Effect of Diabetes Mellitus on Cardiac Resynchronization Therapy and to Prognosis in Heart Failure (from the Prospective Evaluation of Asian With Cardiac Resynchronization Therapy for Heart Failure Study)

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The association of diabetes mellitus (DM) with cardiac resynchronization therapy (CRT) response and cardiovascular outcomes in Asian patients with heart failure (HF) is unclear. This study aims to investigate the effects of DM on CRT response and cardiovascular outcomes in Asian HF patients. Consecutive Asian HF patients receiving CRT were enrolled in the Prospective Evaluation of Asian with CRT for Heart Failure (PEACH) study from 2011 to 2017. CRT response and super-response were defined as decrease in end-systolic volume index ≥15% and ≥30%, respectively. Primary endpoint was time to composite of HF-hospitalization and all-cause mortality. Among 161 patients followed for 3.3 ± 1.5 years (age 66.7 ± 11.2 years, 22% females, mean QRS duration 154.3 ± 22.4 ms, 83% left bundle branch block), 84 (52%) were CRT responders and 57 (35%) were super-responders. Of 82 (51%) patients with DM (100% type 2, mean HbA1c 7.3 ± 1.9%), 35 (43%) were responders. DM attenuated reverse remodeling (CRT response: AOR 0.44, 95% confidence interval [CI] 0.20 to 0.98, p < 0.05; super-response: AOR 0.42, 95% CI 0.18 to 0.97, p <0.05), and DM increased HF-hospitalization and all-cause mortality (AHR 1.68, 95% CI 1.00 to 2.82, p = 0.05). The extent of CRT-response correlates with higher event-free survival (CRT response: AHR 0.5, 95% CI 0.30 to 0.81, p = 0.005; super-response: AHR 0.27, 95% CI 0.14 to 0.52, p < 0.001). In conclusion, the extent of reverse remodeling post-CRT is the strongest predictor of event free survival. However, DM is detrimental to the CRT recipient by attenuating reverse remodeling, inducing end organ dysfunction and is independently associated with worsened clinical outcomes among Asian HF patients. **(Am J Cardiol 2019;124:899−906)**

Diabetes mellitus (DM) and heart failure (HF) often coexist and exert a significant burden on healthcare systems. The global prevalence of DM is expected to rise to 4.4% in 2030,[1] whereas HF is a growing epidemic with a reported prevalence of more than 23 million worldwide.[2] These major public health issues are likely to become more prominent, especially in Asia, as it transitions into an ageing population.[3] Among patients with symptomatic heart failure and broad QRS, cardiac resynchronization therapy (CRT) is an established therapeutic modality in improving survival[4] through its ability to reverse left ventricular (LV) remodelling.[5,6] Although CRT response can be seen early as three months,[7] up to a third of patients remain as non-responders.[8] The impact of DM on left ventricular (LV) function and dimensions have previously been described,[9] with DM conferring a poorer prognosis among HF patients with CRT.[10,11] However, the effect of DM on LV reverse remodeling has been inconsistent,[12,13] and Asian patients are not well represented in large CRT trials. This is particularly pertinent given that DM is 3-fold more common among Southeast Asian patients with HF compared with whites.[14] This study aimed to determine CRT response rates in a cohort of Asian HF patients, and investigates the relation between DM with CRT response and clinical outcomes.

Methods

The Prospective Evaluation of Asian with CRT for Heart Failure (PEACH) study is a prospectively designed, single

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center, observational study of Asian HF patients (ClinicalTrials.gov Identifier: NCT02814942). Consecutive Asian HF patients receiving CRT at an academic medical center were enrolled in the study from 2011 to 2017. Only patients who fulfilled contemporary HF guidelines for CRT and who had paired echocardiograms pre- and post-CRT were included in the study.[4] This included patients with New York Heart Association (NYHA) functional class II to III, QRS duration (QRSd) ≥120 ms and left ventricular ejection fraction (LVEF) ≤35%. The decision to combine CRT with an implantable cardioverter defibrillator (CRT-D) was based on the same international consensus. All patients were above 21 years of age and were able to provide informed consent. The study was performed in accordance with the Helsinki's declaration and approved by the National Healthcare Group Domain Specific Review Board, Singapore.

Patients were assessed at recruitment (index admission for CRT implantation) and followed-up every 6 months in clinic. Baseline demographics, clinical profile and use of guidelines-directed medical therapy were recorded using a comprehensive electronic medical records system (CPSS2, iHIS, Singapore). DM was defined as the presence of a previous diagnosis (fasting plasma glucose ≥7 mmol/L or random plasma glucose ≥11.1 mmol/L or HbA1c ≥6.5%) and/or treatment with antidiabetic medications. The presence of chronic kidney disease (CKD) was defined as estimated glomerular filtration rate of <60 ml/min/1.73m^2. Standard 12-lead electrocardiograms (ECG) were performed and interpreted by experienced electrophysiologists. Serum NT-proBNP levels were drawn on the day of CRT-implantation and repeated during follow-up.

