Impact of cardiac resynchronisation therapy on burden of hospitalisations and survival: a retrospective observational study in the Northern Region of New Zealand

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ABSTRACT
Objective Cardiac resynchronisation therapy (CRT) devices have been shown to improve heart failure (HF) symptoms, survival and improve quality of life (QoL). We evaluated the overall impact of CRT on recurrent hospitalisations and survival in real-world patients with HF.

Design Retrospective observational study.

Setting Northern region of New Zealand.

Participants Patients with HF who underwent CRT device implantation in between 2008 and 2014 were followed up for 1 year.

Interventions CRT.

Primary and secondary outcomes measured Survival, all-cause hospitalisations, length of stay, from which days alive and out of hospital (DAOH) were calculated.

Results 177 patients were included, of whom eight died (4.5%) within 1 year of follow-up. Pre-CRT implantation, 83% of all patients had been hospitalised for a total 248 hospitalisation events. Following CRT, 47 patients (27%) were readmitted to hospital within 1 year (total of 98 admissions; p<0.01 compared with pre-device implant). Length of hospital stay was significantly shorter than in the year prior to CRT implantation at a median of 4 (IQR 3.5–10.5) days (p<0.01). An increase in the median number of DAOH was observed from 362 (IQR 355–364) to 365 (IQR 364–365) (p<0.01) after CRT implant. The improvement in DAOH was seen regardless of gender and type of CRT devices. Greater DAOH was also seen in those with non-ischaemic cardiomyopathy and Caucasians.

Conclusion After CRT implant, patients with HF have greater DAOH with reduction of total hospitalisation and fewer hospital days. These results support CRT devices use as a treatment option for appropriate HF patients. DAOH represents an easily measured, patient-centred endpoint that may reflect effectiveness of interventions in future CRT studies.

INTRODUCTION
Heart failure (HF) is a chronic and progressive condition. HF affects quality of life (QoL) more profoundly than many other chronic diseases.1 Symptom burden, the disabling consequences of HF and the medication regimen (including side effects) all impact on the daily life of HF patients and contribute to impaired QoL.2 As the disease progresses, HF patients show a decline in QoL with increasingly frequent hospitalisations.

Cardiac resynchronisation therapy (CRT) devices have been shown to positively influence symptoms and improve QoL in selective group of patients with HF with left bundle branch block (LBBB).3 An analysis from the Cardiac Resynchronization–Heart Failure (CARE-HF) trial showed that CRT improved long-term QoL and survival in HF patients.4 At baseline, HF patients had a substantially lower mean European Quality of Life-5-Dimensions (EQ-5D) score than a representative age-matched general population (0.60 vs 0.78).4 Three months after randomisation, patients who received CRT had significant improvement in mean EQ-5D score (mean difference 0.08, p<0.0001) compared with those assigned to medical therapy alone. CRT patients had a mean reduction in Minnesota Living with Heart Failure Questionnaire (MLHFQ) score of 10.6 points (p<0.001) at 3 months and this improvement was maintained...
throughout the study. These data support that CRT, in addition to medical therapy, in appropriate patients with HF improves symptoms and QOL that persist for several years.

Objective
The aim of our study was to describe the burden of hospitalisations, using the ‘Days alive and out of hospital’ (DAOH) in HF patients implanted with CRT devices in the Northern Region of New Zealand. We also aimed to determine whether DAOH differs by type of CRT devices, aetiology of HF, gender or ethnicities.

Study design and population
This is a retrospective observational study. The study cohort consisted of consecutive patients implanted with CRT-capable devices between January 2008 to end of year 2014 in the Northern Region of New Zealand. All patients undergoing implantation of de novo CRT-pacemaker (CRT-P) and CRT-defibrillator (CRT-D), all upgrades from pacemakers to CRT-P or CRT-D, upgrades of implantable cardioverter defibrillators (ICD) to CRT-D using transvenous or epicardial left ventricular (LV) lead placement were included. The Northern Region of New Zealand is defined as the four northernmost District Health Board (DHB) areas. Patients undergoing CRT implantation who resided in the Auckland, Counties Manukau, Northland or Waitemata DHBs were included. The four DHBs in Northern Region serve 38% of the total New Zealand population with estimated 1.76 million people in this region. New Zealand has a government-funded health system with universal coverage for all New Zealand residents that includes both acute and elective secondary and tertiary services. Currently there is no health insurance coverage for CRTs in New Zealand. All CRT implantation and follow-up is provided for by the public sector. The indications for CRT-D and CRT-P were based on the published 2010 New Zealand guidelines (Box 1). All referrals for CRT were discussed by the northern region implanting electrophysiologists regarding suitability and appropriateness of CRT support.

