% ($n=13$, 12.9% per person-year) compared to other LVEF subgroups, whereas mortality rate was highest in patients with cardiac MRI-LVEF $\leq 15\%$ ($n=10$, 13.7% per person-year) (figure 4A). If the incidence of ADT was stratified according to similar 2DE-LVEF subgroups (figure 4B), the event rate was more equally distributed among LVEF subgroups. However, patients with 2DE-LVEF $>35\%$ were significantly less likely to experience ADT (log-rank $p=0.02$). Mortality incidence was significantly higher in patients with 2DE-LVEF $\leq 15\%$ ($n=4$, 19.1% per person-year) and 2DE-LVEF 16-20% ($n=2$, 7.8% per person-year) compared to other 2DE-LVEF subgroups. As presented in figure 5A, the incidence of ADT among patients with 2DE-LVEF $\leq 35\%$ was significantly higher compared with patients having a 2DE-LVEF $>35\%$ (10.4% per person-year vs. 2.1% per person-year, respectively, log-rank $p=0.02$). The combined endpoint of ADT or all-cause mortality occurred significantly more frequent in patients with 2DE-LVEF $\leq 35\%$ compared with patients having a 2DE-LVEF $>35\%$ (14.8% per person-year vs. 3.1% per person-year, $p<0.01$) (figure 5B).

Adjusting the cardiac MRI-LVEF eligibility cut-off to 30% would have resulted in 119 of the 149 patients (80%) eligible for ICD therapy. Among patients with cardiac MRI-LVEF $\leq 30\%$, 34 patients experienced ADT, whereas 3 patients with cardiac MRI-LVEF $>30\%$ displayed ADT during follow-up (9.9% per person-year vs. 3.3% per person-year, respectively, log-rank $p=0.06$) (figure 6A). The combined endpoint of ADT or mortality in patients with cardiac MRI-LVEF $\leq 30\%$ occurred significantly more frequent compared with patients having a cardiac MRI-LVEF $>30\%$ (14.6% per person-year vs. 3.3% per person-year, respectively, log-rank $p<0.01$) (figure 6B).

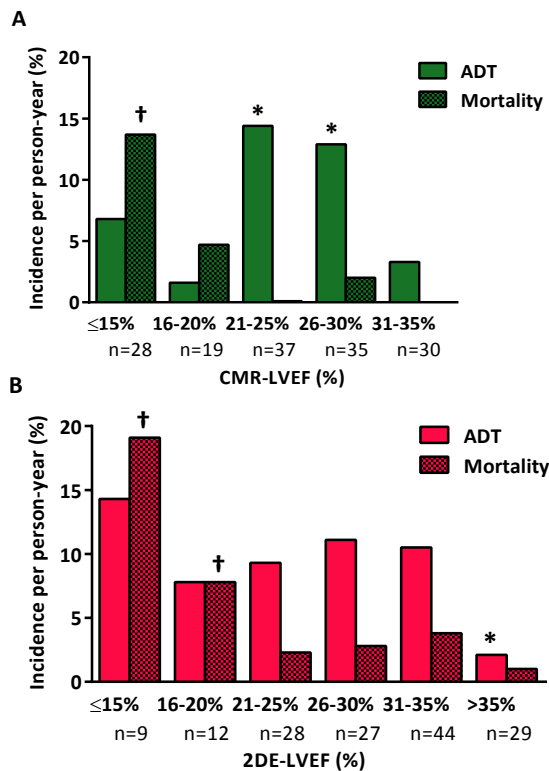


Figure 4. Bar graphs presenting the incidence density of ADT and mortality, stratified according to subgroups of cardiac MRI-LVEF (A) and 2DE-LVEF (B). As shown in figure 4A, patients with cardiac MRI-LVEF 21-25% and 26-30% experienced a higher incidence of ADT compared to other cardiac MRI-LVEF subgroups (* log-rank $p=0.001$), whereas mortality rate was highest in patients with cardiac MRI-LVEF $\leq 15\%$ ([†] log-rank $p<0.001$). Figure 4B demonstrates that patients with 2DE-LVEF $>35\%$ experienced a significantly lower incidence of ADT compared to other subgroups (* log-rank $p=0.02$), while mortality rate was higher in patients with 2DE-LVEF $\leq 15\%$ and 16-20% ([†] log-rank $p<0.001$). Note the difference in subgroup size as depicted below the subgroup bars. 2DE, 2D-echocardiography; ADT, appropriate device therapy; CMR, cardiac magnetic resonance imaging; LVEF, left ventricular ejection fraction.