Interventricular lead distance was obtained as a composite of left ventricular (LV) and right ventricular (RV) lead tip separation distance on posteroanterior (χ, cm) and lateral (Υ, cm) chest X-rays (CXR) performed on the first postimplant day (Figure 1). The composite LV-RV lead separation distance was then derived by the formula: LV-RV lead separation distance (cm) = $\sqrt{(\chi^2 + \Upsilon^2)}$. LV leads implanted were either bipolar or quadripolar in configuration. The LV lead placement was dependent on the availability of suitable target veins and whenever possible, placed in a lateral vein with electrodes in a nonapical position. Device interrogation on routine follow-up was evaluated to assess the percentage duration of biventricular pacing (BVP) and presence of atrial fibrillation (AF). The latter was confirmed by inspection of device electrograms showing irregular atrial activation >220 beats per minute and lasting for >6 minutes. Occurrence of ventricular arrhythmias and application of any implantable cardiac defibrillator (ICD) therapy was also recorded.

Transthoracic echocardiograms were performed in our institutional echocardiography core laboratory pre-CRT and in 6 to 24 months after CRT-implantation. LVEF, left ventricular end-systolic (LVESD) and end-diastolic (LVEDD) dimensions, end-systolic volume index (LVESVI), and LV mass index (LVMI) were measured and classified in accordance with the American and European echocardiography imaging guidelines.[15]

CRT response and super-response were defined as decrease in LVESVI ≥15% and ≥30%, respectively. Although a variety of echocardiographic parameters have been used in the definition of CRT response, these values have been validated as acceptable thresholds of reverse

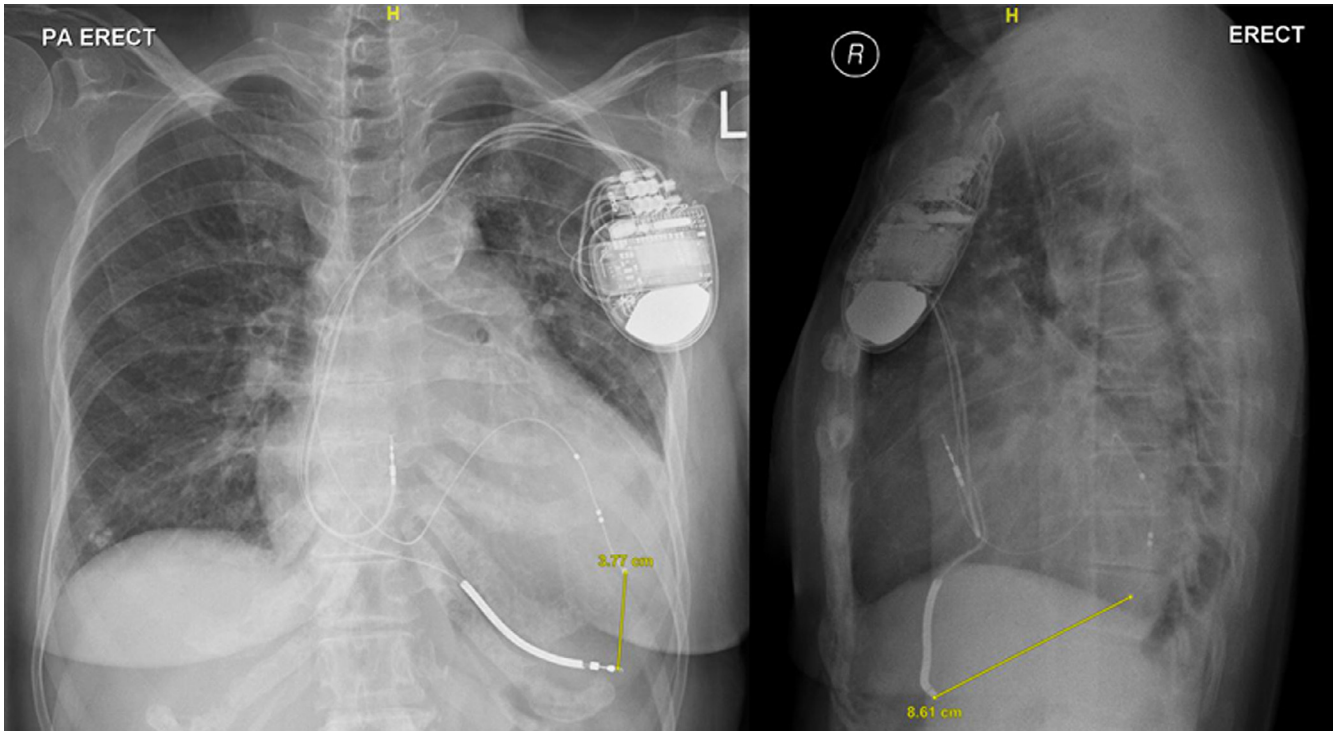

Figure 1. Interventricular lead separation distances obtained from posteroanterior and lateral chest X-rays.

remodeling.[16,17] The primary outcome of this study was a composite of HF-hospitalization or all-cause mortality. Patients in the study were followed from date of CRT implantation to either death or time of drafting this manuscript (April 2019).