Patient and public involvement
This study is based on existing health system data with no direct patient and public involvement.

Study design and data collection
Every New Zealander has a National Health Index (NHI) number, a unique identifier that is assigned to each person who uses health and disability support services in New Zealand. Hospitalisation data for all patients was assessed using the administrative data of Ministry of Health and National Minimum Datasets (NMDS) inpatient hospitalisation data via NHI linkage up to end of year 2015. All-cause mortality data were collected using New Zealand mortality collection and NMDS.

Hospitalisation data for all patients were assessed for a full year prior to implantation (CRT-D or CRT-P) and after implantation or till death at the end of follow-up. An admission was defined as a presentation to hospital requiring an overnight stay. Same day admissions were excluded to prevent influencing per admission length of stay. The total hospital days were calculated by adding the durations of each individual hospital admission to obtain stay. The total hospital days were calculated by adding the durations of each individual hospital stay to obtain total follow-up time.

Box 1 New Zealand Primary Implantable Cardioverter Defibrillator Implantation and Cardiac Resynchronisation Therapy Guidelines

Recommendations for primary ICD implantation in New Zealand:
- Patients with ICM at least 1 month after acute MI or a NICM present for at least 3 months.
- EF <30% measured ≥3 months after optimal heart failure treatment.
- NYHA class II or III.
- On maximal heart failure medications, including ACE inhibitors or angiotensin receptor blockers, beta-blockers and spironolactone as tolerated for at least 3 and preferably 6 months.
- No clinical symptoms or findings that would make them a candidate for a revascularisation procedure.
- At least 3 months remote from any revascularisation procedure.
- No associated disease with a likelihood of survival <18 months.
- Age ≥75 years.

Recommendations for cardiac resynchronisation therapy in New Zealand:
- EF ≥35% after ≥6 weeks of optimal heart failure treatment, with QRS duration >149 ms or is 120–149 ms with two additional criteria for dyssynchrony (aortic pre-ejection delay >140 ms, interventricular mechanical delay >40 ms or delayed activation of the posterolateral left ventricular wall).
- NYHA class III.
- No major cardiovascular event in the prior 6 weeks and be in sinus rhythm.
- No major comorbidity reducing survival <18 months or seriously impairing quality of life.
- EF, ejection fraction; ICD, implantable cardioverter defibrillator; ICM, ischaemic cardiomyopathy; MI, myocardial infarction; NICM, non-ischaemic cardiomyopathy; NYHA, New York Heart Association; EF, ejection fraction; ICD, implantable cardioverter defibrillator; ICM, ischaemic cardiomyopathy; MI, myocardial infarction; NICM, non-ischaemic cardiomyopathy; NYHA, New York Heart Association.
Figure 1 Examples of calculation of days alive and out of hospital.

(for instance 1 year, i.e., 365 days) they were assigned 360 DAOH (figure 1B). If a patient was admitted for 5 days, then rehospitalised for 3 days 90 days later then subsequently died at 110 days after their index hospitalisation, they were assigned 102 DAOH (figure 1C).

Statistical analysis
All calculations were performed using SPSS V.25.0 (IBM Software). Baseline characteristics were summarised either as mean and SD (age and QRS duration), median and interquartile range (IQR) or frequency with percentage depending on the nature of the data. Comparison of continuous data was performed using the two-sample t-test. Length of hospital stay and DAOH were expressed as mean, median and IQR and compared using the Wilcoxon rank-sum test and Mann-Whitney test. A multivariate linear regression model was used to evaluate association between DAOH and baseline patient characteristics. A two-sided p value <0.05 was considered statistically significant.