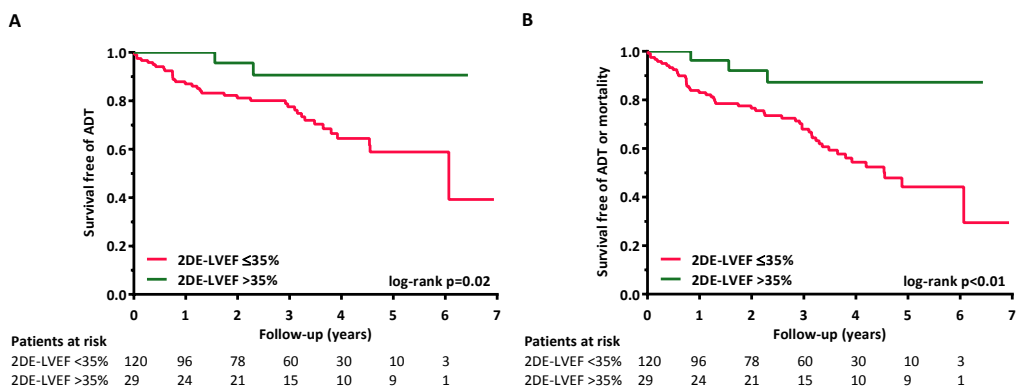


Figure 5. Kaplan-Meier curve analysis demonstrating the occurrence of ADT (A) in patients with 2D-LVEF $\leq 35\%$ compared with 2D-LVEF $> 35\%$ (10.4%/year vs. 2.1%/year, respectively, log-rank $p=0.02$) and the occurrence of the combined endpoint ADT or mortality (B) between patients with 2D-LVEF $\leq 35\%$ and 2D-LVEF $> 35\%$ (14.8%/year vs. 3.1%/year, respectively, log-rank $p<0.01$). 2DE, 2D-echocardiography; ADT, appropriate device therapy; LVEF, left ventricular ejection fraction.

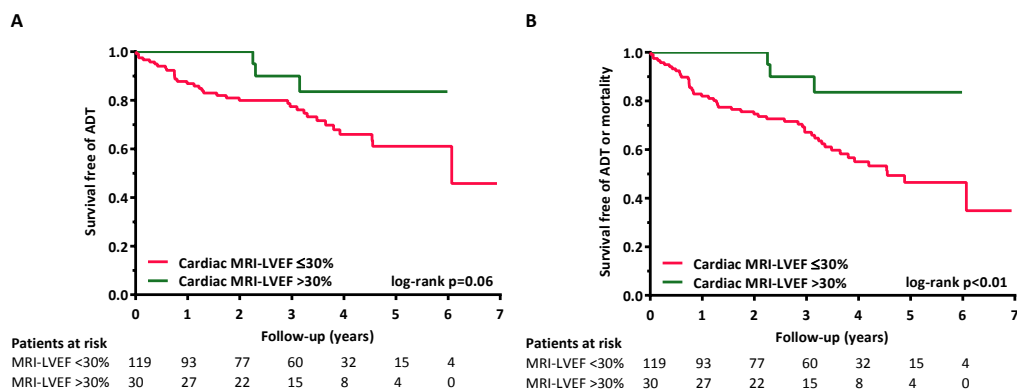


Figure 6. Kaplan-Meier curve analysis demonstrating the occurrence of ADT (A) in patients with cardiac MRI-LVEF $\leq 30\%$ compared with cardiac MRI-LVEF $> 30\%$ (9.9%/year vs. 3.3%/year, respectively, log-rank $p=0.06$) and the occurrence of the combined endpoint ADT or mortality (B) compared between patients with cardiac MRI-LVEF $\leq 30\%$ and cardiac MRI-LVEF $> 30\%$ (14.6%/year vs. 3.3%/year, respectively, log-rank $p<0.01$). ADT, appropriate device therapy, CMR, cardiac magnetic resonance imaging; LVEF, left ventricular ejection fraction.