Exploratory analyses were performed with Chi-square and independent *t* tests, depending on the nature of data. To ascertain how the identified predictors were associated with CRT response, a confirmatory analysis was performed with the generalized structural equation model (gSEM). Optimal cut-off for QRSd for CRT response was determined with respect to sensitivity and specificity. The Binomial and Weibull distributions were applied for analyzing binary and time-to-event outcomes, respectively. A backward elimination model selection procedure incorporated (removal probability >0.05). All statistical tests were performed at 5% level of significance with Stata MP V14 (Stata Corporation, Texas).

Results

Among 271 patients in the PEACH registry, 161 patients met the inclusion criteria (Figure 2) and were included in this analysis (mean follow-up of 3.3 ± 1.5 years, age 66.7 ± 11.2 years, 22% females, mean QRSd 154.3 ± 22.4 ms, 83% left bundle branch block [LBBB], 30% nonischemic cardiomyopathy, LVEF 26.3 ± 7.9%).

CRT response was achieved in 84 (52%) patients, of which 57 (35% of total cohort) were super-responders. Compared with nonresponders, responders were more likely to have LBBB (89% vs 75%, p = 0.02) and BVP >98% (67% vs 47%, p = 0.01). Responders and super-responders were also more likely to be nondiabetic (Responders: 49 [62%] without DM vs 35 [43%] DM, p = 0.01; Super-responders: 36 [46%] without DM vs 21 [26%] DM, p = 0.008). Baseline characteristics of diabetic and nondiabetic patients are shown in Table 1. During follow-up, responders had lower median NT-proBNP (1480 pg/mL vs 3630 pg/mL, p = 0.02), LVEDD (56.1 ± 9.2 mm vs 65.3 ± 9.3 mm, p <0.001), LVESD (43.6 ± 10.4 mm vs 56.4 ± 10.8 mm, p <0.001), LVESVI (54.2 ± 30.9 mL/m^2 vs 94.1 ± 41.7 mL/m^2, p <0.001) and higher LVEF (37.4 ± 13.0% vs 26.4 ± 10.9%, p <0.001) after CRT-implantation compared with nonresponders. LBBB and BVP percentage >98% independently predicted CRT response, whereas QRSd ≥150 ms and BVP >98% predicted super-response (Table 2). Increasing interventricular lead distance, however, was consistently associated with a reduction in CRT response. When assessed in quartiles, only patients with the highest quartile of inter-lead distances demonstrated an attenuated CRT response. Interventricular lead distance ranged from 4.48 cm to 17.18 cm, with the highest quartile consisting of a higher proportion of diabetic nonresponders (Table 3). A positive correlation was seen between interlead distance and LVESVI pre-CRT implantation (r = 0.2, p <0.01). Females, nonischemic cardiomyopathy and type of LV lead (quadripolar vs bipolar) were however not associated with CRT response.

There were 82 (51%) patients with DM (mean HbA1c 8.0 ± 2.1%, mean duration 7.6 ± 4.6 years), among which 35 (43%) achieved CRT-response. Interestingly, of the 35 diabetic responders, 32 (91% of diabetic responders) were super-responders. Of those receiving antidiabetic medications, (26 [32%] on insulin, 64 [78%] on oral hypoglycemic agents (OHGA): 45 [55%] metformin, 37 [45%] sulfonylurea, 8 [10%] dipeptidyl-peptidase-4 inhibitor, 1 (1%) sodium-glucose-cotransporter-2 inhibitor), 12 (15%) were on combination therapy of insulin and OHGA and 21

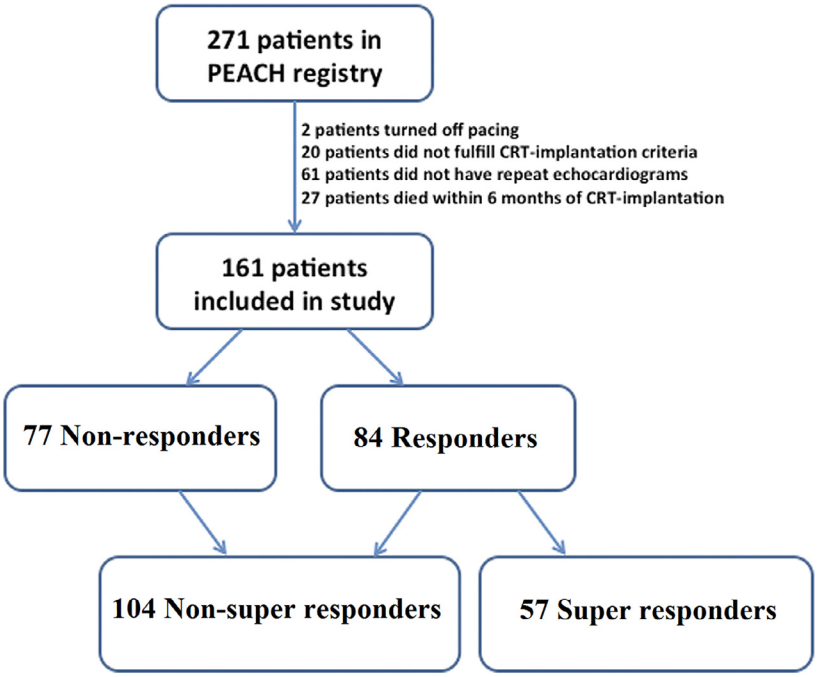

Figure 2. Enrollment and inclusion of patients with CRT in the PEACH study. CRT = cardiac resynchronization therapy; PEACH = Prospective Evaluation of Asian with Cardiac resynchronization therapy for Heart failure.

Table 1
Comparison of baseline characteristics between patients with heart failure with and without diabetes mellitus

Variable	All	Diabetes Mellitus		p Value
		YES (n = 82)	NO (n = 79)	
Age (years)	66.7 ± 11.2	68.4 ± 9.3	64.9 ± 12.8	0.07
Women	35 (22%)	18 (22%)	17 (22%)	0.95
Chinese	104 (65%)	50 (61%)	54 (68%)	0.78
Malay	28 (17%)	15 (18%)	13 (16%)	
Indian	24 (15%)	14 (17%)	19 (13%)	
Other	5 (3%)	3 (4%)	2 (3%)	
QRS duration pre (ms)	154.3 ± 22.4	152.0 ± 21.0	156.8 ± 23.7	0.22
Left bundle branch block	133 (83%)	67 (82%)	66 (84%)	0.76
Angiotensin converting enzyme-inhibitor/ angiotensin II receptor blocker/angiotensin receptor-neprilysin inhibitor	130 (81%)	67 (82%)	63 (80%)	0.75
Beta-blocker	151 (94%)	77 (94%)	74 (94%)	0.95
Spironolactone	69 (43%)	33 (40%)	36 (46%)	0.5
Non-ischemic cardiomyopathy	48 (30%)	16 (20%)	32 (41%)	0.004
Chronic kidney disease	71 (44%)	49 (60%)	22 (28%)	<0.001
Neuropathy	3 (2%)	3 (4%)	0 (0%)	0.09
Retinopathy	9 (6%)	9 (11%)	0 (0%)	0.002
Stroke	22 (14%)	10 (12%)	12 (15%)	0.58
Peripheral vascular disease	13 (8%)	12 (15%)	1 (1%)	0.002
HbA1c (%)	7.3 ± 1.9	8.0 ± 2.1	6.1 ± 0.8	<0.001
Cardiac resynchronization therapy-defibrillator	131 (81%)	65 (80%)	66 (84%)	0.49
Defibrillator therapy	31 (19%)	10 (12%)	21 (27%)	0.02
Biventricular pacing percentage >98%	91 (57%)	47 (58%)	44 (56%)	0.84
New atrial fibrillation	67 (42%)	37 (45%)	30 (38%)	0.36
Type of left ventricular lead [quadripolar]	116 (72%)	61 (74%)	55 (70%)	0.5
Lead separation distance (cm)	10.7 ± 2.3	10.9 ± 2.2	10.5 ± 2.3	0.12
NT-proBNP* pre (pg/mL)	2210 (1040, 5910)	3355 (1025, 6685)	1820 (1060, 4370)	0.22
NT-proBNP* post (pg/mL)	2150 (620, 6840)	3684 (858, 9150)	1499 (529, 3280)	0.005
Left ventricular ejection fraction pre (%)	26.3 ± 7.9	26.1 ± 7.4	26.5 ± 8.4	0.65
Left ventricular ejection fraction post (%)	32.2 ± 13.2	30.9 ± 12.5	33.5 ± 13.9	0.21
Left ventricular end systolic volume index pre (mL/m^2)	87.0 ± 38.4	83.7 ± 36.0	90.3 ± 40.7	0.38
Left ventricular end systolic volume index post (mL/m^2)	73.3 ± 41.5	74.8 ± 37.6	71.7 ± 45.4	0.19
Left ventricular mass index pre (g/m2)	150.9 ± 47.5	152.0 ± 45.8	149.8 ± 49.4	0.68
Left ventricular mass index post (g/m^2)	142.7 ± 46.9	146.4 ± 51.0	139.0 ± 42.2	0.46
Cardiac resynchronization therapy response	84 (52%)	35 (43%)	49 (62%)	0.01
Cardiac resynchronization therapy super-response	57 (35%)	32 (27%)	36 (46%)	0.008
Heart failure-hospitalization	71 (44%)	55 (54%)	27 (34%)	0.01
All-cause mortality	51 (32%)	29 (35%)	22 (29%)	0.31
Composite event†	82 (51%)	50 (61%)	32 (41%)	0.009

* Expressed as median (interquartile range).
† Composite event of heart failure-hospitalization or all-cause mortality

(26%) on two or more OHGAs. Diabetic patients were more likely to have ischemic heart disease (80% vs 59%, p = 0.004), CKD, retinopathy, and peripheral vascular disease. However, LV dimensions and LVMI were similar in the presence or absence of DM. Diabetic patients were at least 56% less likely to achieve reverse remodeling with CRT. Diabetic nonresponders had a higher baseline HbA1c than responders (8.5 ± 2.3% vs 7.4 ± 1.6%, p = 0.02), and a larger proportion in the highest quartile of lead separation (38% vs 14%). However, insulin use (23% vs 38%, p = 0.14), duration of DM (7.7 ± 4.2 vs 7.5 ± 5.0 years, p = 0.69) and mean LVMI (154.1 ± 42.9 vs 150.3 ± 48.5, p = 0.43) did not differ between diabetic responders and diabetic nonresponders, respectively.

There were 71 HF-hospitalizations and 51 all-cause deaths during follow-up. The primary outcome of HF-hospitalization or all-cause mortality occurred in 82 patients (61% DM vs 41% without DM, p <0.01).

The overall primary endpoint occurred more frequently in diabetic subjects (hazard ratio [HR] 2.29, 95% CI 1.22 to 4.31), with Kaplan-Meier curves showing a significant difference between diabetics and non-diabetics on follow-up (Figure 3). When adjusted for patient demographics, clinical covariates, guideline-directed medical therapy, recorded ICD therapies and AF on device interrogations, and CRT response, DM was associated with a 68% increase in primary outcome (Table 4). Similarly, CKD was independently associated

Table 2
Predictors of cardiac resynchronization therapy-response and super-response

	Cardiac resynchronization therapy-response			Super-response		
	Adjusted odds ratio	95% CI	p Value	Adjusted odds ratio	95% CI	p Value
Age	1.01	0.98-1.05	0.54	1.01	0.97-1.05	0.6
Female	1.14	0.43-3.05	0.79	2.53	0.94-6.82	0.07
QRS ≥150 ms	2.15	0.98-4.70	0.06	2.98	1.245-7.09	0.01
Left bundle branch block	3.28	1.24-8.69	0.02	2.11	0.71-6.28	0.18
Non-ischemic cardiomyopathy	1.69	0.62-4.59	0.30	1.01	0.38-2.70	0.99
Diabetes mellitus	0.44	0.20-0.98	0.045	0.42	0.18-0.97	0.04
Chronic kidney disease	0.8	0.35-1.83	0.60	0.49	0.20-1.22	0.12
Lead quartiles*						
2nd	0.72	0.25-2.12	0.55	0.78	0.27-2.26	0.65
3rd	0.51	0.18-1.49	0.54	0.76	0.26-2.27	0.63
4th	0.27	0.09-0.77	0.02	0.23	0.07-0.79	0.02
Type of leads†	0.9	0.38-2.13	0.82	1.65	0.67-4.06	0.28
Biventricular pacing percentage >98%	2.23	1.04-4.81	0.04	2.83	1.23-6.52	0.01

* Compared with first quartile.
† Quadripolar vs bipolar.

Table 3
Distribution of lead quartiles with and without diabetes

Lead quartiles	Without diabetes (n = 79)	Diabetic responders (n = 35)	Diabetic non-responders (n = 47)
1st: 4.48-9.04 cm	22 (28%)	10 (29%)	10 (21%)
2nd: 9.20-10.77 cm	25 (32%)	8 (23%)	8 (17%)
3rd: 10.78-12.14 cm	17 (21%)	11 (35%)	11 (23%)
4th: 12.23-17.18 cm	15 (19%)	5 (14%)	18 (38%)

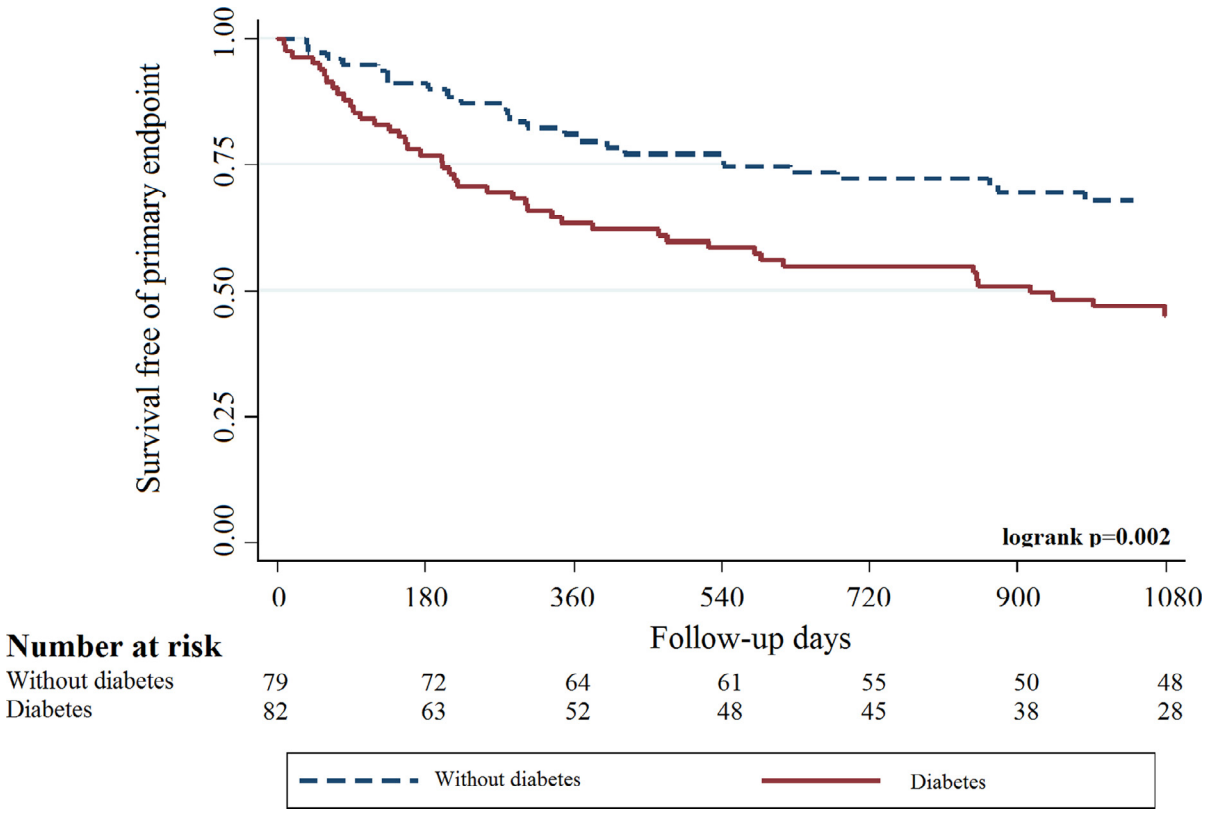

Figure 3. Kaplan-Meier curves of the association of diabetes with primary outcome of composite event of HF-hospitalization or all-cause mortality. CRT = cardiac resynchronization therapy; HF = heart failure.

Table 4
Predictors of composite events of heart failure-hospitalization or all-cause mortality

	Adjusted hazard ratio	95% CI	p Value	Adjusted hazard ratio	95% CI	p Value
Cardiac resynchronization therapy-response*	0.5	0.30-0.81	0.005			
Cardiac resynchronization therapy super-response†				0.27	0.14-0.52	<0.001
Age	0.99	0.97-1.02	0.47	0.99	0.97-1.02	0.54
Female	0.68	0.35-1.33	0.26	0.83	0.42-1.63	0.58
Left bundle branch block	0.71	0.41-1.24	0.23	0.65	0.37-1.16	0.15
Non-ischemic cardiomyopathy	1.14	0.61-2.14	0.67	1.09	0.58-2.06	0.79
Diabetes mellitus	1.68	1.00-2.82	0.05	1.58	0.94-2.66	0.08
Chronic kidney disease	2.6	1.56-4.33	<0.001	2.48	1.47-4.19	0.001
Angiotensin converting enzyme-inhibitor/ angiotensin II receptor blocker/angiotensin receptor-neprilysin inhibitor	0.7	0.41-1.21	0.20	0.62	0.36-1.06	0.08
Beta-blocker	0.77	0.30-1.97	0.58	0.84	0.32-2.17	0.72
Any defibrillator therapy	1.4	0.82-2.39	0.22	1.37	0.81-2.34	0.24
Any new atrial fibrillation	0.69	0.44-1.09	0.11	0.67	0.42-1.05	0.08

* Reduction in end-systolic volume index by ≥15%.
† Reduction in end-systolic volume index by ≥30%.

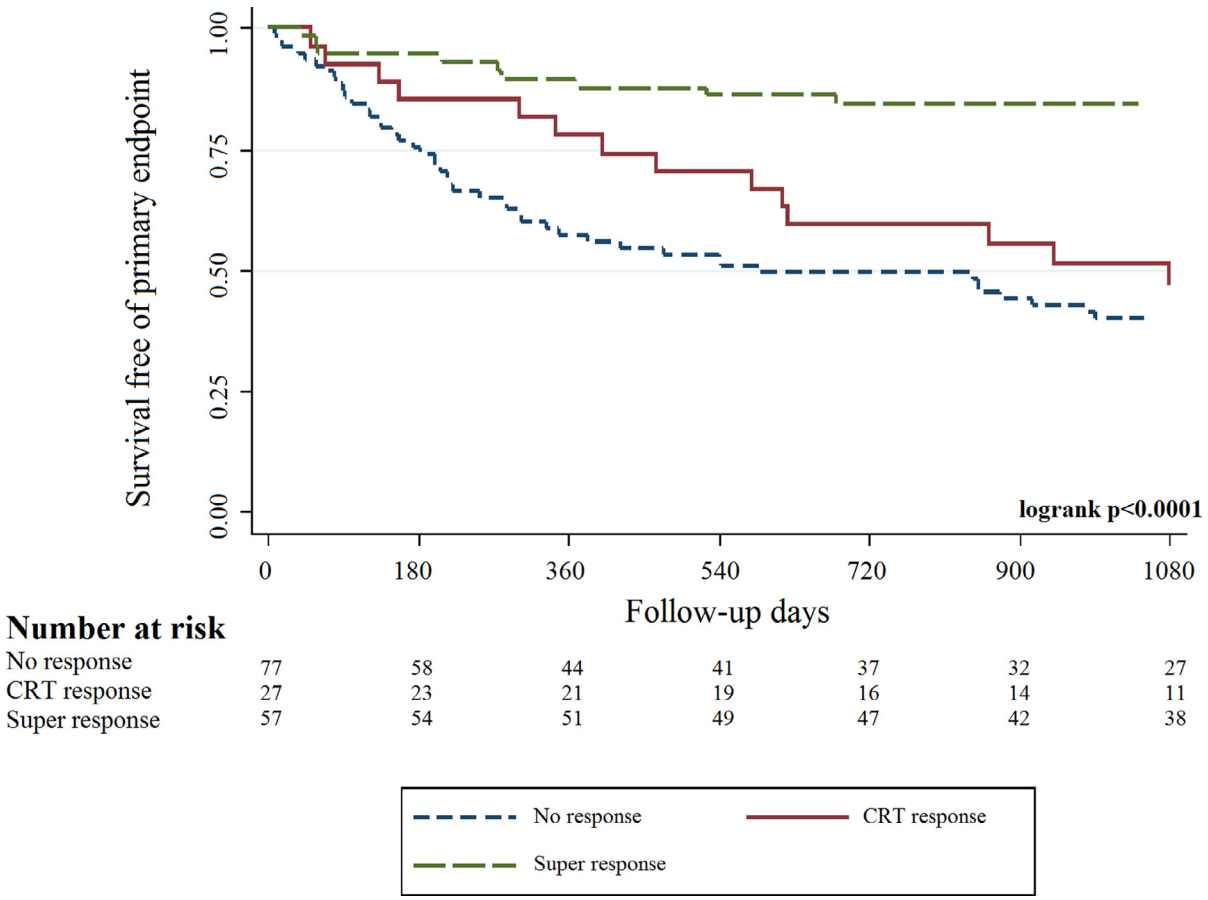

Figure 4. Kaplan-Meier curves of the association of CRT response and super-response with primary outcome of composite event of HF-hospitalization and all-cause mortality. CRT = cardiac resynchronization therapy; HF = heart failure.

with poorer outcomes, with 2.5 times higher likelihood of composite events. CRT-response (HR 0.27, 95% CI 0.14 to 0.51) and super-response (HR 0.13, 95% CI 0.06 to 0.28) were both associated with reduced composite events compared with nonresponse, demonstrated in Kaplan-Meier survival curves (Figure 4). On multivariable adjustment, the degree of CRT-response independently predicted better outcomes, with CRT response showing a 50% reduction, whereas super-response displayed a 73% reduction in composite events (Table 4).

Discussion

This study demonstrated an echocardiographic CRT response and super-response rate of 52% and 35% in Asian HF patients with the degree of CRT response being a strong, independent predictor of increased event free survival. QRSd ≥150 ms, LBBB and BVP >98% were associated with CRT response. Patients with the widest lead separation were less likely to respond. DM is detrimental to CRT recipients by first, diminishing reverse remodeling, second as an independent predictor of HF-hospitalizations and death and finally by increasing microvascular and macrovascular complications.

Compared with studies utilizing the same CRT response definition, our response rate (52%) closely resembles Western HF cohorts (51% to 56%).[6,16] Previous Asian CRT series were however often smaller with varying definitions of CRT response.[18-21] Other important considerations when comparing response to CRT in different HF populations are that Asian patients were 3 times more likely to have DM than whites, with the highest prevalence of DM amongst Southeast Asian patients.[3,14] Given the direct impact of DM on CRT response, differences in CRT response rates between different HF populations may be in part due to the varying prevalence of DM.

The impact of DM on CRT response remains inconsistent in the literature.[12,13,22−24] We demonstrated that Asian HF patients with DM were less likely to achieve reverse remodeling compared with nondiabetic patients, which may in part be due to the significantly higher proportion of ischemic heart disease in our population (80%) of diabetic patients compared with previous Western cohorts (50% to 70%).[13,15,16,18] Although Höke et al. found that insulin use reduced CRT-response,[12] we did not find a difference in CRT response with insulin use, in keeping with other studies.[13,23] Insulin therapy has been suggested to be a measure of disease chronicity and DM control, but we did not observe differences in insulin use and duration of DM among diabetic responders and nonresponders. Instead, we found that baseline HbA1c levels were significantly higher among diabetic nonresponders, reflecting that nonresponders more likely had suboptimal glycemic control regardless of insulin use. Shah et al. found that patients with HbA1c ≤7.0% had higher event free survival in the first 90 days but not at 2-year follow-up, suggesting an interaction between postoperative response and peri-implantation HbA1c.[25] It is highly plausible that better glycemic control could improve CRT response in DM, which should be tested prospectively.

Intuitively, lead positioning with maximal lead separation should improve interventricular synchrony, based on studies that showed greater benefits with lateral or posterolateral lead placement and greater RV/LV lead separation.[26,27] Unlike previous studies, lead separation in our cohort was strongly associated with reduced CRT-response, but seen only in the highest quartile of interlead distance, which also had a correspondingly highest baseline LVESVI. These observations suggest that as the LV dilates progressively, it may reach a threshold where it becomes too stretched to undergo CRT-induced reverse remodeling. Interestingly, a larger proportion of patients in the highest quartile of lead separation were diabetic nonresponders, suggesting a possible role in this subgroup of patients.

The association of DM with long-term survival has been conflicting[10,12,13,23,24] with some studies suggesting the use of insulin rather than the diagnosis of DM predictive of poorer outcomes.[11,13,23] Higher mortality rates observed with insulin were attributed to hypoglycemic episodes and increased microvascular and macrovascular complications as a consequence of disease chronicity and severity in patients receiving insulin.[11,23] LVESV reduction as a marker of reverse remodeling was the best predictor of long-term survival amongst other clinical and echocardiographic parameters.[5] The extent of LVESV reduction correlated with increased likelihood of event-free survival in our study, with super-responders 73% less likely to have a primary event. By limiting the extent of reverse remodeling, DM may further contribute indirectly to adverse outcomes in addition to its intrinsic prognostic risk among HF patients.

The prevalence of CKD was twice higher with DM, along with other DM-associated microvascular and macrovascular complications. The REVERSE study reported a smaller magnitude of CRT response among patients with CKD and poorer prognosis with CKD in HF,[28] whereas a large real-world registry of CKD patients showed reduced mortality and HF-hospitalizations with CRT.[29] To the contrary, CKD did not diminish CRT response in our cohort, but is a competing cause of mortality and HF-hospitalizations as shown, with the risk of death correlating with worsening renal impairment. These observations would imply that whilst CKD patients still benefit from CRT, CKD may attenuate the clinical and probably cost-effectiveness of CRT.

There were several limitations to our study. The small sample size may have rendered the study underpowered to detect statistical differences in individual endpoints of the primary outcome. Less objective clinical endpoints such as NYHA status and 6-minute walk distance were not evaluated in this study. All-cause mortality was chosen rather than cardiovascular mortality as part of the composite endpoint as there is a very low rate of patients undergoing postmortem examination due to cultural barriers in Singapore. Hence, determination of the cause of death may be imprecise.

Taken in conjunction, the presence of DM is detrimental to the CRT recipient in several ways: first, by limiting the extent of reverse remodeling after CRT implantation; second, causing renal impairment which is an independent predictor of adverse outcomes; third through the increased incidence of microvascular and macrovascular complications and last, as an independent predictor of HF-hospitalizations and reduced survival.

Disclosures

The authors have no conflicts of interest to disclose.

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