RESULTS
From 2008 to 2014, 177 patients were implanted with either CRT-D or CRT-P devices. Baseline characteristics of patients were shown in table 1: three-quarters of the patients were male and 81% Caucasians. CRT-D was the most common device implanted (82%). Patients were more likely to have non-ischaemic cardiomyopathy (NICM) (51%) with a mean left ventricular ejection fraction (LVEF) of 26%±8%. Twenty-six patients had permanent atrial fibrillation (AF) in whom 13 had had atrioventricular (AV) nodal ablation. Shown in table 2 are the baseline characteristics of patients who received CRT-P and CRT-D. In general, patients receiving CRT-P were older, more likely to be female Caucasians, have pacemaker-induced cardiomyopathy but better LVEF, higher prevalence of permanent AF and previous history of AV nodal ablation, and have smaller body habitus than those who received CRT-D. Follow-up data were available for all patients, and eight patients (4.5%) died within

| Table 1 Baseline characteristics of patients implanted with CRT | n=177 |
|---|---|
| Median age (years) (IQR) | 64.4 (57.5–70.6) |
| Gender | |
| Male (%) | 135 (76.3) |
| Female (%) | 42 (23.7) |
| Ethnicity (%) | |
| NZ European/other European | 143 (80.8) |
| Maori | 10 (5.6) |
| Pacific Island | 17 (9.6) |
| Asian | 7 (4) |
| Type of device | |
| CRT-P | 32 (18.1) |
| CRT-D | 145 (81.9) |
| Aetiology | |
| Ischaemic cardiomyopathy | 40 (22.6) |
| Non-ischaemic cardiomyopathy | 90 (50.8) |
| Pacing-induced cardiomyopathy | 32 (18.1) |
| Valvular heart disease | 6 (3.4) |
| Complex congenital heart disease | 2 (1.1) |
| Cardiac sarcoidosis | 4 (2.3) |
| Other causes | 3 (1.7) |
| Mean LVEF (%±SD) | 26.4±7.9 |
| NYHA functional class I/II/III | 18 (10%)/79 (45%)/80 (45%) |
| Median height (m) (IQR) | 1.74 (1.67–1.78) |
| Median weight (kg) (IQR) | 85.1 (75.8–96.8) |
| Median BMI (m/kg²) (IQR) | 28.3 (25.5–32.2) |
| Permanent AF (%) | 26 (15) |
| Paroxysmal AF (%) | 20 (11.3) |
| AV node ablation (%) | 13 (7.4) |
| Diabetes mellitus (%) | 42 (23.7) |
| Hypertension (%) | 47 (26.6) |
| QRS morphology (%) | |
| LBBB | 135 (76.3) |
| Paced | 42 (23.7) |
| Mean QRS duration (ms) | 176.3±25.2 |
| Median eGFR (mL/min/1.73m²) | 66 (54.5–85.5) |
| Stages of chronic kidney disease, n (%) | |
| 1 | 37 (20.9) |
| 2 | 84 (47.5) |
| 3 | 54 (30.5) |
| 4 | 2 (1.1) |

AF, atrial fibrillation; AV, atrioventricular; BMI, body mass index; CRT, cardiac resynchronisation therapy; CRT-D, CRT with defibrillator; CRT-P, CRT with pacemaker; eGFR, estimated glomerular filtration rate; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; NZ, New Zealand.
1 year (three were from HF deaths, and five from cardiovascular deaths attributable to myocardial infarction (MI) or cerebrovascular accidents).

**Hospitalisations**

Pre-CRT implantation, there were 248 hospitalisation events among 147 (83.1%) patients. This resulted in total of 1126 hospital days with a median length of hospital day of 7 (3.5–10.5). After excluding implant admission (ie, all contiguous admissions preimplant and postimplant date and included interhospital transfers and periods of rehabilitation after implant prior to first discharge home), the number of total admissions post-CRT implant decreased to 98 episodes in 47 (26.6%) patients after first discharge within the first-year follow-up (p<0.01). Total hospital days had decreased from 1126 to 605 with a relative 46% reduction in total bed days. Length of hospital day was also significantly shorter than in the year prior to CRT implantation at a median of 4 (2–6) (p<0.01).

**Days alive and out of hospital prior and after device implantation**

Table 3 showed the DAOH of the whole study cohort and according to gender, ethnicity, aetiology of HF and type of devices. An increase in the median number of DAOH was observed from 362 (355–364) to 365 (364–365) (p<0.01).
### Table 3  Hospital admissions pre-CRT and post-CRT implantation at 1 year according to gender, ethnicity, aetiology of heart failure and type of devices

| Characteristics | 1 year prior to implant | 1 year postimplant | P value |
|-----------------|------------------------|--------------------|---------|
| **Total cohort (n=177)** | | | |
| Total hospital admissions | 248 | 98 | <0.01 |
| Total patient admitted | 147 | 47 | <0.01 |
| Total hospital days | 1126 | 605 | <0.01 |
| Length of hospital stay (median (IQR) days) | 7 (3.5–10.5) | 4 (2–6) | 0.03 |
| DAOH (median (IQR)) | 362 (355–364) | 365 (364–365) | <0.01 |
| DAOD (mean±SD) | 358.6±8.4 | 354.7±44.8 | 0.24 |
| Number of deaths (%) | 0 | 8 (4.5) | not applicable |
| **Gender** | | | |
| **Male (n=135)** | | | |
| Total hospital admissions | 193 | 78 | <0.01 |
| Total patient admitted | 113 | 39 | <0.01 |
| Total hospital days | 889 | 396 | <0.01 |
| Length of hospital stay days (median (IQR) days) | 5 (2.5–7.5) | 4 (2–6) | 0.69 |
| DAOH (median (IQR)) | 362 (355–364) | 365 (363–365) | <0.01 |
| DAOD (mean±SD) | 358.4±8.6 | 354.5±45.7 | 0.15 |
| Number of deaths (%) | 0 | 6 (4.4) | not applicable |
| **Female (n=42)** | | | |
| Total hospital admissions | 55 | 20 | <0.01 |
| Total patient admissions | 34 | 8 | <0.01 |
| Total hospital days | 237 | 209 | <0.01 |
| Length of hospital stay (median (IQR) days) | 3.5 (2–5) | 7.5 (4–11) | 0.14 |
| DAOH (median (IQR)) | 363 (354.8–364) | 365 (365–365) | <0.01 |
| DAOD (mean±SD) | 359.4±7.8 | 355.5±42.4 | 0.39 |
| Number of deaths (%) | 0 | 2 (4.8) | not applicable |
| **Ethnicity** | | | |
| **NZ European/other European (n=143)** | | | |
| Total hospital admissions | 189 | 69 | <0.01 |
| Total patient admitted | 118 | 35 | <0.01 |
| Total hospital days | 813 | 389 | <0.01 |
| Length of hospital stay (median (IQR) days) | 3.5 (2–9) | 3 (1.5–4.5) | 0.28 |
| DAOH (median (IQR)) | 363 (357–364) | 365 (364–365) | <0.01 |
| DAOD (mean±SD) | 359.3±8.2 | 357.1±40.2 | 0.50 |
| Number of deaths (%) | 0 | 5 (3.5) | not applicable |
| **Maori (n=10)** | | | |
| Total hospital admissions | 21 | 12 | 0.26 |
| Total patient admitted | 10 | 4 | <0.01 |
| Total hospital days | 128 | 76 | 0.35 |
| Length of hospital stay (median (IQR) days) | 14.5 (7–21) | 10 (5–15) | 0.02 |
| DAOH (median (IQR)) | 350 (347.5–356) | 365 (346–365) | 0.39 |

Continued
after CRT implant. Postimplant, the patients had significantly more time out of hospital than they did in the year prior to implant. This increase in DAOH was seen for both men and women, Caucasians, patients with NICM and both patients with CRT-D and CRT-P. For Māori patients, CRT implant was associated with reduction in...
total patient admissions and length of hospital stay but not DAOH (table 3).

Influences of gender
At the time of implant, median age between men and women was similar (64.4 (57.2–70.8) vs 64.9 (59.2–69.7) years, p=0.89). There were more CRT-P devices implanted in women (28.6% vs 14.8%, p=0.04). There was no difference in total hospital admissions, total hospital days, length of hospital days and DAOH between gender prior to implant (table 4). Postimplant, women had lower total hospital days (209 vs 396, p=0.04) compared with men. However, the length of hospital day was longer in women compared with men (7.5 (4–11) vs 4 (2–6), p=0.03). There were no gender differences observed in DAOH.

Influences of type of devices
CRT-D devices were the most common devices implanted in our study cohort (81.9%). CRT-D patients have more admissions prior to implant (118 vs 29, p<0.01), and 38 (26.2%) of these patients had either survived a cardiac arrest or had occurrence of symptomatic ventricular arrhythmias (table 4). At 1-year follow-up, CRT-D patients continued to have more total hospital admissions (92 vs 6, p<0.01), total hospital days (589 vs 16, p=0.01) and shorter DAOH (p=0.04) compared with CRT-P patients. There were more deaths at follow-up in CRT-D group (8 vs 0, p<0.01).

