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Can cardiac resynchronization therapy be used as a tool to reduce sudden cardiac arrest risk?

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ABSTRACT

Patients with cardiomyopathy and reduced left ventricular (LV) ejection fraction are at risk of heart failure (HF) symptoms and sudden cardiac arrest (SCA). In selected HF patients, cardiac resynchronization therapy (CRT) provides LV reverse remodeling and improves the cellular and molecular function. However controversial results have been published regarding the effect of CRT on the residual ventricular arrhythmia risk. Indeed, the decrease in SCA risk is inconsistent and some factors strongly influence the residual post implantation arrhythmic risk. Conversely, proarrhythmic effect of CRT has been previously described. In this review we aim to describe the relationship between CRT implantation and the SCA risk decrease and discuss the patients who only require cardiac resynchronization therapy-pacemaker and those who need a concomitant implantable cardioverter defibrillator.

Contents

Abbreviations: ce-CMR, contrast-enhanced cardiac magnetic resonance; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy-defibrillator; CRT-P, cardiac resynchronization therapy-pacemaker; HF, heart failure; ICD, implantable cardioverter defibrillator; ICM, ischemic cardiomyopathy; LBBB, left bundle branch block; LV, left ventricular; LVEF, left ventricular ejection fraction; NICM, non-ischemic cardiomyopathy; QoL, quality of life; RBBB, right bundle branch block; SCA, sudden cardiac arrest; VA, ventricular arrhythmia; VT, ventricular tachycardia.

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Introduction

Patients with cardiomyopathy and reduced left ventricular (LV) ejection fraction (LVEF) are at risk of heart failure (HF) symptoms and ventricular arrhythmias (VA), leading to sudden cardiac arrest (SCA).[1,2] In selected HF patients with LVEF impairment and wide QRS, cardiac resynchronization therapy (CRT) has been shown to decrease mortality, morbidity and to improve quality of life (QoL).[3–8] Indeed, in CRT-responders, resynchronization positively impacts the failing heart, leading to LV reverse remodeling and improving the cellular and molecular function,[9,10] and leading to improvement in symptoms.

Controversial results have been published regarding the effect of CRT on the residual VA risk. Some studies demonstrated a reduction of appropriate implantable cardioverter device (ICD) therapy,[5,11–13] mostly related to positive LV remodeling. However, the decrease in VA risk is inconsistent, influenced by pre- and post-implantation factors (such as baseline echocardiography parameters or cardiac fibrosis).[14] Furthermore, proarrhythmic effect of CRT has been raised in some cases, mediated by heterogeneous trans-mural myocardial repolarization and prolonged action potential duration.[15,16]

This review aims at focusing on the residual VA and SCA risk in HF patients after CRT implantation, and describing the parameters influencing this response and discussing the requirement of a concomitant ICD implantation in patients likely to be super-responders.

The benefit of CRT in HF patients

Impact on morbidity and mortality

Numerous landmark trials established the efficacy of CRT in patients with HF. The MUSTIC (Multisite Stimulation in Cardiomyopathies) trial was the first to evaluate the benefit of CRT in 67 severe HF patients (New York Heart Association/NYHA functional class III). Indeed, biventricular pacing significantly improved exercise tolerance, QoL and decreased by two thirds the hospitalization rate.[3] Similarly, the MIRACLE (Multicenter Insync Randomized Clinical Evaluation) trial assessed the benefit of CRT in 453 patients with advanced HF (NYHA functional class III/IV), LVEF ≤ 35%, and QRS width ≥ 130 ms.[4] CRT was associated with LV chronic reverse remodeling, improvement of the QoL and a 40% decrease of the composite of death or HF hospitalization. Similar results were reported in the CARE-HF (Cardiac Resynchronization in Heart Failure) trial among a population of patients with NYHA functional class III/IV status, LVEF <35% and QRS width > 120 ms. CARE-HF was notable for demonstrating a benefit of CRT pacing in regard to overall mortality, in a trial which did not involve ICD therapy.[5] The benefit of CRT in patients with mildly symptomatic HF was assessed in the REVERSE-HF (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction), MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) and RAFT (Resynchronization-Defibrillation for Ambulatory Heart Failure) trials, including mostly patients with NYHA functional class I/II. In this population, CRT was associated with LV reverse remodeling and a reduction of 25%–50% in HF hospitalization.[5–7] Among these studies of mild-HF CRT recipients, the RAFT trial was the only one to observe a positive impact on mortality, with a 25% risk reduction.[8] Currently, CRT is highly recommended for symptomatic HF patients in sinus rhythm with severe LVEF and wide left bundle branch block (LBBB; >150 ms) (class I, level A) but also with a lower level in patients with QRS duration between 130 and 150 ms (class I, level B). For patients without LBBB the class of recommendation is lower.[17]

LV reverse remodeling induced by CRT

In HF patients, some parameters (such as reduced LVEF, myocardial adverse remodeling or wide intrinsic QRS duration), have been associated with the occurrence of VA.[18,19] Interestingly, CRT implantation positively impacts these factors. Indeed, the LV remodeling induced by CRT has been evaluated in various studies and diverse LV parameters such as LV volumes and function or mitral valve regurgitation have been shown to be improved. In a sub-analysis of 323 patients included in the MIRACLE study, authors showed that after 6 months of follow-up, CRT significantly reduced end-diastolic and end-systolic volumes, reduced the LV mass and increased LVEF.[20] Similarly, LV remodeling of 262 CRT recipients included in the REVERSE cohort were analyzed. After 24-months of follow-up, the LV end-systolic volume index and LV end-diastolic volume index were reduced by 30% and 20%, respectively. In addition, LV function was significantly improved, suggesting that CRT may prevent disease progression in HF patients.[6] Recently, a sub-analysis of 356 CRT candidates included in the PREDICT-CRT study demonstrated that the volumetric response assessed at 1-year after CRT was strongly associated with long-term mortality. In fact, LV end-systolic volume was an independent predictor of survival with an 8% reduction of mortality for every 10% decrease in end-systolic volume.[21] Currently, a significant decrease in LV end-systolic volume index between 15 and 25% at 6-months, with or without increase in LVEF, defines a positive echocardiographic CRT response.[22,23]

Beyond echocardiographic reverse remodeling, CRT implantation also induces an electrical reverse remodeling with a decrease of the intrinsic QRS duration. Indeed, patients who exhibited a decrease in intrinsic QRS duration by ≥20 ms at 12-months after CRT implantation experienced better clinical and echocardiographic responses.[24]

CRT response is variable between candidates

Despite major technical improvements, the benefit of CRT is inconsistent between candidates and some patients may still experience a deterioration of the LV function over time (around 15%). Conversely, between 10% and 25% are described as “super-responders” and experience an exceptional improvement with a normalization or near-normalization of LVEF, associated with a better survival.[21,25,26] Many factors have been described to influence CRT response, such as female gender, body mass index <30 kg/m, non-ischemic cardiomyopathy (NICM), wider QRS or LBBB and lack of dilated left atria.[25] However, despite a better understanding in cardiac dyssynchrony and a better selection in patients eligible for CRT, up to 30% still do not respond to therapy. Consequently, pathologic LV remodeling and electrical/structural substrates induced by the cardiomyopathy still persist or remain unchanged in some patients. As a result, residual VA risk seems variable in CRT patients and remains complex to evaluate.

Residual risk of VAs in CRT recipients

VA risk in HF patients

VAs are common in HF patients with reduced LVEF. For instance, among the >5000 patients implanted with an ICD in primary prevention included in the DAI-PP (Défibrillateur Automatique Implantable-Prévention Primaire) study, 22.3% of those experienced at least one VA episode during 3-year follow-up.[27] Additionally, the related VA risk does not seem to be related to the etiology of the underlying cardiomyopathy, a similar incidence of appropriate ICD therapy having been described in patients with ischemic cardiomyopathy (ICM) and NICM (76.4 vs. 78.6 per 1000 person-years, respectively).[26] Similarly, as described in the DANISH study (Danish ICD Study in Patients With Dilated Cardiomyopathy) among a NICM cohort, ICD implantation does not impact mortality but does significantly reduce the occurrence of SCA.[28] Of note, the majority of non-ICD patients (58%) were treated with CRT-pacemaker (CRT—P) and could explain the similar survival between both groups. Conversely, data suggest that NICM are at lower risk of SCA, especially when medical therapy is optimized.[29] In addition, Barra et al. showed in a European cohort of >5000 patients that NICM patients may not benefit from additional primary prevention ICD

therapy, as opposed to those with ICM.[30] Overall, the related risk of SCA has declined over time among HF patients with reduced LVEF. A recent meta-analysis of >40,000 patients showed a 44% decrease in the rate of SCA across the trials published between 1995 and 2004.[31] This evolution is consistent with the increasing number and use of guidelines-directed drugs therapies which contribute to reduce the risk of SCA but the role of CRT implantation in this evolution remains unclear.

Beneficial effect of CRT on the occurrence of VA

Various studies have evaluated the impact of CRT on the evolution of VA risk in HF patients. Indeed, as previously described in a cohort of 31 CRT-D recipients, biventricular pacing was associated with a 66% decrease in appropriate ICD therapies compared to 34 patients implanted with an ICD without CRT.[32] Furthermore, CRT tended to decrease the occurrence of non-sustained VAs. Similarly, Ouellet et al. evaluated the VA risk among MADIT-CRT patients and showed that CRT was associated with a 29% reduction in the occurrence of first VA. Of note, the beneficial anti-arrhythmic effect of CRT was higher among patients with LBBB with a 2-fold lower risk compared to non-LBBB patients.[33]

This reduced risk of life-threatening VA has been strongly correlated to the degree of LV remodeling induced by CRT. This data is supported by a sub-analysis of the MADIT-CRT trial which explored the risk of subsequent VA between low and high echocardiographic CRT responders (defined as >25% reduction of the LV end systolic volume). After 2-years of follow-up, results showed that "high" echocardiographic CRT responders presented a significantly lower risk of VA compared to "low" echocardiographic responders or ICD recipients[11] (Fig. 1, panel A). Similarly, Hsu J et al. found a decreased VA risk according to the CRT response with a 1-year risk of ICD therapy of 5%, 12% and 24% in the super-responders, responders and hypo-responders, respectively.[34] Recently, the VA risk was evaluated among the patients included in the MADIT-CRT study with normalized LVEF (>50%) after CRT implant. Among the 55 (7.2%) patients having achieved a LVEF>50%, only 1 patient had VA ≥200 bpm and none were shocked by the ICD, representing an absolute low risk of VA.[35] The benefit of super-responders with LVEF normalization has also been assessed in a multicenter study of 629 CRT-Defibrillator (CRT-D) recipients. Thirty-seven patients were defined as super-responder (LVEF > 50%) and were followed for 6.2 years. Results showed a significantly lower 5-year rate of anti-tachycardia pacing and ICD shocks compared to non-super responders (2.7% vs. 22.1% and 2.7% vs. 14.3%, respectively).[12] A recent meta-analysis including 6 studies and a total of 1740 patients assessed a rate of appropriate ICD therapy in patients with LVEF improvement ≥45% at 2.3/100 person-years which was >3-fold lower compared to patients with LVEF improvement <45% (8.3/100 person-years).[36] Of note, the threshold rate of arrhythmic mortality/100 person-years that is associated with net benefit from ICD has been estimated at 3%, suggesting that some patients at low arrhythmic risk could be implanted with CRT-P rather than CRT-D, or down-graded to a CRT-P at the time of device replacement (Fig. 1, panel B). To summarize, data demonstrated that only CRT-patients with complete or near LVEF normalization are at very low VA risk. Typically, patients who achieved LVEF normalization were more often female with NICM, LBBB QRS morphology, lower creatinine level, and less advanced LV pathological remodeling at baseline (i.e. less dilated LV/atrium and higher LVEF).[35] Conversely, patients who experienced LVEF improvement >35% but without normalization had a decreased but not eliminated VA risk.[37]

The relationship between echocardiographic response and VA events has been investigated. In a cohort of 198 CRT recipients,

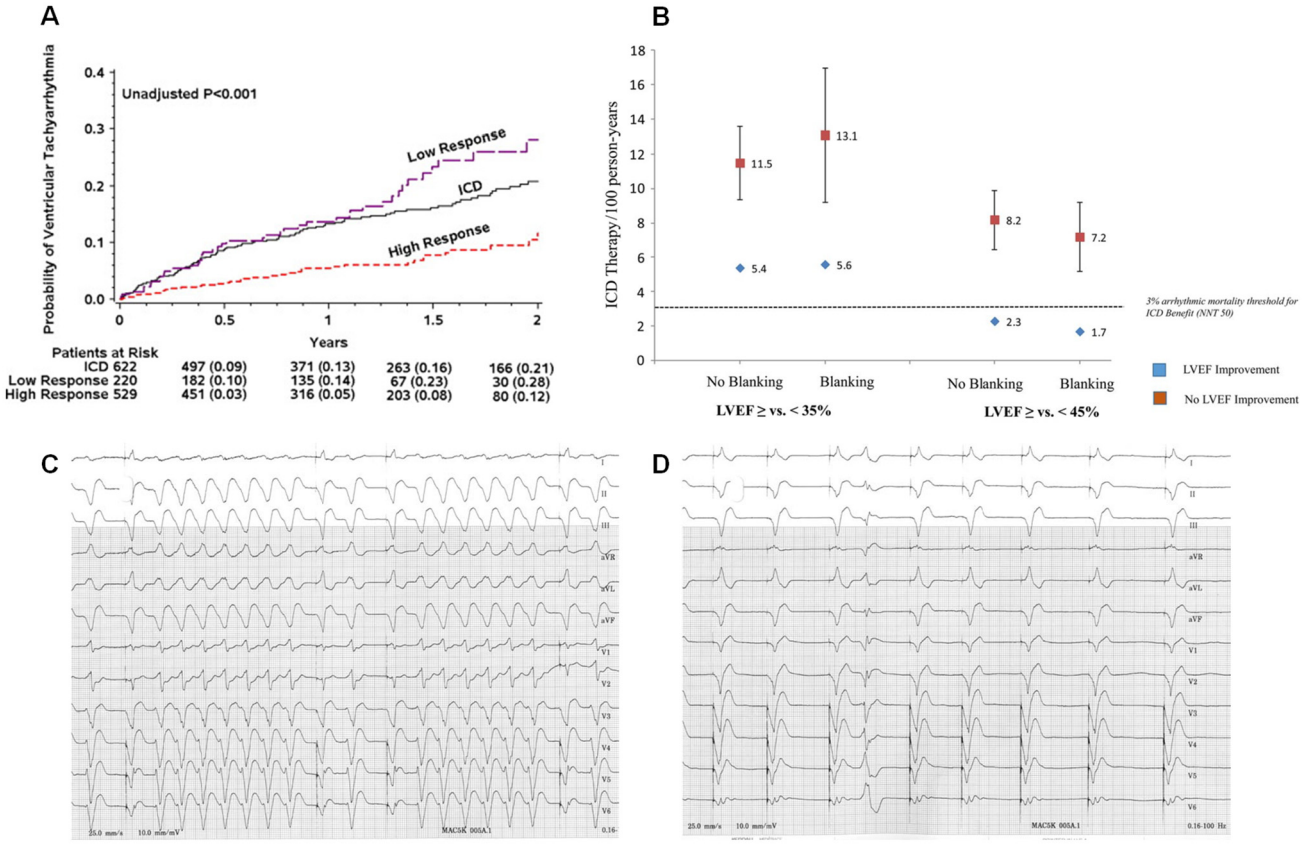

Fig. 1. Impact of CRT on the VA risk in HF patients according to the LV remodeling (Panel A and B). CRT pro-arrhythmia effect in a patient with LV lead on (Panel C) and LV lead of and VVI 40 bpm programming (Panel D). Panel A: from Barsheshet et al.[11] Reproduced with permission of editor. Panel B: from Chatterjee et al.[36] Reproduced with permission of editor. Panel C and D: from Nayak et al.[41] Reproduced with permission of editor.

anatomical responders (defined as reduction in LV end systolic volume of ≥15%) experienced approximately 30% and 50% fewer single premature ventricular contraction beats and non-sustained ventricular tachycardia (VT) runs, respectively. These results suggest that anatomic remodeling is associated with a decrease of VT triggers in CRT responders.[38] Additionally, in NICM patients with LBBB, CRT improves the septal ventricular myocardial perfusion which might explain at least part of the observed reduction in arrhythmic burden.[39] Lastly, LV reverse remodeling could improve the underlying arrhythmic substrate.

Beyond the LVEF improvement, positive echocardiographic remodeling is associated with molecular and cellular functional enhancement which could impact the risk of VA. Indeed, in a dyssynchronous HF animal model, CRT partially restored ryanodine receptor and transverse tubular system density leading to more homogeneous diastolic calcium sparks.[40] Additionally, reverse calcium regulatory genes were evaluated in 24 CRT recipients who had endomyocardial biopsies before CRT implantation and 4 months later. As compared with baseline, CRT responders experienced significant improvement of the sarcoplasmic reticulum calcium ATPase 2α (SERCA2a) and phospholamban (PLB) gene expression. Of note, non-responders did not have comparable positive molecular remodeling.[41] Similarly, among 7 patients, CRT significantly increased the PLB gene expression and trended to an increase in SERCA2a gene expression, improving cardiomyocyte calcium homeostasis.[10] The impact of CRT on structural myocardial substrate has also been previously assessed and a significant decrease in the pathologic hypertrophic gene expression has been reported.[10] Recently, in a HF dog model, CRT attenuated LV fibrosis and decreased pro-fibrotic factors both in serum and myocardial tissue.[40] Lastly, CRT therapy influences the electrical substrate by reducing the regional heterogeneity of action potential duration leading to fewer early after depolarizations.[9]

In the light of these results, response to CRT promotes the electrical/structural substrate reverse remodeling and improves calcium homeostasis leading to better excitation-contraction coupling. The LV molecular enhancement might be implicated in the decreased VA risk, but, to the best of our knowledge, no study has specifically evaluated this potential relation so far.

Influence of the LV lead location on arrhythmic outcomes

Beyond LV reverse remodeling, the impact of the LV lead position on the occurrence of VA after CRT implantation has also been evaluated, with variable results. A sub-analysis of the MADIT-CRT study showed that CRT with posterior or lateral LV lead placement is associated with decreased risk of arrhythmic events compared to patients with anterior LV lead location.[42] However, such impact may be explained by baseline differences between both groups. In fact, patients with anterior lead location had a higher rate of right bundle branch block (RBBB) compared to the lateral/posterior group and authors have suggested that pacing the anterior LV wall in patients with RBBB may not reduce electrical heterogeneity to the same amount as in patients with LBBB. Additionally, patients with anterior lead location were more likely to have had a prior myocardial infarction, and anterior LV pacing close to scar tissue could potentially increase electrical instability. Conversely, another study with 187 enrolled patients showed that anterior LV lead had no impact on the incidence of VA after CRT implantation.[43]

Paradoxical proarrhythmic effect of CRT

Although LV remodeling decreases the occurrence of VAs, a potential pro-arrhythmic effect of CRT has also been described (CRT proarrhythmic effect is illustrated Fig. 1, Panels C and D). This data was supported by Nayak et al. who enrolled 91 CRT recipients and described that VAs initiated by biventricular pacing occurred in 8 (4%) patients after a mean time of 16 days following device implantation. Consequently, the authors defined the concept of "CRT-induced proarrhythmia" as VT or electrical storm within 1 month of implantation.[44] In another study, 74 CRT recipients who required subsequent VA ablation were enrolled and 8 (12.5%) of those patients met the CRT-induced VAs definition. Interestingly, VAs occurred in very short time of 0.5 (0–2.5) days after CRT implant. During the ablation procedure, re-entry was the underlying mechanism among all patients with CRT-associated pro-arrhythmia. In addition, LV lead location within epicardial scar was significantly more frequent in the proarrhythmia group (80% vs. 17% on epicardial unipolar scar) and ablation was performed within the epicardial scar close to the LV lead in the 8 patients.[45] Authors have suggested that LV lead positioned on epicardial scar could pace near areas of slow conduction or critical isthmuses and induce re-entrant VT.

CRT has also been associated with myocardial electrophysiological disorders. In animal studies, epicardial LV pacing through the coronary sinus has been associated with prolonged QT interval, increased transmural dispersion of repolarization, and more R-on-T extrasystoles, occasionally leading to torsades de pointes.[46] Similar results were found in a canine model with a two-fold increase in transmural dispersion of repolarization when pacing from the epicardium compared to the endocardium.[47] Recently, ECG indices of dispersion and repolarization were measured in 64 patients receiving CRT and increased repolarization heterogeneity was independently associated with higher risk of VA.[48] Interestingly, LV reverse remodeling seems to decrease the repolarization heterogeneity while CRT non-responders showed a progressive increase in repolarization dispersion during follow-up.[49] Some authors have also hypothesized that CRT is intrinsically pro-arrhythmic but LV remodeling is able to produce a net anti-arrhythmic effect. Recent data from a meta-analysis included 23 studies and >8000 patients demonstrated that without LV reverse remodeling, the rate of VAs was 24% higher in CRT patients than in the ICD-only group. Results suggest that the effect of CRT on VA risk is complex and while CRT produces an overall anti-arrhythmic effect following LV reverse remodeling, it can also be potentially pro-arrhythmic in its absence.[50] Similarly, a sub-analysis of MADIT-CRT showed that CRT low-responders exhibited a 40% increase in 2-year VT risk compared with the ICD-only group.[11]

A variable VA risk occurs after CRT implantation. Indeed, some patients exhibit super-response to CRT associated with an extremely low residual VA risk. Conversely, paradoxical effect with myocardial electrical destabilization could emerge in CRT recipients leading to increased occurrence of VA episodes. Low-responder patients seem especially at risk of CRT-related pro-arrhythmia. Data suggest that some HF patients with reduced LVEF should only be implanted with CRT—P, whereas others need to receive concomitant defibrillator with CRT (CRT-D). The challenge is how to determine which CRT candidates are also likely to benefit from placement of a device which also has defibrillator function.

Is CRT without defibrillator sufficient to protect HF candidates to CRT?

In HF patients with reduced LVEF and prolonged QRS, CRT-P alone or combined with defibrillators (CRT-D) will induce LV remodeling, improve symptoms/survival and is a class I recommendation under current guidelines.[17] Currently, most candidates for CRT implantation also meet ICD criteria and up to 80% of patients are implanted with CRT-D in primary prevention in clinical practice.[51] However, among these patients, CRT-P could be sufficient to reduce the rate of VAs and protect from SCA. Consequently, the challenge in clinical practice is to implant the appropriate device in the appropriate patient.

How to predict the VA residual risk after CRT implantation

Identifying patients with residual risk of SCA after CRT implantation is crucial and predictors or new diagnostic tools are warranted to determine patients at risk of SCA who may benefit from an ICD back-up. Killu et al. suggested three pre-CRT implantation predictors of appropriate

ICD therapy in CRT-D recipients: male gender, baseline LV end-systolic volume and LVEF.[12] Of note, female super-responders have a 5-year incidence rate of appropriate ICD therapy of 0%. Similarly, Ruwald et al. identified 6 predictors of LVEF normalization (>50%) among CRT recipients: female gender, LBBB, no previous myocardial infarction, baseline LVEF > 30%, baseline LV end-systolic volume ≤ 170 ml and baseline left atrial volume index ≤45 ml/m^2. Among the population, 42 patients had all factors and none experienced VAs during follow-up.[35] In addition, in a Spanish cohort including 196 patients implanted with CRT followed during 30.1 months, super-responders had lower VA rate compared to non-super-responder group (5.9% vs. 24.4%, respectively) and 4 VA predictors were described: baseline QRS duration > 160 ms, amiodarone, previous history of VA and non-super-responder patients (LVEF < 45%).[52] Controversial data have been published regarding the impact of CRT on VA burden according to the underlying cardiomyopathy etiology. Indeed, in a population of 115 CRT patients, ischemic cardiomyopathy was surprisingly associated with a 2-fold lower risk of the appropriated ICD therapy risk.[53] Conversely, the impact of the cardiomyopathy etiology was evaluated in a population of 689 patients. The cohort was divided in four groups: patients with ICM vs. NICM and patients implanted with an ICD vs. CRT-D. Results showed that ICM patients with CRT-D have similar cumulative probability of appropriate ICD therapy compared to those with only ICD. However, non-ischemic patients with CRT-D have a 2-fold lower risk of 2-years appropriate ICD incidence compared to the ICD group (24.7% vs. 41.6%, respectively).[54] The authors suggest that CRT implantation is associated with a marked reduction in appropriate ICD therapies in the non-ischemic patients group. However, in this study the 2-years incidence of VAs remains high and affects 1 in 5 patients in both groups, suggesting that cardiomyopathy etiology as the only one predictor of residual VA risk after CRT implantation is not selective enough. Fig. 2 synthetizes the main VA risk predictors previously described.

Currently, in light of the literature, it seems difficult to fully predict the residual risk of VA after CRT implantation which is mainly driven by predictors of super-response. On the other hand, super-response predictors are mostly based on echocardiography parameters

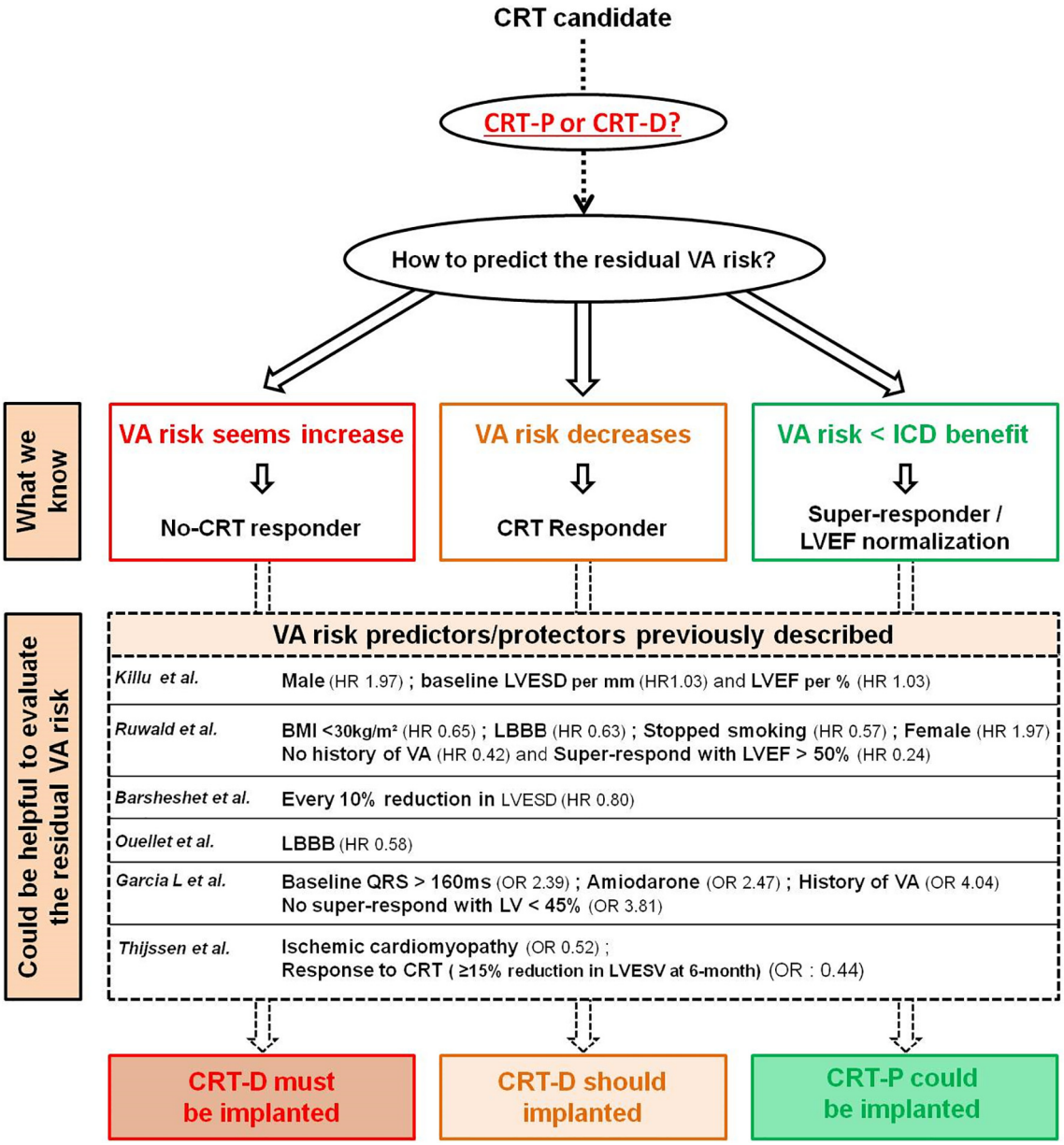

Fig. 2. How to predict the residual ventricular arrhythmia risk after CRT implantation: summary of the current literature. BMI = Body mass index; CRT = Cardiac resynchronization therapy; CRT-P = Cardiac resynchronization therapy with pacemaker; CRT-D = Cardiac resynchronization therapy with defibrillator; ICD = Implantable cardioverter defibrillator; LV = Left ventricular; LVEF = Left ventricular ejection fraction; LBBB = Left bundle branch block; LVESD = Left ventricular end-systolic dimension; VA = Ventricular arrhythmia.

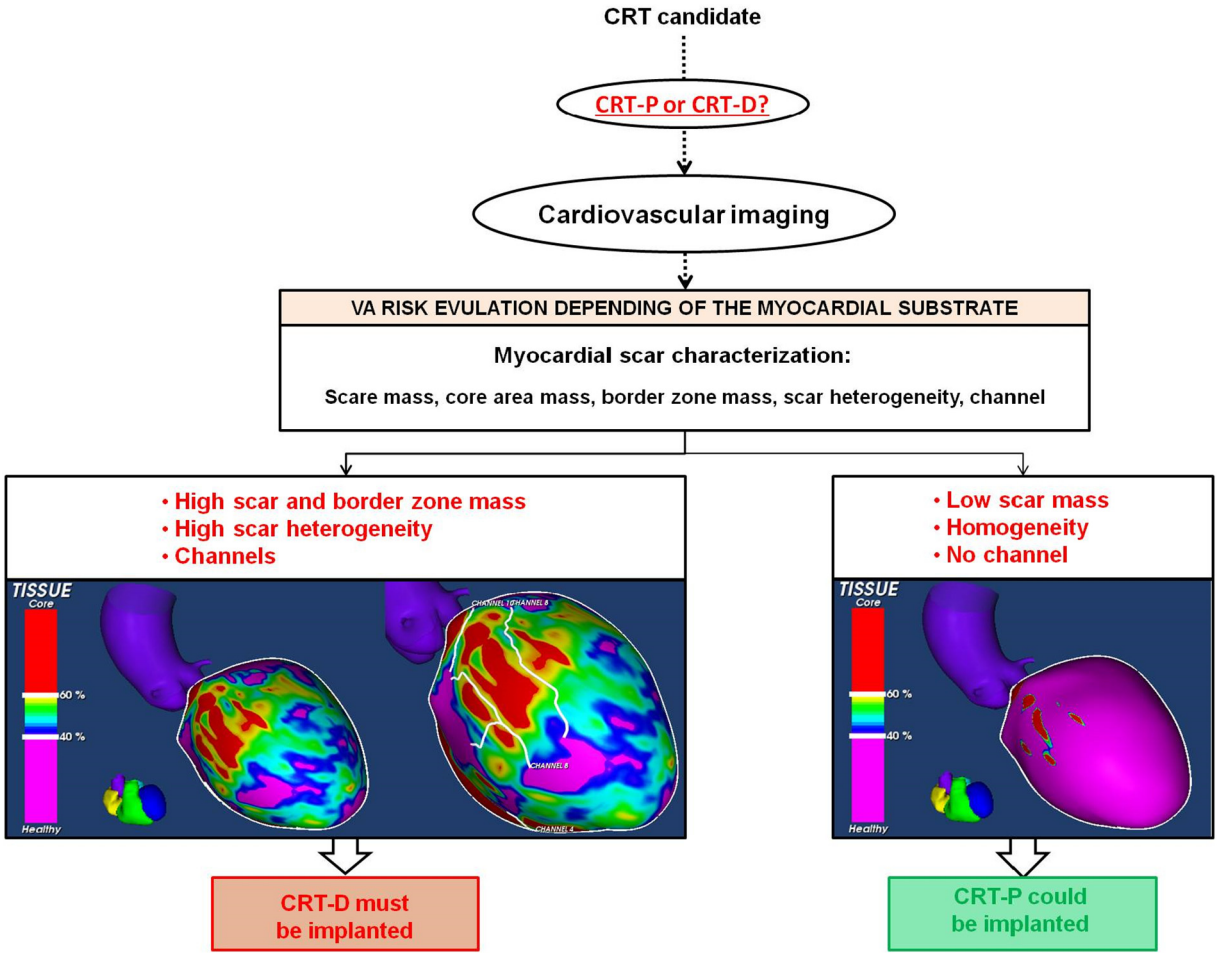

Fig. 3. Future directions for residual ventricular arrhythmia risk evaluation in patients eligible to CRT. CRT = Cardiac resynchronization therapy; CRT-P=Cardiac resynchronization therapy with pacemaker; CRT-D = Cardiac resynchronization therapy with defibrillator; VA = Ventricular arrhythmia.

associated with inter-physician variability. However new imaging diagnostic tools may be helpful to predict patients at high VA risk. Indeed, analysis of myocardial scar tissue by contrast-enhanced cardiac magnetic resonance (ce-CMR) was correlated to VA occurrence risk in CRT candidates, regardless of the etiology of the cardiomyopathy. In a cohort of 78 patients, the presence of >16% scar and a border zone >9.5 g were independent predictors of appropriate ICD therapy and SCA, respectively associated with a 7.8 and 4.6-fold increased risk. Of note, a scar mass > 16% had 100% sensitivity and 81% specificity for 1-year prediction of appropriate ICD therapy while a border zone mass > 9.5 g had a sensitivity and specificity of 100 and 93%, respectively, with a 43% positive predictive value and 100% negative predictive value for 1-year appropriate ICD therapy.[55] ceCMR seems promising to identify a very low-risk subgroup or CRT patients that will not benefit from a back-up ICD. Similarly, in a population of 217 CRT candidates, pre-procedural scar analyzed using ce-CMR was performed to assess the residual VAs risk and SCA among this population. A total of 25 (11.5%) patients experienced appropriate ICD therapy or SCA during 35.5 months of follow-up. Regarding the ce-CMR analysis, none of the 92 patients without myocardial scar experienced ICD therapies or SCA. Additionally, among the 125 patients with late gadolinium enhancement, total scar mass, core mass, and border zone mass were significantly greater in the group with ICD therapies or SCA. Furthermore, border zone channels mass was higher in patients with VAs or SCA. Lastly, the authors developed two nice algorithms based on scar mass > 10 g and the presence of border channel for the first one and based on scar mass > 10 g and border zone mass > 5.3 g for the second one. Both algorithms identified patients at high risk with 100% sensitivity, 81.3% specificity and 36.2% positive predictive value for the first algorithm and 100% sensitivity, 79.3% specificity and 33.3% positive predictive value for the second algorithm. Interestingly, these algorithms can be used in ICM and NICM patients.[56] Data suggest that assessment of the myocardial substrate is crucial to predict the VA risk after CRT implantation and probably more relevant than baseline patient characteristics or echocardiography itself. However, randomized studies are required to confirm the usefulness of scar characterization for the identification of CRT candidates that could benefit from adding defibrillator or not to the CRT device. Fig. 3 illustrates the potential impact of the use of cardiovascular imaging to accurately evaluate the VA risk after CRT implantation.

Conclusions

CRT has substantially improved the prognosis of HF patients who are candidates for the therapy. LV reverse remodeling and especially super-response with LVEF normalization are undeniably associated with a decrease in VAs and SCA risk. Data suggest that CRT-P is a sufficient tool to protect selected HF patients from SCA. However, identifying CRT candidates who do not need concomitant ICD implantation remains challenging. Cardiac imaging and myocardial scar analysis seems promising to evaluate the residual risk for VA and SCA after CRT implant and will probably serve to further risk-stratify these patients in the future.

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