Profound differences in prognostic impact of left ventricular reverse remodeling after cardiac resynchronization therapy relate to heart failure etiology

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BACKGROUND An ischemic etiology of heart failure (HF) has been associated with reduced left ventricular reverse remodeling after cardiac resynchronization therapy (CRT).

OBJECTIVE The purpose of this study was to assess the relationship between the etiology of HF and reverse remodeling and outcome after CRT.

METHODS Consecutive patients undergoing CRT implantation between October 1, 2008 and August 14, 2015 were retrospectively evaluated. Coronary angiography classified ischemic vs nonischemic etiology. *Reverse remodeling* was defined as the changes in left ventricular ejection fraction (LVEF) after 6 months. Clinical outcome was assessed 1 year after implantation using a combined end point of all-cause mortality and HF readmission.

RESULTS A total of 685 patients were included (300/385 for ischemic/nonischemic etiology). Compared with patients with ischemic cardiomyopathy, patients with nonischemic cardiomyopathy exhibited a greater degree of improvement in LVEF (8.4% ± 10.4% vs 15.8% ± 12.3%; $P < .001$). After correcting for differences, an ischemic etiology of HF predicted less reverse remodeling ($P < .001$) and a higher rate of mortality or HF readmission (hazard ratio 1.63; 95% confidence interval [CI] 1.12–2.73; $P = .011$). Nevertheless, in comparison to a greater degree of improvement in LVEF, a lesser degree of improvement in LVEF (0%–5%) was associated with a higher risk of all-cause mortality and HF hospitalization in patients with nonischemic cardiomyopathy (odds ratio 9.78; 95% CI 1.95–49.04; $P = .006$) but not in patients with ischemic cardiomyopathy (odds ratio 3.58; 95% CI 0.85–15.18; $P = .083$). The most accurate cutoff for improvement in LVEF predicting good clinical outcome was 5.5% in ischemic cardiomyopathy vs 10.5% in nonischemic cardiomyopathy.

CONCLUSION CRT results in reverse remodeling in both patients with ischemic and nonischemic cardiomyopathy, but to a lesser extent in the former. Patients with an ischemic etiology are at an intrinsically higher risk of mortality and HF hospitalization, but derive benefit on outcome at a lesser degree of reverse remodeling.

KEYWORDS Ischemic cardiomyopathy; Nonischemic cardiomyopathy; Cardiac resynchronization therapy; Reverse remodeling; Outcome

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Introduction

Cardiac resynchronization therapy (CRT) alleviates electromechanical dyssynchrony in patients with heart failure with reduced ejection fraction (HFrEF), thereby beneficially affecting functional status, cardiac structure (reverse remodeling), and outcome.[1–8] It is clear that more pronounced left ventricular reverse remodeling induced by CRT favorably influences prognosis.[9–11] As a result, it has become increasingly popular in clinical practice to measure left ventricular reverse remodeling as an end point or even a predictor of success in patients undergoing CRT. Randomized controlled trials have consistently pointed out that up to 30% of patients do not exhibit a meaningful effect on left ventricular reverse remodeling.[12] However, such patients may still exhibit some degree of reverse remodeling, but at a lower extent than so-called responders. Nonresponders are known to have a higher risk of heart failure hospitalization and all-cause mortality.[9] However, this group also constitutes of patients with an intrinsically higher risk of heart failure hospitalizations and mortality (ischemic cardiomyopathy, right bundle branch block, etc). Therefore, any potential benefit of CRT might be diminished by their inherently higher risk of adverse outcome. Patients with ischemic

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cardiomyopathy form such a subgroup of patients that have shown a reduced capability to mount a left ventricular reverse remodeling response in randomized controlled trials.[9–11] As a result, physicians might wrongly think that CRT has a diminished effect on outcome in patients with ischemic cardiomyopathy because of the lesser degree of reverse remodeling attained. However, in the CRT trials that have demonstrated a reduction in the combined end point of heart failure hospitalizations and all-cause mortality with CRT, no interaction was seen for ischemic etiology on outcome.[2,3,6,7] As such, the relationship between left ventricular reverse remodeling and outcome in patients with ischemic vs nonischemic cardiomyopathy might be different. This analysis sought to determine the intrinsic relationship between left ventricular reverse remodeling response and clinical outcome according to heart failure etiology in a contemporary population undergoing CRT.

Methods

Study population

Consecutive patients with HFrEF undergoing CRT implantation in a single tertiary care center (Ziekenhuis Oost-Limburg, Genk, Belgium) between October 2008 and August 2015 were retrospectively evaluated. CRT indications were in compliance with the European Society of Cardiology guidelines.[13] After implantation, all patients underwent a similar prespecified follow-up and CRT optimization protocol, as published previously by our group.[14,15] Briefly, all patients received identical optimization of heart failure care, including uptitration of neurohormonal blockers, downtitration of loop diuretics, as well as echocardiographically guided AV and VV optimization of their device settings. Patients received a first follow-up appointment 6 weeks after implantation and a second follow-up at 6 months. Afterward, the follow-up intensity was reduced to once every 9 months if clinically stable. For the present analysis, patients were grouped according to heart failure etiology. Differentiation between an ischemic and a nonischemic etiology of HFrEF was made before CRT implantation in all patients on the basis of coronary angiography. The present study is in compliance with the Declaration of Helsinki. Given the retrospective nature of the study design, the need for written informed consent was waived by the local ethics committee. The manuscript was drafted according to the Strengthening the Reporting of Observational Studies in Epidemiology statement for observational studies.[16]

Baseline characteristics and follow-up

Demographic characteristics and clinical data just before CRT placement, medical therapy, baseline laboratory results, baseline electrocardiography, and echocardiography were retrospectively collected from the individual electronic medical record. Cardiac reverse remodeling was evaluated by comprehensive 2-dimensional echocardiography examinations (Philips Medical Systems, iE33w, Andover, MA) performed by experienced cardiac sonographers. Left ventricular reverse remodeling was measured as the change in left ventricular ejection fraction (LVEF) 6 months after CRT implantation. LVEF was obtained using the modified Simpson's biplane method in the apical 2- and 4-chamber views. All reported echocardiography measurements were averaged from 3 consecutive cycles (or 5 if atrial fibrillation was present) and assessed as recommended by the American Society of Echocardiography.[17]

Study specific end points

To assess the relationship between left ventricular reverse remodeling and outcome, the LVEF change from baseline until 6 months of follow-up was handled as a continuous value. *Good clinical outcome* was defined as the absence of all-cause mortality or heart failure readmission after 1 year. *Heart failure hospitalization* was defined as hospitalization for congestion (at least 2 signs or symptoms of congestion), necessitating the use of intravenous diuretics or hospitalization for low-output heart failure lasting at least 24 hours.

Statistics

Continuous variables are expressed as mean ± SD if normally distributed or median (interquartile range) if not normally distributed. Normality was checked using the Shapiro-Wilk statistic. Categorical data were expressed as numbers and percentages and compared using the Pearson χ^2 test or Fisher exact, as appropriate. Continuous variables were compared using the Student t test or Mann-Whitney U test, as appropriate. Linear regression analysis was used to determine the extent of differential left ventricular reverse remodeling (standardized coefficients) attributed to ischemic vs nonischemic etiology after correcting for differences in baseline characteristics. The Kaplan-Meier method was used to construct survival curves, with the log-rank test used for comparison between groups. Adjusted hazard ratios were calculated by Cox regression analysis after correcting for differences in baseline characteristics. Binary logistic regression analysis was used to determine the adjusted odds ratio for discrete categorical groups of LVEF improvement on clinical outcome according to heart failure etiology. The optimal relationship between change in LVEF (continuous variable) and the absence of mortality and heart failure admission after 1 year was investigated using receiver operating characteristics (ROCs). The optimal cutoff point was searched by identifying the Youden index point (sensitivity + specificity – 1). Adjustment of ROC curves for differences in baseline characteristics was done by introducing statistically different baseline variables into a linear regression model and saving the multivariate residual (the linear predictor). Afterwards it was determined if the multivariate residual affected the area under the curve, which was not the case. Thus making ROC-curve adjustment unnecessary. Statistical significance was always set at a 2-tailed probability level of $<.05$. Statistical analyses were performed using SPSS version 22 (IBM Corp, Chicago, IL).

Results

Study population and reverse remodeling

A total of 685 patients underwent CRT implantation between October 2008 and August 2015. Angiographic analysis revealed an ischemic etiology of HFrEF in 300 patients (44%), leaving 385 patients (56%) with nonischemic cardiomyopathy. The baseline characteristics of the population are listed in Table 1. Patients with ischemic cardiomyopathy were older, were more often men, had more cardiovascular risk factors, suffered more frequently from chronic kidney disease and chronic obstructive pulmonary disease, and more often had a history of stroke. In addition, patients with ischemic cardiomyopathy less often demonstrated left bundle branch block morphology on the electrocardiogram. Figure 1 illustrates the change in LVEF after 6 months according to HFrEF etiology. Repeat echocardiography reporting LVEF was available in 95% of patients alive at 6 months follow-up. Patients with ischemic vs nonischemic cardiomyopathy exhibited significantly less improvement in LVEF (8.4% ± 10.3% vs 15.8% ± 12.3%, respectively; $P < .001$). After correcting for differences in baseline characteristics (age, male sex, chronic obstructive pulmonary disease, hypertension, dyslipidemia, diabetes, stroke, anemia, left bundle branch block, glomerular filtration rate, left ventricular end-diastolic diameter, and defibrillator use), 5.13% of the difference in LVEF change between ischemic and nonischemic cardiomyopathy was explained by the ischemic etiology (95% confidence interval [CI] 3.05–7.21; $P < .001$), with the remaining 2.27% difference explained by other covariates.

Table 1 Baseline characteristics of the population

Variable	Total population (N = 685)	Ischemic etiology (n = 300)	Nonischemic etiology (n = 385)	*P*
Demographic characteristics				
Age (y)	71.8 ± 9.3	74 ± 9	71 ± 11	<.001
Octogenarians	178 (26)	92 (31)	86 (22)	.014
Sex: male	463 (68)	249 (83)	213 (56)	<.001
BMI (kg/m^2)	27.5 ± 4.9	27 ± 5	27 ± 5	.523
Duration HF (mo)	30.6 ± 45.1	30 ± 39	31 ± 49	.600
Comorbidities				
Atrial fibrillation	255 (37)	114 (38)	141 (37)	.712
Anemia	207 (31)	113 (38)	94 (25)	<.001
Iron deficiency	301 (56)	144 (59)	157 (53)	.164
COPD	116 (17)	65 (22)	51 (13)	.008
Hypertension	547 (80)	258 (86)	289 (75)	<.001
Dyslipidemia	480 (70)	239 (80)	240 (62)	<.001
Diabetes	181 (26)	109 (36)	71 (18)	<.001
Stroke	49 (7)	29 (10)	20 (5)	.023
CKD (GFR <60) mL/min	314 (46)	163 (54)	150 (39)	<.001
History of valve surgery	94 (14)	41 (14)	53 (14)	.970
Laboratory analysis				
Sodium level (mmol/L)	139 ± 4	139 ± 4	139 ± 11	.570
Hemoglobin level (g/dL)	13.3 ± 1.7	13.2 ± 1.8	13.4 ± 1.6	.043
GFR (mL/min)	64 ± 24	58 ± 25	66 ± 24	<.001
NYHA class				.154
II	267 (39)	113 (38)	154 (40)	
III	387 (57)	168 (56)	220 (57)	
IV	29 (4)	19 (6)	10 (3)	
QRS duration (ms)	156 ± 30	153 ± 30	155 ± 29	.494
LBBB	517 (76)	210 (71)	307 (80)	.005
Echocardiography				
LVEF (%)	29 ± 9	30 ± 9	30 ± 9	.408
LVEDD (cm)	6.5 ± 1.0	6.1 ± 1.0	6.0 ± 1.0	.036
LVESD (cm)	5.6 ± 1.2	5.7 ± 1.2	5.4 ± 1.2	.020
Medication				
ACE-I or ARB	581 (85)	248 (83)	333 (87)	.202
β-Blocker	571 (84)	251 (84)	320 (83)	.754
Aldosterone antagonist	422 (62)	186 (62)	236 (62)	.798
Device-related features				
CRT-pacemaker	326 (48)	128 (43)	231 (60)	.001
CRT-defibrillator	361 (52)	172 (57)	154 (40)	.001
Posterolateral LV lead position	621 (90)	271 (90)	349 (71)	.316

Values are presented as mean ± SD or as n (%).

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; GFR = glomerular filtration rate; HF = heart failure; LBBB = left bundle branch block; LV = left ventricular; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter.

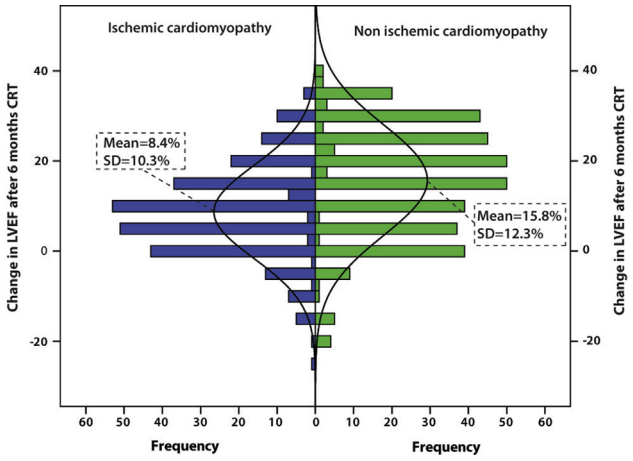

Figure 1 Distribution of change in LVEF after 6 months in ischemic vs nonischemic cardiomyopathy. CRT = cardiac resynchronization therapy; LVEF = left ventricular ejection fraction.

Clinical outcome overall

Figure 2 illustrates the Kaplan-Meier curves for freedom from all-cause mortality and heart failure admission. In total, 675 patients (98.5%) had follow-up data available to construct curves. Patients with ischemic cardiomyopathy had a higher incidence of all-cause mortality or heart failure readmission after 1 year of follow-up (63 events [21%] vs 42 events [11%]; $P < .001$). After adjusting for differences in baseline characteristics (as mentioned previously), ischemic cardiomyopathy was associated with a hazard ratio of 1.63 (95% CI 1.12–2.73; $P = .011$) for the combined end point of all-cause mortality and heart failure admission.

Reverse remodeling vs outcome

The adjusted odds ratio for all-cause mortality and heart failure readmission according to the degree of reverse left ventricular remodeling is depicted in Figure 3 for patients with an ischemic vs a nonischemic etiology. Patients with the most extensive reverse remodeling (LVEF 15%–20%) were set as the categorical comparator in the model. Less extensive reverse remodeling was associated with a significantly higher odds for the end point of heart failure admission or all-cause mortality overall. However, for patients with ischemic cardiomyopathy, an LVEF improvement of 0%–5% was not associated with a statistically higher adjusted odds ratio for the combined end point (odds ratio 3.58; 95% CI 0.85–15.18; $P = .083$). This in contrast to patients with nonischemic cardiomyopathy, in whom the same degree of reverse remodeling was associated with a higher odds for poor outcome (odds ratio 9.78; 95% CI 1.95–49.04; $P = .006$), indicating a differential effect between left ventricular reverse remodeling and outcome according to heart failure etiology. To further evaluate the relationship between reverse remodeling and outcome, we performed ROC curve analysis to determine what amount of left ventricular reverse remodeling optimally predicted freedom from all-cause mortality and heart failure hospitalization after 1 year. Figure 4 illustrates the ROC curve analysis for patients with an ischemic (Figure 4A) and a nonischemic (Figure 4B) etiology to assess the capacity of reverse left ventricular remodeling to predict clinical outcome. The most accurate cutoff for improvement in LVEF predicting good clinical outcome was 5.5% in patients with ischemic cardiomyopathy vs 10.5% in patients with nonischemic cardiomyopathy. In an adjusted multivariate linear regression model, the differences in baseline characteristics did not affect this cutoff point.

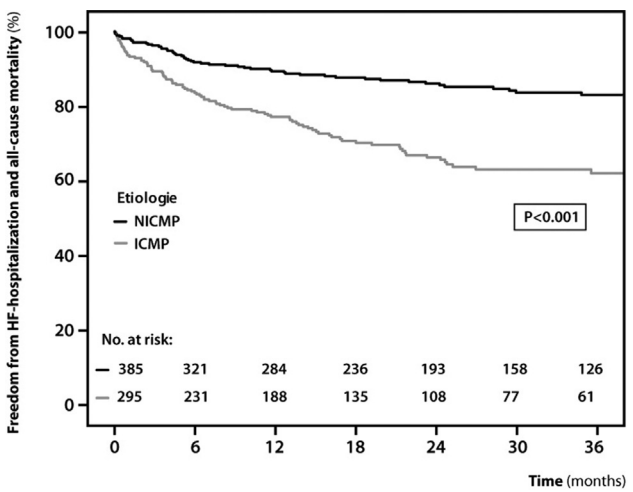

Figure 2 Kaplan-Meier curves for freedom from HF admission and all-cause mortality. HF = heart failure; ICMP = ischemic cardiomyopathy; NICMP = nonischemic cardiomyopathy.

Discussion

This large observational study of contemporary patients undergoing CRT reports on the importance of HFrEF etiology during the assessment of the impact of reverse left ventricular remodeling on outcome. Our data indicate that patients with ischemic cardiomyopathy exhibit diminished left ventricular reverse remodeling and a higher absolute risk of all-cause mortality or heart failure readmissions. However, the reduced reverse remodeling response observed after CRT in patients with ischemic cardiomyopathy did *not* translate into a reduced risk reduction for the clinical outcome. Indeed, in patients with ischemic cardiomyopathy, smaller improvements in LVEF were associated with a reduction in all-cause mortality or heart failure readmissions already at 1 year, which is in contrast to patients with an nonischemic etiology of heart failure, in whom only more extensive reverse remodeling was associated with good clinical outcome.

One of the central objectives in heart failure (and medicine in general) is to reduce mortality and morbidity. Although considered as the criterion standard end point in randomized controlled trials, measuring an effect on mortality or morbidity is less intuitive in clinical practice. The intrinsic desire to measure a treatment effect is even more pronounced when implementing device-based treatment options, because of their perceived higher economic burden and more invasive approach. As a result, measurement of left ventricular reverse remodeling has become popular in patients undergoing CRT to determine the treatment effect and potentially allocate therapy itself.[12] Yu

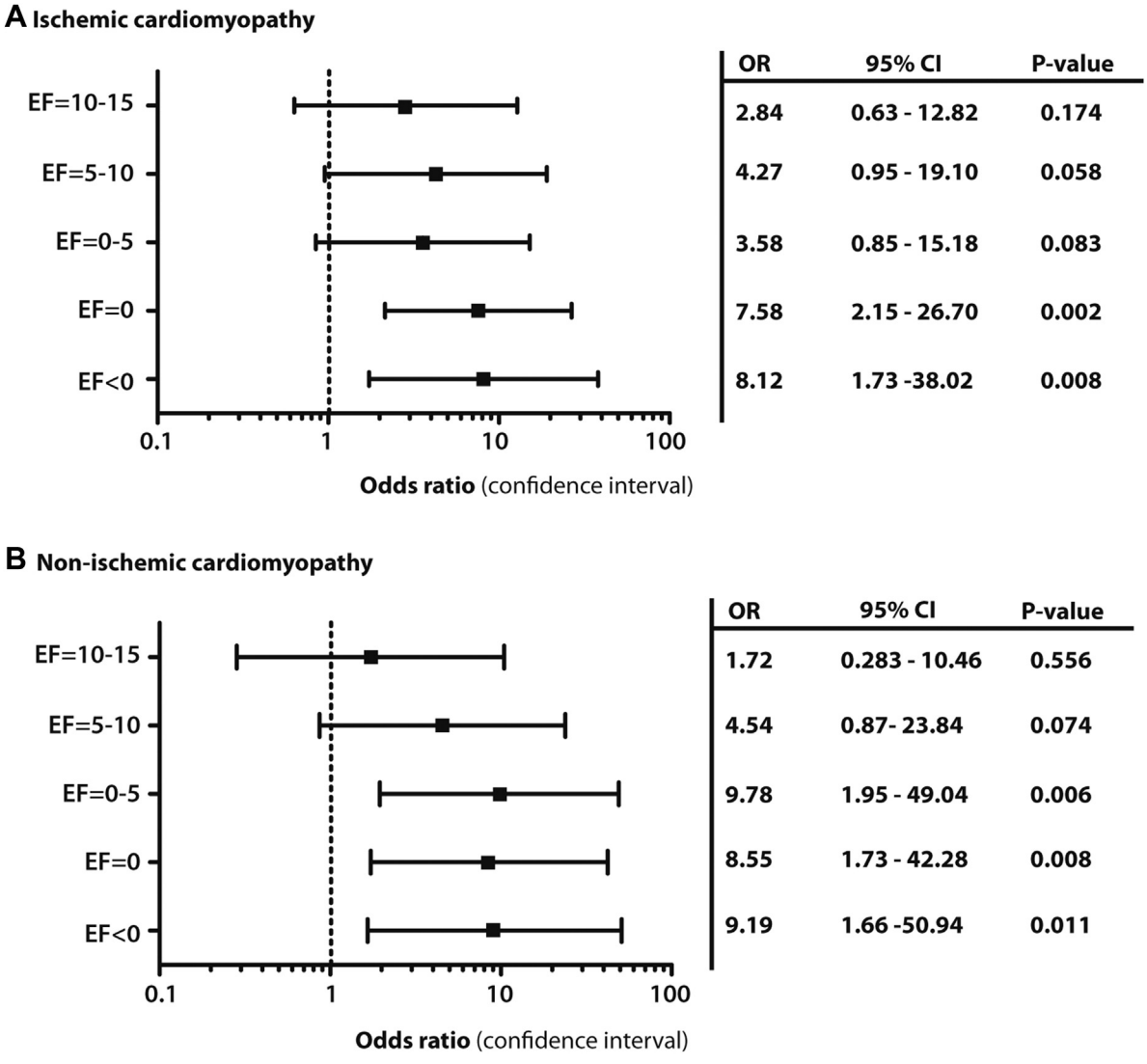

Figure 3 Adjusted odds ratio for heart failure admission and all-cause mortality after 1 year vs the degree of left ventricular reverse remodeling in (**A**) ischemic cardiomyopathy and (**B**) nonischemic cardiomyopathy after 6 months of cardiac resynchronization therapy. Odds ratios were adjusted for the differences in baseline characteristics. The x-axis is log-scaled. CI = confidence interval; EF = ejection fraction; OR = adjusted odds ratio.

et al[11] have demonstrated that left ventricular reverse remodeling predicts a lower rate of cardiovascular mortality with a sensitivity of 87% and specificity of 69% (thereby outperforming other metrics such as symptomatic improvement). However, some patients might still be classified as echocardiographic nonresponders, despite deriving a beneficial effect on mortality or morbidity. Previous reports assessing the extent of left ventricular reverse remodeling have led many to believe that patients with ischemic cardiomyopathy derive less benefit from CRT. Indeed, well-cited subanalyses of the Multicenter InSync Randomized Clinical Evaluation (MIRACLE), Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronization Therapy (MADIT-CRT), and CArdiac REsynchronization-Heart Failure (CARE-HF) studies have shown that patients with ischemic cardiomyopathy exhibit less left ventricular reverse remodeling, measured as a change in LVEF and left ventricular end-diastolic or end-systolic volume.[9–11] Therefore, physicians might wrongly think that patients with ischemic cardiomyopathy undergoing CRT will derive less benefit on outcome since ischemic cardiomyopathy is associated with less reverse remodeling and less reverse remodeling is associated with poor outcome. Yet, in the trials capable of demonstrating a beneficial effect of CRT on outcome (CARE-HF, Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure [COMPANION], MADIT-CRT, and Resynchronization–Defibrillation for Ambulatory Heart Failure Trial [RAFT]), no treatment interaction was noted for the etiology of heart failure and outcome (all-cause mortality and heart failure hospitalization).[2,3,6,7] Thus, generating our hypothesis that it is a false syllogism that patients with an ischemic cardiomyopathy derive less benefit on outcome from CRT. Supporting this concept, an elegant analysis from the CARE-HF study demonstrated that patients with ischemic cardiomyopathy had a similar relative risk reduction for heart failure hospitalization and all-cause mortality as patients with nonischemic cardiomyopathy.[18]

Our analysis adds further insights into this novel and emerging concept of a disproportional effect of CRT on left

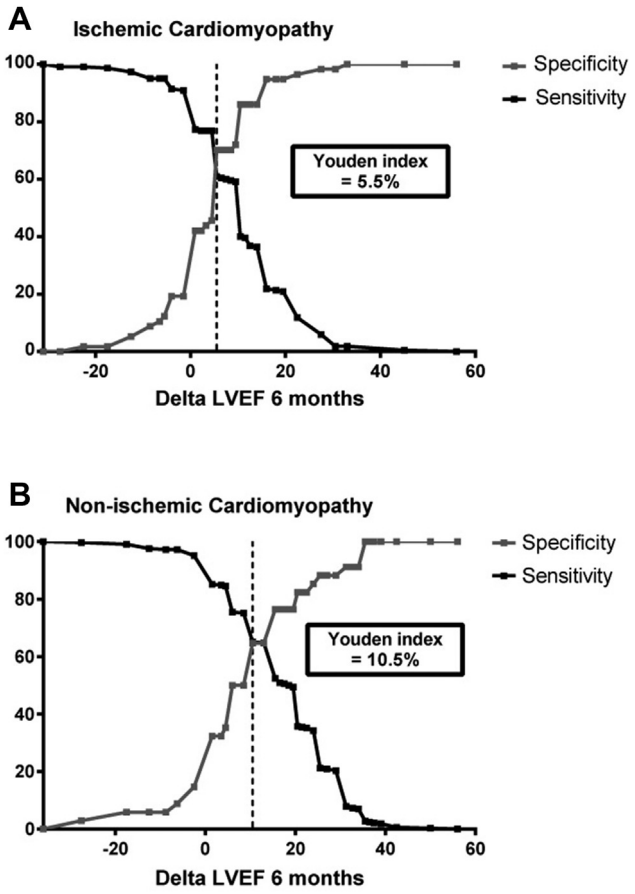

Figure 4 Optimal cutoff between reverse remodeling and freedom from 1-year mortality or heart failure admission in ischemic vs nonischemic cardiomyopathy. The receiver operating characteristic relationship between change in LVEF and absence of 1-year mortality or heart failure admission for (**A**) ischemic cardiomyopathy and (**B**) nonischemic cardiomyopathy. The dotted intersect line indicates the Youden index point (optimal cutoff point). LVEF = left ventricular ejection fraction.

ventricular reverse remodeling and outcome in patients with ischemic vs nonischemic cardiomyopathy. Indeed, our results clearly indicate that patients with ischemic cardiomyopathy exhibit less improvement in LVEF after 6 months of CRT in comparison to patients with nonischemic cardiomyopathy. Importantly, this reduced capability to reverse remodeling was sustained, even after correcting for baseline characteristics, inclusive of known predictors of diminished reverse remodeling such as male sex, non–left bundle branch block configuration, poor kidney function, and baseline left ventricular dilation. This diminished reverse remodeling capacity in ischemic cardiomyopathy is often attributed to the extent of myocardial scarring not amenable to resynchronization.[19] In addition, patients with ischemic cardiomyopathy more often present with a non–left bundle branch configuration (as in our cohort).[18] Finally, it has been shown that even patients with ischemic cardiomyopathy and left bundle branch block often exhibit less electromechanical dyssynchrony (using a broad range of techniques, including strain imaging, cardiac magnetic resonance imaging, and direct contact mapping).[20–22] Therefore, it is obvious that the myocardial substrate in patients with ischemic cardiomyopathy is less amenable for resynchronization and thus reverse remodeling on a chamber level.

Nevertheless, this reduced capacity to reverse remodel did not withhold patients with ischemic cardiomyopathy from deriving important benefits on clinical outcome. Surely, patients with ischemic cardiomyopathy after CRT exhibited a higher event rate, but it is paramount to emphasize that this also relates to the higher baseline risk before CRT. Indeed, in the control arm of the CARE-HF trial randomized to optimal medical therapy, patients with ischemic vs nonischemic cardiomyopathy exhibited an event rate of ~50% vs 25% after 1 year, respectively.[18] Therefore, the absolutely higher event rate in patients with ischemic cardiomyopathy after CRT might more closely relate to the intrinsically higher baseline risk and is not reflective of a diminished effect of CRT on outcome. More importantly, our analysis indicates that patients with ischemic cardiomyopathy already exhibited a lower adjusted odds ratio for all-cause mortality and heart failure admission at a lesser degree of reverse remodeling, while the same degree of reverse remodeling was associated with a higher adjusted odds ratio for the same end point in patients with nonischemic cardiomyopathy.

To further underscore the differential effect of the etiology on left ventricular reverse remodeling and outcome, we used the discriminative capability of ROC statistics to determine the optimal relationship between a continuous predictive value (change in LVEF) and a binary outcome value (1-year survival and freedom from heart failure hospitalization). Intriguingly, patients with ischemic cardiomyopathy had already experienced an optimal gain in outcome at lower levels of left ventricular reverse remodeling than did patients with nonischemic cardiomyopathy (Figure 4). This differential effect of CRT on reverse remodeling vs outcome might be explained by the observation that CRT itself improves more than just a dyssynchronous contraction pattern at the chamber level. Animal models of CRT have shown that CRT abbreviates sodium currents, improves repolarizing potassium currents, and diminishes intracellular calcium overload, leading to a reduction of a proarrhythmogenic phenotype.[23] This was also clinically observed in the long-term follow-up of the CARE-HF patient population.[24] Furthermore, CRT reduces proapoptotic signaling, thereby reducing disease progression.[23] Indeed, both disease progression and a proarrhythmogenic phenotype are characteristic of ischemic cardiomyopathy. Positron emission tomography studies indicative of improved cardiac metabolism after CRT have not shown a convincing difference between ischemic and nonischemic cardiomyopathy, indicating that the changes on a molecular level (molecular reverse remodeling) might span beyond the effects of alleviating electromechnical dyssynchrony at the chamber level (chamber level reverse remodeling).[25]

Study limitations

Several study limitations should be taken into account. First, this was a retrospective study. In the absence of a control group (such as with randomized controlled trials), it is not possible to calculate a absolute risk reduction of CRT on

outcome in patients with or without an ischemic etiology. Preferably the risk reduction effect would be used as a marker for the effect on outcome as it takes into account the intrinsically higher baseline risk in patients with ischemic cardiomyopathy. Second, left ventricular systolic volume was not available in our population. Since the start of our CRT clinic, we used LVEF changes to document reverse remodeling. This stems forward from the initial CRT studies (MIRACLE and MIRACLE-ICD) that used LVEF and left ventricular end-diastolic diameter as entry criteria and outcome end point for follow-up.[8] Furthermore, numerous studies have shown a good relationship between LVEF changes and outcome; therefore, the validity of the conclusion should not be affected.[26,27] In addition, it is more intuitive to group patients in different blocks of LVEF improvement (eg, 0%, 0%–5%, and 5%–10%) than for changes in percentage of left ventricular systolic volume. Third, we chose an outcome end point with short follow-up (1 year) and this might not be reflective of the effect at longer periods of follow-up. However, we explicitly chose this short duration to have a more tangible relationship between reverse remodeling measured at 6 months and the outcome variable. Fourth, we classified patients only as ischemic or nonischemic on the basis of the results of coronary angiography. However, the nonischemic group encompasses a broad spectrum of different patients (valvular, pacing induced, toxic, primary dilated cardiomyopathy, etc). Nevertheless, this distinction has not been made in the literature assessing the impact of the etiology on reverse remodeling after CRT. Fifth, baseline differences were present (as expected) between patients with ischemic cardiomyopathy and those with nonischemic cardiomyopathy, but every analysis performed was appropriately adjusted. Finally, this study should be interpreted as hypothesis generating, as the study was not designed to determine whether differential processes beyond alleviation of dyssynchrony modulated outcome in patients with ischemic cardiomyopathy.

Conclusion

Ischemic cardiomyopathy independently predicts less left ventricular reverse remodeling after CRT. However, this does not translate to a diminished benefit on outcome, as patients with ischemic cardiomyopathy exhibited benefit on outcome at a lesser degree of left ventricular reverse remodeling.

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