Influence of aetiology of HF
Among the cohort of patients, half (50.8%) had underlying NICM and 22.6% had ICM. Patients with ICM were older (median age 66.1 (59.1–71.3) vs 62.8 (56.3–69.7), p=0.09) but this was not statistically significant. Six patients with ICM died within 1 year compared with two with NICM (15% and 2% respectively; p=0.01). At 1-year follow-up, NICM patients had less total hospital days (212 vs 297, p<0.01) compared with those with ICM but there was no difference between total hospital admissions, total patient admissions, length of hospital day and DAOH (table 4).

Influences of ethnicity
The majority of the patients were Caucasians (80.8%). Maori patients consisted of only a minority of CRT device recipients (5.6%). Prior to implant, Maori patients have longer length of hospital stay (14.5 (7–21) vs 3.5 (2–9) days, p<0.01) and shorter DAOH (350 (347.5–356) vs 363 (357–364), p<0.01) compared with Caucasians (table 4).

At 1-year follow-up, there was no difference between the groups in terms of total hospital admissions (p=0.06), total patient admissions (p=0.15), total hospital days (p=0.11), length of hospital stay (p=0.22) and DAOH (p=0.23) between the two groups (table 4).

Table 5 showed the results of multivariable linear regression that accounted for 20% of the variance in the difference between the DAOH prior and post CRT implant (adjusted R2=0.14, F (17,159)=2.35, p=0.030). A significant increase in DAOH was associated with higher QRS duration at implant among New York Heart Association (NYHA) class I patients (p=0.0065). Similarly, a significant reduction in DAOH was found for history of AF and ICM (p=0.0091).

DISCUSSION
We report here the burden of hospitalisations in a real-world cohort of patients with HF receiving CRT therapy. Prior to device implantation, the patients in our study had frequent hospitalisations. During 1-year post-CRT implantation, hospitalisations were reduced by two-thirds, length of hospital stay decreased and total bed days were virtually halved. Mortality rates were low and overall there was a significant increase in DAOH. Health-related QoL in patients with HF is an important outcome as it reflects the impact of HF on individual’s daily lives. NYHA classification has been used traditionally to assess functional status in patients with HF. Although simple, it is subject to interobserver variability, captures only a limited range of health status and is applied from a physician’s perspective instead of the patient’s. The MLHFQ is a commonly used standard assessment instrument in clinical practice. However, the MLHFQ does have limitations that include lack of responsiveness to clinical change and sensitivity when differentiating across different levels of HF symptom burden and objective measures of the functional capacity of the heart compared with NYHA and LVEF. The Kansas City Cardiomyopathy Questionnaire (KCCQ) is another self-administered, 23-item questionnaire that quantifies physical limitation, symptoms (frequency, severity and recent change over time), QoL, social interference and self-efficacy. KCCQ has been validated in stable and decompensated patients with HF, and its sensitivity was substantially greater than that of the MLHFQ and the 36-Item Short Form Health Survey questionnaires. The KCCQ score also provides significant incremental predictive ability over NYHA for HF outcomes.

Recurrent hospitalisations can adversely impact on QoL but assessing numbers or rates of admissions alone does not consider the overall burden of disease. DAOH could be used to measure QoL in patients with HF. It captures the number and duration of all hospitalisations as well as mortality, provides a readily comprehensible summary of treatment difference and therefore has the potential to add statistical power to detecting treatment differences. It also gives greater weight to the impact of survival: for example, if a patient has a short hospitalisation in week 1 because of worsening HF symptoms but survives and is not hospitalised for the remainder of their follow-up, they will have a greater DAOH. A recent study by Boriani et al reported the long-term ‘real world’ outcomes in patients with HF with ICDs and CRT-Ds devices using mortality, hospitalisations and DAOH. In this study, comorbidities were one of the key determinants of the DAOH. By reporting DAOH, this study has made it possible to assess
Table 4  Comparison of hospital admissions and DAOH pre-CRT and post-CRT implantation between gender, ethnicity, aetiology of heart failure and type of devices

|                         | Male (n=135) | Female (n=42) | P value |
|-------------------------|--------------|---------------|---------|
| Median age (IQR)        | 64.4 (57.2–70.8) | 64.9 (59.2–69.7) | 0.89    |
| Type of devices (%)     |              |               |         |
| CRT-P                   | 20 (14.8)    | 12 (28.6)     | 0.04    |
| CRT-D                   | 115 (85.2)   | 30 (71.4)     |         |
| Total hospital admissions prior | 193         | 55            | 0.4     |
| Total patient admissions prior | 113        | 34            | 0.42    |
| Total hospital days prior | 889        | 237           | 0.66    |
| Length of hospital days prior (median IQR) | 5 (2.5–7.5) | 3.5 (2–5) | 0.53 |
| DAOH prior (median IQR) | 362 (355–364) | 363 (345.8–364) | 0.52    |
| DAOH prior (mean±SD)    | 358.4±8.6    | 359.4±7.8     | 0.67    |
| Total hospital admissions post | 78          | 20            | 0.78    |
| Total patients admissions post | 39         | 8             | <0.01   |
| Total hospital days post | 396         | 209           | 0.04    |
| Length of hospital days post (median IQR) | 4 (2–6)     | 7.5 (4–11)   | 0.03    |
| DAOH after implant (median IQR) | 365 (363–365) | 365 (365–365) | 0.22 |
| DAOH after implant (mean±SD) | 354.5±45.7 | 355.5±42.4 | 0.89 |
| Number of deaths at 1 year follow-up (%) | 6 (4.4)      | 2 (4.8)       | 0.86    |

|                         | NZ European/other European (n=143) | Maori (n=10) | P value |
|-------------------------|-----------------------------------|--------------|---------|
| Median age (IQR)        | 65.5 (58.7–71.2)                  | 59.9 (55.2–66.2) | 0.17    |
| Type of devices (%)     |                                   |              |         |
| • CRT-P                 | 30 (21)                           | 2 (20)       | 0.88    |
| • CRT-D                 | 113 (79)                          | 8 (80)       |         |
| Total hospital admissions prior | 189         | 21            | 0.79    |
| Total patient admissions prior | 118       | 10            | <0.01   |
| Total hospital days prior | 813        | 128           | 0.68    |
| Length of hospital days prior (median IQR) | 3.5 (2–9) | 14.5 (7–21) | <0.01 |
| DAOH prior (median IQR) | 363 (357–364)                     | 350 (347.5–356) | <0.01  |
| DAOH prior (mean±SD)    | 359.3±8.2                          | 352.2±6.1    | 0.68    |
| Total hospital admissions post | 69         | 12            | 0.06    |
| Total patient admissions post | 35       | 4             | 0.15    |
| Total hospital days post | 389      | 76             | 0.11    |
| Length of hospital days post (median IQR) | 3 (1.5–4.5) | 10(5–15) | 0.22 |
| DAOH after implant (median IQR) | 365 (364–365) | 365 (346–365) | 0.23 |
| DAOH after implant (mean±SD) | 357.1±40.2 | 335.2±74.1  | 0.01    |
| Number of deaths at 1-year follow-up (%) | 5 (3.5)      | 1 (10)        | 0.18    |

|                         | ICM (n=40) | NICM (n=90) | P value |
|-------------------------|-----------|-------------|---------|
| Median age (IQR)        | 66.1 (59.1–71.3) | 62.8 (56.3–69.7) | 0.09    |
| Type of devices (%)     |          |             |         |
| CRT-P                   | 3 (7.5)  | 2 (2.2)     | 0.04    |
| CRT-D                   | 37 (92.5)| 88 (97.8)   |         |

Continued
the global burden of hospitalisation during follow-up, and enable us to summarise the absolute treatment effect of ICDs and CRT-Ds on mortality and morbidity.15 Assessing outcomes beyond survival is becoming increasingly important in an era where indications for CRT devices are expanding. DAOH puts emphasis on deaths occurring early in follow-up and captures the duration of all hospitalisations. In our study, patients implanted with CRT actually spent fewer days in hospital, with a reduction in total hospital bed-days over 1-year period (605 vs 1126 days, p<0.01). Therefore CRT, using these measures of impact, has the potential not only for significant patient benefit but also reducing hospital costs as a result of the reduction of total hospitalisation and hospital bed-days with a greater DAOH, ie, patients spent more time out of hospital alive.

We have shown that CRT implantation is associated with increase in DAOH regardless of gender and type of devices, consistent with previous studies that women derived similar benefits from CRT as men and CRT with or without ICD have major impact on morbidity and mortality.16–18 In our study, patients with NICM have less total hospitalisations, shorter length of hospital days and increased DAOH. NICM is a known predictor of better

| Table 4  | Continued |
|----------|-----------|-----------|
|          | ICM (n=40) | NICM (n=90) | P value |
| Total hospital admissions prior | 61 | 116 | 0.73 |
| Total patient admissions prior | 35 | 70 | <0.01 |
| Total hospital days prior | 298 | 487 | 0.41 |
| Length of hospital days prior (median (IQR)) | 6 (3–9) | 4.5 (2–7) | 0.09 |
| DAOH prior (median (IQR)) | 361 (354.3–364) | 363 (356.8–364) | 0.09 |
| DAOH prior (mean±SD) | 357.6±9.7 | 359.6±7.5 | 0.09 |
| Total hospital admissions post | 35 | 51 | 0.07 |
| Total patient admissions post | 13 | 27 | 0.58 |
| Total hospital days post | 297 | 212 | <0.01 |
| Length of hospital days post (median (IQR)) | 7 (3.5–10.5) | 3 (1.5–4.5) | 0.55 |
| DAOH after implant (median (IQR)) | 365 (360.8–365) | 365 (361.8–364) | 0.58 |
| DAOH after implant (mean±SD) | 337.1±69.7 | 356.3±40.3 | 0.58 |
| Number of deaths at 1-year follow-up (%) | 5 (12.5) | 2 (2.2) | <0.01 |

| CRT-D (n=145) | CRT-P (n=32) | P value |
|---------------|--------------|---------|
| Median Age (IQR) | 63.4 (56.8–69.2) | 69.3 (60.3–73.9) | 0.04 |
| Total hospital admissions prior | 200 | 48 | 0.99 |
| Total patient admissions prior | 118 | 29 | <0.01 |
| Total hospital days prior | 919 | 207 | 0.82 |
| Length of hospital days prior (median (IQR)) | 5 (2.5–7.5) | 4 (2–6) | 0.47 |
| DAOH prior (median (IQR)) | 363 (355–364) | 362 (355–364) | 0.47 |
| DAOH prior (mean±SD) | 358.7±8.5 | 358.5±8.4 | 0.47 |
| Total hospital admissions post | 92 | 6 | <0.01 |
| Total patient admissions post | 43 | 4 | <0.01 |
| Total hospital days post | 589 | 16 | 0.01 |
| Length of hospital days post (median (IQR)) | 4 (2–6) | 4 (2–6) | 0.06 |
| DAOH after implant (median (IQR)) | 365 (363–365) | 365 (365–365) | 0.04 |
| DAOH after implant (mean±SD) | 350.9±49.6 | 362±3.9 | 0.01 |
| Number of deaths at 1-year follow-up (%) | 8 (5.5) | 0 | <0.01 |

CRT, cardiac resynchronisation therapy; CRT-D, CRT with defibrillator; CRT-P, CRT with pacemaker; DAOH, days alive and out of hospital; ICM, ischaemic cardiomyopathy; NICM, non-ischaemic cardiomyopathy; NZ, New Zealand.
response to CRT, thus our findings are consistent with published data.19 20 In our study, there was no difference in total hospital days and length of stay post CRT implant in patients with ICM despite the reduction in hospitalisations. This could be explained by the fact that patients with ICM had more comorbidities (older, more cardiac arrest and lower LVEF). Patients with ICM have more vascular risk factors and therefore have high probabilities of staying in hospital for other interventions. This could also affect the total hospital days and length of stay. They also have more CRT-D devices implanted. Despite improvement in DAOH after implant, CRT-D patients still had more total hospital admissions, total hospital days and shorter DAOH compared with those with CRT-P. About 26% of these ICM patients with CRT-D had had a cardiac arrest or symptomatic ventricular arrhythmias. There is also cumulative evidence that implanting CRT-D devices is associated with a higher perioperative and postoperative risk of major complications compared with CRT-P.21 22 Almost 2/3 of CRT-P patients have pacemaker-induced cardiomyopathy. An upgrade to CRT can potentially prevent the reverse remodelling associated with chronic right ventricular pacing. Response to CRT further decreases the risk for ventricular arrhythmias, sudden cardiac death and all-cause mortality. All these factors likely account for the differences in DAOH between the two groups.

For Maori patients with HF, CRT implant was associated with reduction in total patient admissions and length of hospital stay but not DAOH (table 3). Compared with the Caucasian patients, the median length of hospital stay was longer and the median DAOH (p<0.01) was shorter prior to CRT implant. Post CRT implant, these were not statistically significant. Maori patients in generally are disproportionately represented in adverse health outcomes with higher rates of admission and mortality from HF when compared with the non-Maori population.23 However, the number of Maori patients with CRT in our study was small. Additional studies with a larger number of Maori patients are needed to determine if there are other unmeasured confounders that might contribute to ethnicity differences and outcomes in our population. Taking socio-economic factors into account in future studies, not only ethnicity, would also allow to clarify the reasons of such differences noted.

Two pairs of clinical variables were found with significant interactions: (1) NYHA class I symptoms and QRS duration at implant and (2) History of AF and ICM. A significant increase in DAOH was associated with higher QRS duration at implant among NYHA class I patients.

### Table 5  Results of a multiple regression analysis predicting difference between the days alive and out of hospital prior and post-CRT implant

| Variables                              | β  | SE  | P value |
|----------------------------------------|----|-----|---------|
| Age at implant                         | −0.01 | 0.34 | 0.97    |
| NZ European (reference non-European)   | −9.99 | 9.46 | 0.29    |
| Maori (reference non-Maori)            | 10.1  | 15.3 | 0.56    |
| Gender                                 | 2.03  | 8.08 | 0.80    |
| LVEF at implant                        | 0.07  | 0.46 | 0.87    |
| eGFR at implant                        | −0.32 | 0.20 | 0.11    |
| QRS Duration at implant                | 0.14  | 0.15 | 0.35    |
| ICM                                    | −3.76 | 12.3 | 0.76    |
| NICM                                   | 2.34  | 10.34| 0.82    |
| Type of devices                        | 10.55 | 11.96| 0.38    |
| Primary prevention                     | −11.54| 8.32 | 0.17    |
| NYHA class I (reference class II)      | 144.89| 60.97| 0.01    |
| NYHA class III (reference class II)    | 4.91  | 6.93 | 0.45    |
| History of AF                          | −3.38 | 8.81 | 0.70    |
| History of AV node ablation            | −5.87 | 13.68| 0.67    |
| History of AF*ICM                      | −43.46| 16.46| <0.01   |
| NYHA class I*QRS duration at implant   | 0.99  | 0.36 | <0.01   |

β, standardised coefficients beta; AF, atrial fibrillation; AV, atrioventricular; CRT, cardiac resynchronisation therapy; eGFR, estimated glomerular filtration rate; ICM; ischaemic cardiomyopathy; LVEF, left ventricular ejection fraction; NICM, non-ischaemic cardiomyopathy; NYHA, New York Heart Association; SE, coefficient SEs; NZ, New Zealand.
NYHA class I patients have minimal HF symptoms, therefore the chance of hospitalisation will be much reduced. QRS duration has been used as an enrolment criterion in multiple CRT clinical trials. Response to CRT seems to increase as the QRS duration becomes longer, with greatest benefit in QRS duration ≥150 ms. In the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) study, CRT-D was better than optimal HF therapy at all QRS durations, although the effect was greater with increasing QRS duration.\(^\text{17}\) In the CARE-HF study, CRT therapy was better than pharmacological therapy alone at all QRS durations, although the benefit was greater in those with a QRS duration ≥160 ms.\(^\text{16}\) Similarly, in Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT), the benefit of CRT-D compared with an ICD alone was confined to those with QRS duration ≥150 ms.\(^\text{24}\)

The multivariable analyses for prediction of DAOH demonstrated that history of AF and the presence of ICM was associated with lower DAOH. In our study, there was no difference in DAOH post CRT implant in patients with ICM despite the reduction in hospitalisations as these patients have more comorbidities with high probabilities of staying in hospital for other interventions. The benefits of CRT appear to be attenuated in patients with AF. They exhibit loss of AV synchronicity, a higher risk for insufficient CRT delivery because of uncontrolled ventricular rates, inappropriate ICD shocks, inadequate symptomatic improvement, repeated hospitalisation and increased mortality.\(^\text{25, 26}\) Furthermore, in patients with AF, phases of effective biventricular capture alternate with phases of competing AF rhythm, which causes spontaneous, fusion or pseudofusion beats.\(^\text{27}\) Such beats render the pacing counters inaccurate for assessing true biventricular capture beats. The combination of these two variables would result in lower DAOH.

HF adversely affects QoL in HF patients and results in significant morbidity and mortality.\(^\text{26}\) CRT has been shown in multiple studies to improve symptoms, QoL and survival in patients with HF who remain symptomatic despite optimal medical therapy, and who have LVEF ