EDITOR'S CHOICE

Difference in long-term clinical outcome after cardiac resynchronisation therapy between ischaemic and non-ischaemic aetiologies of heart failure

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ABSTRACT

Objective: To examine the impact of heart failure (HF) aetiology on long-term outcome after cardiac resynchronisation therapy (CRT).

Design: Prospective cohort study.

Setting: University hospital.

Patients: 119 patients (44% with ischaemic and 56% non-ischaemic aetiology) who underwent CRT.

Interventions: Clinical follow-up for 39 (24) months.

Main outcome measures: Cardiovascular mortality, HF and cardiovascular hospitalisation were compared by Kaplan-Meier curves between the two groups, followed by Cox regression analysis for prognostic predictor(s).

Results: 41 (34%) patients died, in whom cardiovascular causes were identified in 32 (27%) patients. The ischaemic group had a higher cardiovascular mortality (log-rank $\chi^2 = 4.293$, $p = 0.038$) and cardiovascular hospitalisation (log-rank $\chi^2 = 5.123$, $p = 0.024$) when compared with the non-ischaemic group, though no difference was found in HF hospitalisation (log-rank $\chi^2 = 0.019$, $p = 0.892$). At three months, left ventricular reverse remodelling occurred in 52% of the ischaemic group and 55% of the non-ischaemic group ($\chi^2 = 0.128$, $p = 0.720$). By Cox regression analysis, ischaemic aetiology and absence of reverse remodelling at three months were independent predictors of cardiovascular mortality (HR = 2.698, $p = 0.032$; HR = 3.541, $p = 0.030$) and cardiovascular hospitalisation (HR = 1.905, $p = 0.015$; HR = 2.361, $p = 0.004$). Furthermore, these two factors had an incremental value in predicting cardiovascular mortality when compared with either alone (left ventricular reverse remodelling, log-rank $\chi^2 = 10.275$ vs 6.311, $p = 0.05$; Ischaemic aetiology, log-rank $\chi^2 = 10.275$ vs 4.293, $p<0.05$).

Conclusion: Ischaemic aetiology of HF is an independent predictor of higher cardiovascular mortality and hospitalisation after CRT. This may implicate the progressive nature of coronary heart disease leading to a worse outcome despite similar short-term benefits of CRT.

Cardiac resynchronisation therapy (CRT) is an established treatment for patients with advanced heart failure (HF) who have electromechanical delay. Its beneficial effects on cardiac function, exercise capacity, quality of life, left ventricular (LV) reverse remodelling and long-term prognosis, including mortality and cardiovascular hospitalisation, have been confirmed in large clinical trials.[1–7] In the MIRACLE study, a lesser degree of reduction of LV volumes at one-year follow-up was observed in ischaemic than non-ischaemic patients.[8 9] However, it is not known whether there is any attributable difference in aetiology on long-term prognosis after CRT. In the CARE-HF study, when compared with ischaemic patients, non-ischaemic patients showed a greater extent of reduction in the estimated absolute risk for death or unplanned hospitalisation after receiving CRT, though aetiology of HF was not found to be an independent predictor for the outcome measure of CRT.[10] On the other hand, early LV reverse remodelling occurring at 3–6 months after CRT detected by echocardiography has been shown to herald the improvement of long-term survival, apart from symptomatic improvement.[3–5 8 11] Therefore, the main objective of the present study was to compare the long-term clinical outcome in patients with ischaemic and non-ischaemic aetiologies of HF after CRT. This will be tested in the multivariate model to examine if HF aetiology is an independent determinant of prognosis on top of short-term LV reverse remodelling.

METHODS

Patients

This study prospectively enrolled 119 patients with advanced HF (mean age 65 (SD 13) years, 75% men) who underwent CRT and were followed up for at least three months. Four patients died (one refractory HF, two sudden cardiac death (SCD), and one pneumonia) before the three-month follow-up, and were excluded from analysis as there was no echocardiographic follow-up data. The inclusion criteria for CRT included refractory HF despite optimal medical therapy, LV systolic dysfunction with ejection fraction <40%, and QRS duration >120 ms. Coronary heart disease was confirmed in 52 patients (44%), who had past history of myocardial infarction and/or positive findings on coronary angiogram or underwent percutaneous coronary intervention. For the other 67 patients (56%), non-ischaemic aetiology was confirmed by the normal coronary angiography. CRT devices were implanted as previously described.[3 12] Only five patients in the ischaemic group and four patients in the non-ischaemic group had biventricular defibrillator devices, while all the others received biventricular pacemakers. Echocardiographic study with tissue Doppler imaging (TDI) and clinical assessment were performed serially before device implantation and at three months after CRT. Patients who had a decrease in LV end-systolic volume (LVESV) of ⩾15% were defined as responders of LV reverse remodelling, and the others were classified as non-responders. The study protocol was approved by the ethics

Table 1 Baseline clinical and echocardiographic characteristics in heart failure patients secondary to ischaemic and non-ischaemic aetiologies

Parameters	Ischaemic (n = 52)	Non-ischaemic (n = 67)	p Value
Age (years)	65 (12)	64 (13)	0.699
Gender, % of patients			
Male	75	73	$\chi^2 = 0.002$
Female	25	27	p = 0.962
NYHA class, % of patients			
III	87	85	$\chi^2 = 0.003$
IV	13	15	p = 0.950
Quality of life score	30 (20)	31 (22)	0.830
6-Minute hall-walk distance (metres)	306 (113)	338 (107)	0.135
Heart rhythm, % of patients			
Sinus	90	88	$\chi^2 = 0.180$
Atrial fibrillation	10	12	p = 0.671
LVEDV (cm^3)	181 (76)	183 (66)	0.894
LVESV (cm^3)	134 (65)	138 (62)	0.726
LV ejection fraction (%)	27.2 (6.8)	26.4 (9.2)	0.604
QRS duration (ms)	131 (31)	137 (37)	0.354
Ts-SD (ms)	35 (12)	39 (14)	0.142

LV, left ventricular; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; NYHA, New York Heart Association; Ts-SD, standard deviation of the time to peak myocardial systolic velocity among the 12 left ventricular segments.

committee of the university and written informed consent was obtained from all patients.

Echocardiography

Echocardiography with TDI was performed (Vivid 7, Vingmed-General Electric, Horten, Norway) at baseline and three months after CRT. The atrioventricular interval was optimised by Ritter's method at day 1 after implantation to reach maximal transmitral diastolic filling.[13] The LV volumes and ejection fraction were assessed by biplane Simpson's equation using the apical four-chamber and two-chamber views where the length of the ventricular image was maximised. At least three consecutive beats of sinus rhythm and 5–7 beats of atrial fibrillation were measured and the mean was calculated. LV sphericity indices, myocardial performance index and mitral regurgitation were measured as previously described.[3 14] Furthermore, in the ischaemic group, wall motion score of individual LV segment was assessed (1 = normal; 2 = hypokinetic; 3 = akinetic; 4 = dyskinetic; 5 = aneurysm) and hence wall motion score index of the 16 segments was calculated as previously described.[15]

Two-dimensional colour TDI was performed in the apical views (apical four-chamber, two-chamber and three-chamber views) and myocardial velocity curves were reconstituted (EchoPac PC, version 6.1.0, Vingmed-General Electric, Horten, Norway). The time to the peak systolic velocity at ejection phase was measured in each segment and systolic dyssynchrony was defined by calculating the dyssynchrony index (Ts-SD)—that is, the standard deviation of time to the peak systolic velocity among the 12 LV segments.[3 16–18]

Assessment of cardiovascular events during long-term follow-up

All patients were followed up regularly (every two to three months) in the HF clinic, with clinical assessment, ECG recording and device interrogation to ensure biventricular pacing was maintained. The occurrence of cardiovascular events was adjudicated by two cardiologists blinded to the echocardiographic findings. Only those events happening after the three-month follow-up were included in the analyses, in order to investigate the impact of short-term changes in cardiac function or clinical status on long-term prognosis. The cause of death was ascertained by reviewing the clinical record and investigation results, report of the close relatives and postmortem findings. Among cardiovascular hospitalisation and/or death, HF was defined according to clinical symptoms (limitation of activity, fatigue, and dyspnoea or orthopnoea), physical signs (oedema, elevated jugular venous pressure, rales or third heart sound with gallop) or radiological evidence of pulmonary congestion.[19] The diagnosis of acute coronary syndrome was based on the current guidelines, including the presence of typical chest pain or discomfort, and elevation of cardiac enzymes such as creatine kinase-MB or troponin T and compatible ECG changes. In addition, cardiac arrhythmia, SCD and cerebrovascular accident were also included in cardiovascular causes of hospitalisation and/or death.

Statistical analysis

Results are presented as mean (SD). The paired or unpaired t test was used when appropriate in the comparison of continuous variables between baseline and three months, or between the ischaemic and non-ischaemic groups. The Wilcoxon or Mann-Whitney test was adopted for the comparison of ordinal parameters accordingly. Comparison of proportions was performed using Pearson χ^2 analysis. Multivariate logistic regression was used to find the independent predictor(s) for short-term LV reverse remodelling. Differences in long-term event-free survival between the ischaemic and non-ischaemic groups were compared by Kaplan-Meier survival curves where the log-rank χ^2 values were presented. Cox regression multivariable survival analysis was used to evaluate potential predictor(s) for cardiovascular mortality. A p value <0.05 was considered statistically significant.

RESULTS

The baseline demographic, clinical and echocardiographic parameters are shown in table 1. These parameters were all comparable between ischaemic and non-ischaemic groups without statistical differences. In addition, the wall motion score index was 2.0 (0.3) (range 1.4–2.8) in the ischaemic patients. On the first day after CRT, the optimised

Table 2 Comparison of reverse remodelling and changes in other echocardiographic and clinical parameters at three months after cardiac resynchronisation therapy between ischaemic and non-ischaemic patients

Parameters	All patients (n = 119)	p Value	Ischaemic (n = 52)	p Value	Non-ischaemic (n = 67)	p Value	Ischaemic vs non-ischaemic p Value
ΔLVEDV (cm^3)	−21 (31)	<0.001	−17 (27)	<0.001	−25 (33)	<0.001	0.169
ΔLVESV (cm^3)	−26 (30)	<0.001	−21 (26)	<0.001	−31 (33)	<0.001	0.082
ΔLV ejection fraction (%)	7.4 (6.9)	<0.001	5.9 (6.0)	<0.001	8.6 (7.4)	<0.001	0.032
ΔSphericity index, end-diastole	0.09 (0.23)	<0.001	0.06 (0.22)	0.060	0.11 (0.23)	0.001	0.288
ΔSphericity index, end-systole	0.13 (0.29)	<0.001	0.10 (0.28)	0.018	0.16 (0.31)	<0.001	0.294
ΔMitral regurgitation (%)	−10 (17)	<0.001	−8 (16)	0.003	−12 (17)	<0.001	0.219
ΔMPI	−0.15 (0.26)	<0.001	−0.12 (0.29)	0.016	−0.16 (0.24)	<0.001	0.348
ΔLV filling time (ms)	59 (147)	<0.001	38 (125)	0.057	76 (161)	0.001	0.204
ΔQuality of life score	−9 (22)	<0.001	−7 (18)	0.015	−11 (24)	<0.001	0.267
Δ6-minute hall-walk distance (metres)	32 (81)	<0.001	22 (93)	0.141	40 (70)	<0.001	0.256
ΔNYHA class, % of patients							
Improvement of two classes	10		8		12		
Improvement of one class	63	<0.001	56	<0.001	67	<0.001	0.092
No improvement	24		34		18		
Deterioration of one class	3		2		3		

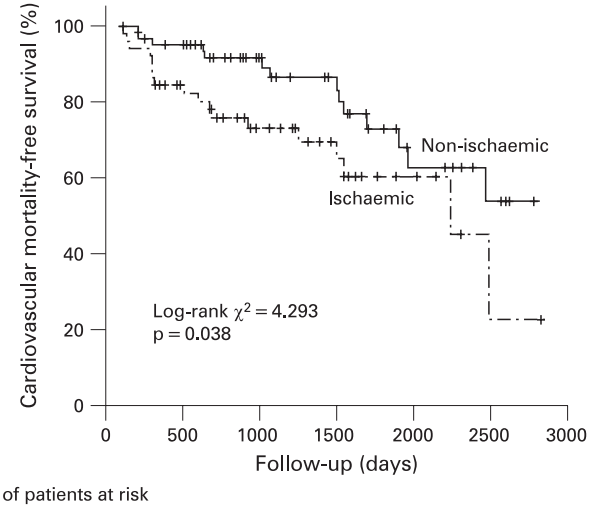
Δ, changes between three-month follow-up and baseline; LV, left ventricular; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; MPI: myocardial performance index; NYHA, New York Heart Association.

atrioventricular interval was 97 (26) ms, which was not different between ischaemic and non-ischaemic groups (95 (29) vs 98 (23) ms, p = 0.559).

Short-term reverse remodelling and its relation with systolic dyssynchrony and ischaemic or non-ischaemic aetiology

At three months after CRT, LV reverse remodelling was achieved with a significant improvement in LV function and geometry, as well as clinical status (all p<0.001) (table 2). Sixty-four patients (54%) were found to be the volumetric responders, and the prevalence in the ischaemic group and non-ischaemic group was 52% and 55%, respectively ($\chi^2 = 0.128$, p = 0.720). In the non-ischaemic group, all the measured clinical and echocardiographic parameters were observed to be improved. Similarly, favourable improvement was evident in most of the parameters in the ischaemic group, with the exception of end-diastolic sphericity index, LV filling time and 6-minute hall-walk distance. Moreover, in the ischaemic group, the wall motion score index was similar between the volumetric responders (n = 27) and non-responders (n = 25) (2.0 (0.3) vs 2.1 (0.3), p = 0.548). When the extent of improvement was compared between the two aetiological groups, LVESV had a trend of greater reduction in the non-ischaemic group (p = 0.082), which gave rise to a greater increase in LV ejection fraction than in the ischaemic group (p = 0.032) (table 2).

In the multivariate logistic regression analysis model for the prediction of short-term LV reverse remodelling response, severity of systolic dyssynchrony at baseline as measured by Ts-SD was the only independent covariate (RR = 1.191, 95% CI: 1.119 to 1.267; p<0.001). Other factors including ischaemic versus non-ischaemic aetiology of HF, LV ejection fraction, QRS duration, age, gender and other clinical parameters were not significant. While Ts-SD ⩾33 ms was adopted to define a significant dyssynchrony,[16 20] it was observed in 60% of the ischaemic group and 64% of the non-ischaemic group ($\chi^2 = 0.256$, p = 0.611).



Number of patients at risk

Non-ischaemic	67	59	36	27	12	6
Ischaemic	52	39	24	14	6	1

Figure 1 Kaplan-Meier survival analysis showing a higher cardiovascular mortality in the ischaemic than non-ischaemic group after cardiac resynchronisation therapy.

Clinical outcome of patients during long-term follow-up

The mean duration of follow-up was 39 (24) months (range 3–92 months). One hundred and three patients (87%) were followed up for more than one year, while ischaemic and non-ischaemic patients had a comparable period of follow-up (36 (22) vs 43 (25) months, p = 0.128). Forty-one patients (34%) died, in whom cardiovascular causes were identified in 32 (27%), including HF in 12, SCD in 12, acute coronary syndrome in two, cardiogenic shock in one, ventricular fibrillation in two and cerebrovascular accident in three patients. The number of deaths was 22 (42%) in the ischaemic group, with cardiovascular deaths in 18 (35%) patients. These figures were 19 (28%) and 14 (21%), respectively, in the non-ischaemic group. In the ischaemic group the cardiovascular causes of death was HF in five, SCD in eight, acute coronary syndrome in two, ventricular fibrillation in one and cerebrovascular accident in two patients, and the corresponding figures were seven, four, 0, one, one in the non-ischaemic group, plus cardiogenic shock in one patient.

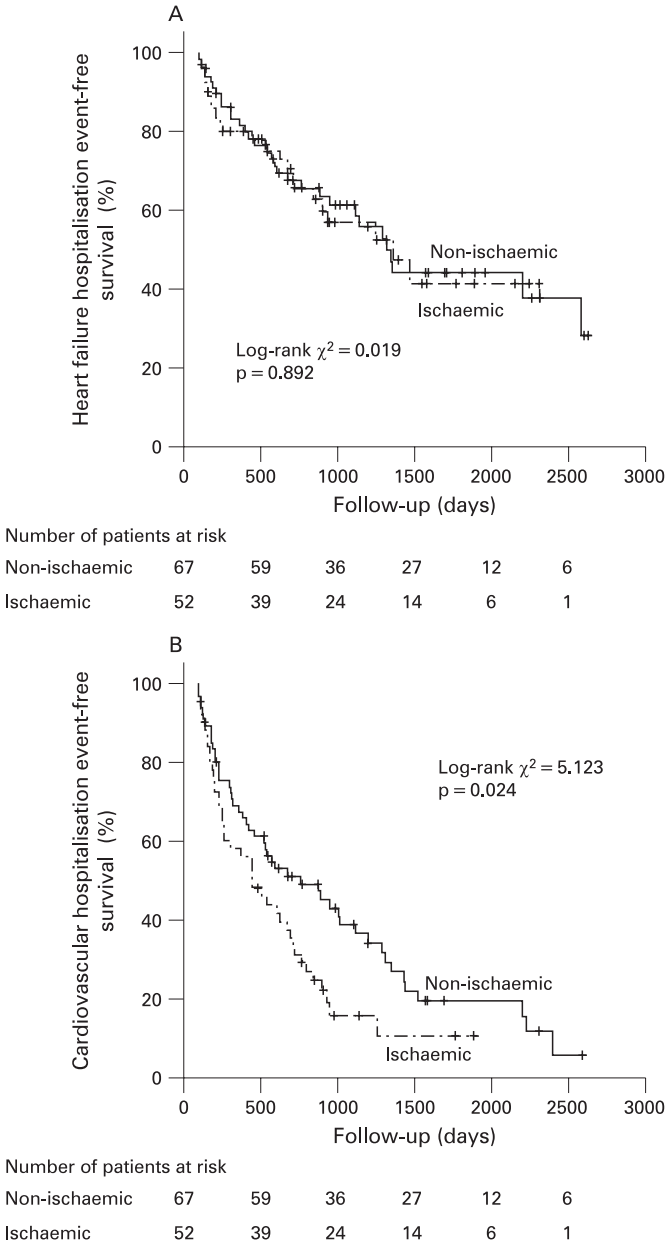


Figure 2 Kaplan-Meier analysis for (A) heart failure (HF) hospitalisation event-free survival and (B) cardiovascular hospitalisation event-free survival that compared between the ischaemic and non-ischaemic groups. The ischaemic group had a lower cardiovascular hospitalisation event-free survival while the HF hospitalisation event-free survival was comparable between the two groups.

In the ischaemic group, 18 patients who had a cardiovascular death showed a trend of higher wall motion score index than those survived (2.1 (0.3) vs 2.0 (0.3), p = 0.075), though it was not statistically significant. In Kaplan-Meier survival analysis, it was demonstrated that patients with ischaemic aetiology had a significantly higher cardiovascular mortality (log-rank $\chi^2 = 4.293$, p = 0.038) (fig 1), as well as all-cause mortality (log-rank $\chi^2 = 3.910$, p = 0.048) during long-term follow-up than those with non-ischaemic aetiology.

During the long-term follow-up, 54 patients were hospitalised for fatal and non-fatal congestive HF, which included 23 patients (44%) in the ischaemic group and 31 patients (46%) in the non-ischaemic group (p = 0.992). There was no difference in HF event-free survival between the two groups by Kaplan-Meier survival analysis (log-rank $\chi^2 = 0.019$, p = 0.892) (fig 2A). Altogether there were 89 patients admitted for cardiovascular causes during long-term follow-up, with 41 patients (79%) in the ischaemic group and 48 patients (72%) in the non-ischaemic group (p = 0.220). However, the Kaplan-Meier survival analysis showed a significantly lower cardiovascular hospitalisation event-free survival in the ischaemic group when compared with the non-ischaemic group (log-rank $\chi^2 = 5.123$, p = 0.024) (fig 2B).

Further investigation was performed by Kaplan-Meier survival analysis to examine the time course of changes in HF as well as cardiovascular hospitalisation event-free survival in the first, second and third-year follow-up in both ischaemic and non-ischaemic groups. It was observed that there was no difference in both event rates in the first-year follow-up between ischaemic and non-ischaemic groups. However, a significantly lower cardiovascular hospitalisation event-free survival was observed in the ischaemic group in the second and third-year follow-up (table 3).

Predictors of long-term event-free survival

By using Cox multivariate regression analysis to predict long-term cardiovascular event-free survival, a group of covariates were selected into the model as shown in table 4. These included clinical characteristics, aetiology of HF, as well as the three-month changes in echocardiographic parameters and clinical status. It was shown that ischaemic aetiology and the absence of short-term LV reverse remodelling at three months were independent predictors of cardiovascular mortality during long-term follow-up. Moreover, these two factors were found predictive of cardiovascular hospitalisation while the lack of LV reverse remodelling was the only predictor of HF hospitalisation (table 4).

Since ischaemic aetiology and the lack of LV reverse remodelling at three months appeared to be independent

Table 3 Comparison of the heart failure (HF) and cardiovascular hospitalisation event-free survival in ischaemic and non-ischaemic patients after cardiac resynchronisation therapy at the end of first, second and third-year follow-up

Hospitalisation event-free survival (% of patients)	Ischaemic (n = 52)	Non-ischaemic (n = 67)	Ischaemic vs non-ischaemic
First-year follow-up:			
HF related	74%	80%	log-rank $\chi^2 = 1.053$, p = 0.305
Cardiovascular related	51%	61%	log-rank $\chi^2 = 2.316$, p = 0.128
Second-year follow-up:			
HF related	65%	68%	log-rank $\chi^2 = 0.432$, p = 0.511
Cardiovascular related	27%	49%	log-rank $\chi^2 = 6.150$, p = 0.013
Third-year follow-up:			
HF related	54%	67%	log-rank $\chi^2 = 2.729$, p = 0.099
Cardiovascular related	10%	44%	log-rank $\chi^2 = 11.443$, p = 0.001

Table 4 Prediction of long-term cardiovascular events using multivariate Cox regression analysis

	Cardiovascular mortality		HF hospitalisation		Cardiovascular hospitalisation	
Parameters	**HR (95% CI)**	**p Value**	**HR (95% CI)**	**p Value**	**HR (95% CI)**	**p Value**
Age	1.029 (0.995 to 1.064)	0.099	1.022 (0.998 to 1.046)	0.079	1.012 (0.994 to 1.032)	0.196
Female gender	1.498 (0.589 to 3.805)	0.396	1.565 (0.778 to 3.147)	0.209	1.242 (0.710 to 2.175)	0.448
Sinus rhythm	0.409 (0.146 to 1.149)	0.090	1.637 (0.568 to 4.715)	0.361	0.932 (0.452 to 1.919)	0.848
Ischaemic aetiology	2.698 (1.092 to 6.667)	0.032	1.216 (0.638 to 2.318)	0.552	1.905 (1.135 to 3.196)	0.015
ΔLVESV <15%	3.541 (1.131 to 11.079)	0.030	2.385 (1.106 to 5.142)	0.027	2.361 (1.314 to 4.243)	0.004
ΔLV ejection fraction <5%	1.155 (0.436 to 3.059)	0.772	1.014 (0.490 to 2.098)	0.969	0.750 (0.421 to 1.334)	0.327
ΔQuality of life score	1.000 (0.980 to 1.021)	0.967	1.005 (0.989 to 1.022)	0.532	1.008 (0.996 to 1.021)	0.195
ΔNYHA class	1.084 (0.510 to 2.300)	0.834	1.013 (0.585 to 1.754)	0.963	1.141 (0.744 to 1.750)	0.546

CI, confidence interval; HF, heart failure; HR, hazard ratio; LV, left ventricular; LVESV, left ventricular end-systolic volume; MPI: myocardial performance index; NYHA, New York Heart Association.

long-term prognosticators of CRT, patients were divided further into four groups with respect to the status of short-term LV reverse remodelling and aetiology of HF. This included non-ischaemic patients with reverse remodelling (group 1, n = 37), non-ischaemic patients without reverse remodelling (group 2, n = 30), ischaemic patients with reverse remodelling (group 3, n = 27) and ischaemic patients without reverse remodelling (group 4, n = 25). The cardiovascular mortality compared by Kaplan-Meier survival analysis was shown to be different among these groups (log-rank $\chi^2 = 10.275$, $p = 0.016$) (fig 3). Further analysis revealed that the non-ischaemic patients with reverse remodelling had the lowest cardiovascular mortality (group 1 vs group 2: log-rank $\chi^2 = 4.993$, $p = 0.025$; group 1 vs group 3: log-rank $\chi^2 = 4.513$, $p = 0.034$; group 1 vs group 4: log-rank $\chi^2 = 10.332$, $p = 0.001$). The differences among the other three groups were not statistically significant.

Furthermore, the absence of LV reverse remodelling and ischaemic aetiology have incremental prognostic values. Combining both parameters became significantly superior in predicting cardiovascular mortality when compared with either single factor (fig 4).

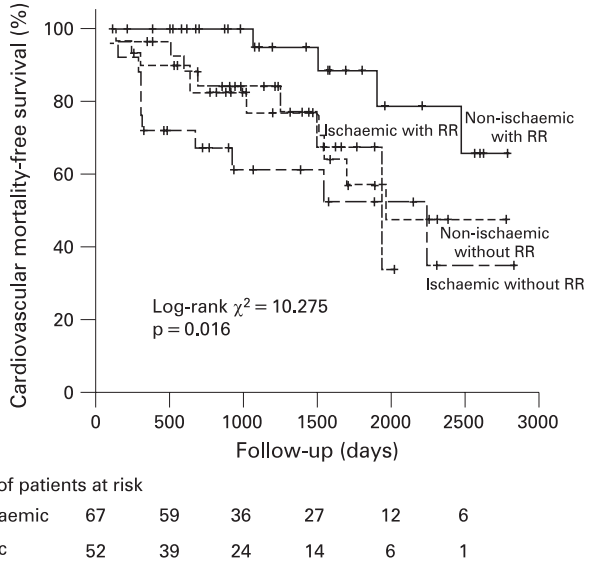


Figure 3 Comparison of cardiovascular mortality by Kaplan-Meier survival analysis among the four groups of patients—non-ischaemic patients with left ventricular reverse remodelling (RR) (n = 37), non-ischaemic patients without RR (n = 30), ischaemic patients with RR (n = 27) and ischaemic patients without RR (n = 25). The non-ischaemic patients with RR had the best cardiovascular death event-free survival.

DISCUSSION

This study illustrated the impact of HF aetiology on long-term prognosis after CRT. During the follow-up with a mean duration of over three years, ischaemic patients were associated with a significantly higher cardiovascular event rate than non-ischaemic patients. Interestingly, the difference in cardiovascular hospitalisation became more apparent when patients were followed up for longer periods, in particular after two years. Furthermore, the prognostic importance of HF aetiology appeared to be independent of short-term LV reverse remodelling.

Ischaemic aetiology is associated with worse long-term clinical outcome after CRT

In our study, ischaemic patients were found to have higher cardiovascular mortality and lower cardiovascular event-free survival during the long-term follow-up after CRT. It is intriguing to note that cardiovascular hospitalisation event-free survival was not different in the first year between the two aetiological groups, though the survival curve continued to diverse over time and therefore in the second and third year, the event-free survival became significantly lower in the ischaemic group. From our observation, we postulate that CRT improves the uncoordinated contraction in both ischaemic and non-ischaemic aetiologies of

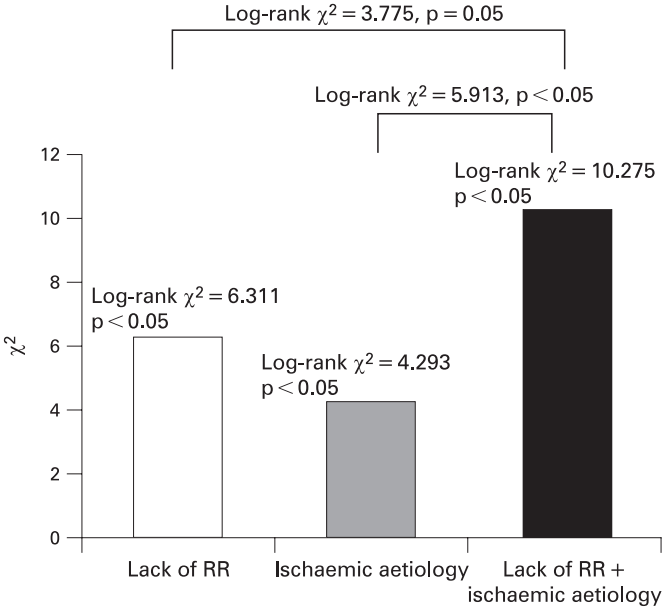


Figure 4 Incremental predictive value of combining the lack of early left ventricular reverse remodelling (RR) and ischaemic aetiology for cardiovascular mortality on top of the individual predictor.

HF when significant systolic dyssynchrony is present. This leads to an early improvement of haemodynamics, increase in systolic function and favourable LV reverse remodelling which heralds the improvement of long-term prognosis leading to a lower mortality and a lower cardiovascular hospitalisation event rate. On the other hand, CRT is not a treatment for myocardial ischaemia itself. As a result, when the underlying coronary heart disease progresses, it might lead to the subsequent development of fatal and non-fatal cardiovascular events, which include acute coronary syndrome, arrhythmia and so on. This effect will only be revealed when patients were followed up for a long period of time.

In the current study, although the ischaemic group showed a trend of lesser degree of improvement in LVESV at three months, the volumetric responder rate was similar between the two groups by using a reduction of LVESV ⩾15%. Therefore, the impact of heart failure aetiology on long-term prognosis may operate independently of whether short-term LV reverse remodelling has occurred or not. In fact, the InSync/InSync-ICD Italian Registries observed a significantly higher all-cause mortality in ischaemic patients during three-year follow-up even when CRT benefits on clinical symptoms and echocardiographic parameters persisted.[21] In the MIRACLE study, LV reverse remodelling occurred at six months and persisted in both ischaemic and non-ischaemic cardiomyopathy at 12 months, though this occurred to a lesser degree in ischaemic patients.[9] It is not clear, however, from the study whether such inferiority in medium-term cardiac response would result in a worse long-term prognosis in ischaemic aetiology of HF. The recent analysis of CARE-HF failed to identify ischaemic aetiology as an independent predictor for worse prognosis after CRT.[10] Nevertheless, the study found a higher estimated absolute risk in ischaemic than in non-ischaemic patients (0.63 vs 0.41) for death from any cause or unplanned hospitalisation for cardiovascular events.[10]

HF aetiology and short-term LV reverse remodelling after CRT

Although previous studies have demonstrated short-term LV reverse remodelling response after CRT,[7–9 11] the present study observed that there were no significant differences between ischaemic and non-ischaemic cardiomyopathy, in both the extent of changes of LV volume and the proportion of responders. Of note, there was also no difference in the severity of baseline dyssynchrony between ischaemic and non-ischaemic groups, as shown by the dyssynchrony index (Ts-SD), a finding consistent with our pervious observations.[17]

Difference in LV reverse remodelling response with respect to different aetiologies had been reported in previous studies. In the MIRACLE study, it has been suggested that non-ischaemic patients had a greater degree of reverse remodelling with a higher ejection fraction than ischaemic patients after CRT for 6-12 months.[8 9] Our current study also found that the gain in ejection fraction is greater in the non-ischaemic group. This is in contrast to the study by Molhoek *et al* who did not report any difference in ejection fraction at six-month follow-up.[22] On the other hand, previous studies did not provide insight into whether there was any difference in the severity of systolic dyssynchrony. As previous studies also demonstrated that baseline dyssynchrony was a major determinant of short-term reverse remodelling response, the observed difference in response between the two aetiologies in various studies could have been the result of the difference in severity of systolic dyssynchrony.[17]

Our current study also illustrated the independent and incremental values of HF aetiology and short-term LV reverse remodelling response on long-term prognosis after CRT. Therefore, the best clinical outcome occurs in non-ischaemic patients who have also shown early LV reverse remodelling at three months after CRT.

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Competing interests: None.

Ethics approval: Obtained.

Patient consent: Written informed consent was obtained from all patients.

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