DISCUSSION

The aim of this study was to determine the clinical consequences of cardiac MRI-based LVEF assessment for device eligibility according to current guidelines. 2DE significantly overestimated LVEF compared with cardiac MRI in patients with ischemic and dilated CMP, resulting in 19% more patients eligible for ICD therapy if LVEF was assessed by

cardiac MRI using a cut-off of 35% for device eligibility. In patients with a 2DE-LVEF >35% but cardiac MRI-LVEF \leq 35%, a low ADT rate was observed. Moreover, application of a cardiac MRI-LVEF cut-off of \leq 30% for device eligibility resulted in an ADT rate which was comparable to a 2DE-LVEF cut-off of \leq 35%. These results support the need for cardiac MRI-specific LVEF cut-off values for device eligibility.

Although clinical guidelines for ICD implantation for primary prevention are based on studies predominantly using 2DE, similar LVEF eligibility cut-off values are used for other imaging modalities.³ Due to the superior reproducibility and accuracy of cardiac MRI¹⁷, this imaging modality is increasingly used in clinical practice and is often considered to be the gold standard for LVEF assessment. Moreover, late gadolinium enhanced-cardiac MRI allows for detailed scar tissue characterization which has been frequently linked to ventricular arrhythmias and may further enhance risk stratification.¹⁸ Thus, it is reasonable to assume that cardiac MRI will become a prevailing method for eligibility assessment in primary prevention ICD implantation. Studies that have compared LV volume and function calculations using 2DE and cardiac MRI consistently demonstrate that cardiac MRI assessed ventricular volumes are larger as compared with 2DE.^{6-13, 19} Although conflicting results have been published regarding LVEF differences, most studies report an overestimation of LVEF by 2DE in patients with impaired LVEF when taking cardiac MRI as a reference standard.^{6, 7, 10-12} Consistent with the results from this study, Joshi et al.¹¹ and Gruszczynska et al.¹⁰ reported a significant overestimation of LVEF by 2DE ranging from 3 to 5% compared with cardiac MRI. Furthermore, comparable to most of these studies, this discrepancy becomes more substantial in patients with more severely reduced LVEF.^{7, 10} The differences in LVEF assessment between 2DE and cardiac MRI are likely to have consequences for device eligibility, in particular for patients with borderline LVEF values (30-35%). The present study demonstrated that 19% of 149 patients were not eligible for ICD therapy if LVEF assessment was based on 2DE. These findings confirm the results obtained by Joshi et al.¹¹, who found a reclassification of 21% regarding device eligibility when cardiac MRI was used for LVEF evaluation. In patients with 2DE-LVEF 30-35% specifically, this reclassification increased to 41% of the patients and usually was in favour of ICD implantation.

It remains unclear, however, whether the use of cardiac MRI for LVEF assessment will lead to an improved selection of patients with highest benefit from ICD implantation. One may hypothesize that due to the increase in eligible patients, the rate of ADT may actually decrease resulting in lower benefit from ICD implantation. The results obtained in the current study demonstrate a low rate of 2.1 % ADT annually in reclassified patients with a 2DE-LVEF >35% but cardiac MRI-LVEF \leq 35% during the follow-up. Previous studies have reported low event rates in patients with ICD implantation and improved LVEF.²⁰⁻²² Kini et al.²⁰ demonstrated that patients with improvement in LVEF above 35% show an incidence of ADT of 2.8% annually whereas patients with LVEF <35% experienced 10.7% ADT annually. These results are consistent with the incidence rates of ADT observed in

the current study. Patients with cardiac MRI-LVEF of 21-30% received the highest ADT rate, whereas the corresponding 2DE-LVEF ranged between <15 and 35% leading to the highest ADT rate. This is likely to be the result of the LVEF-overestimation by 2DE. In addition, the superior reproducibility of cardiac MRI may result in a refined selection of patients at highest risk for appropriate ICD therapy.^{7,11,17}

These data suggest the need for a specific cardiac MRI-based LVEF threshold for device eligibility. As shown, a cardiac MRI-LVEF cut-off of $\leq 30\%$ would have resulted in a number of eligible patients and an incidence of ADT that was comparable with using a conventional 2DE-LVEF cut-off of $\leq 35\%$. In patients not eligible according to a cardiac MRI-LVEF cut-off of 30%, the ADT rate was low (3.3% annually). Similarly, patients with 2DE-LVEF above the conventional eligibility cut-off of 35% who received an ICD, as cardiac MRI-LVEF was below 35%, showed a comparable low ADT incidence of 2.1% per person-year. Whether this lower risk for ventricular arrhythmias is acceptable to refrain from ICD implantation remains to be evaluated by a risk-benefit analysis. Nonetheless, Rayatzadeh et al.¹² demonstrated that none of the patients who received an ICD for primary prevention with a cardiac MRI-LVEF $>30\%$ but 2DE-LVEF $\leq 35\%$ experienced ventricular arrhythmias, suggesting the application of a cardiac MRI-based LVEF threshold of $\leq 30\%$ for ICD eligibility.

Several limitations of this study need to be acknowledged. First, this was a retrospectively designed cohort study. Only patients who received both a cardiac MRI and 2DE prior to ICD implantation were included in the current study, which may have introduced a selection bias. However, none of the patients underwent LVEF assessment using both imaging modalities due to inadequacy of either 2DE or cardiac MRI. Cardiac MRI was generally performed prior device implantation irrespective of 2DE findings. Furthermore, the included patient population reflects a typical cohort of patients referred for primary prevention ICD implantation as presented in the baseline characteristics table. Secondly, LVEF assessments by 2DE as well as cardiac MRI were evaluated by multiple readers which may have influenced the comparison of cardiac MRI and 2DE. However, all LVEF assessments were measured according to routine clinical standards, therefore reflecting the 'real-world' clinical practice. Thirdly, 2DE and cardiac MRI assessment were not measured simultaneously. Although the median time between both imaging modalities was only 5 days, non-reported events may have occurred that have affected the comparison between cardiac MRI and 2DE. Finally, the current study only compared the difference of LVEF assessment between 2DE and cardiac MRI. It would be of interest to include several other imaging modalities, such as nuclear imaging, 3D-echocardiography and cardiac computed tomography which are also used in daily clinical practice for LVEF assessment. The clinical consequences for device eligibility and follow-up of these imaging modalities remain unclear.

REFERENCES

1. Moss AJ, Zareba W, Hall WJ et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med* 2002;346(12):877-883.
2. Bardy GH, Lee KL, Mark DB et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med* 2005;352(3):225-237.
3. Epstein AE, DiMarco JP, Ellenbogen KA et al. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices): developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. *Circulation* 2008;117(21):e350-e408.
4. Russo AM, Stainback RF, Bailey SR et al. ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR 2013 appropriate use criteria for implantable cardioverter-defibrillators and cardiac resynchronization therapy: a report of the American College of Cardiology Foundation appropriate use criteria task force, Heart Rhythm Society, American Heart Association, American Society of Echocardiography, Heart Failure Society of America, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. *J Am Coll Cardiol* 2013;61(12):1318-1368.
5. McMurray JJ, Adamopoulos S, Anker SD et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2012;33(14):1787-1847.
6. Bellenger NG, Burgess MI, Ray SG et al. Comparison of left ventricular ejection fraction and volumes in heart failure by echocardiography, radionuclide ventriculography and cardiovascular magnetic resonance; are they interchangeable? *Eur Heart J* 2000;21(16):1387-1396.
7. de Haan S, de Boer K, Commandeur J, Beek AM, van Rossum AC, Allaart CP. Assessment of left ventricular ejection fraction in patients eligible for ICD therapy: Discrepancy between cardiac magnetic resonance imaging and 2D echocardiography. *Neth Heart J* 2014;22(10):449-455.
8. Gardner BI, Bingham SE, Allen MR, Blatter DD, Anderson JL. Cardiac magnetic resonance versus transthoracic echocardiography for the assessment of cardiac volumes and regional function after myocardial infarction: an intrasubject comparison using simultaneous intrasubject recordings. *Cardiovasc Ultrasound* 2009;7:38.

10. Greupner J, Zimmermann E, Grohmann A et al. Head-to-head comparison of left ventricular function assessment with 64-row computed tomography, biplane left cineventriculography, and both 2- and 3-dimensional transthoracic echocardiography: comparison with magnetic resonance imaging as the reference standard. *J Am Coll Cardiol* 2012;59(21):1897-1907.
11. Gruszczynska K, Krzych LJ, Golba KS et al. Statistical agreement of left ventricle measurements using cardiac magnetic resonance and 2D echocardiography in ischemic heart failure. *Med Sci Monit* 2012;18(3):MT19-MT25.
12. Joshi SB, Connelly KA, Jimenez-Juan L et al. Potential clinical impact of cardiovascular magnetic resonance assessment of ejection fraction on eligibility for cardioverter defibrillator implantation. *J Cardiovasc Magn Reson* 2012;14:69.
13. Rayatzadeh H, Patel SJ, Hauser TH et al. Volumetric left ventricular ejection fraction is superior to 2-dimensional echocardiography for risk stratification of patients for primary prevention implantable cardioverter-defibrillator implantation. *Am J Cardiol* 2013;111(8):1175-1179.
14. Li C, Lossnitzer D, Katus HA, Buss SJ. Comparison of left ventricular volumes and ejection fraction by monoplane cineventriculography, unenhanced echocardiography and cardiac magnetic resonance imaging. *Int J Cardiovasc Imaging* 2012;28(5):1003-1010.
15. Lang RM, Bierig M, Devereux RB et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18(12):1440-1463.
16. Cantillon DJ, Wilkoff BL. Antitachycardia pacing for reduction of implantable cardioverter-defibrillator shocks. *Heart Rhythm* 2015;12(6):1370-1375.
17. Wilkoff BL, Williamson BD, Stern RS et al. Strategic programming of detection and therapy parameters in implantable cardioverter-defibrillators reduces shocks in primary prevention patients: results from the PREPARE (Primary Prevention Parameters Evaluation) study. *J Am Coll Cardiol* 2008;52(7):541-550.
18. Grothues F, Smith GC, Moon JC et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. *Am J Cardiol* 2002;90(1):29-34.
19. Scott PA, Rosengarten JA, Curzen NP, Morgan JM. Late gadolinium enhancement cardiac magnetic resonance imaging for the prediction of ventricular tachyarrhythmic events: a meta-analysis. *Eur J Heart Fail* 2013;15(9):1019-1027.

20. Nowosielski M, Schocke M, Mayr A et al. Comparison of wall thickening and ejection fraction by cardiovascular magnetic resonance and echocardiography in acute myocardial infarction. *J Cardiovasc Magn Reson* 2009;11:22.
21. Kini V, Soufi MK, Deo R et al. Appropriateness of primary prevention implantable cardioverter-defibrillators at the time of generator replacement: are indications still met? *J Am Coll Cardiol* 2014;63(22):2388-2394.
22. Manfredi JA, Al-Khatib SM, Shaw LK et al. Association between left ventricular ejection fraction post-cardiac resynchronization treatment and subsequent implantable cardioverter defibrillator therapy for sustained ventricular tachyarrhythmias. *Circ Arrhythm Electrophysiol* 2013;6(2):257-264.
23. Ruwald MH, Solomon SD, Foster E et al. Left Ventricular Ejection Fraction Normalization in Cardiac Resynchronization Therapy and Risk of Ventricular Arrhythmias and Clinical Outcomes: Results From the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy (MADIT-CRT) Trial. *Circulation* 2014;130(25):2278-2286.

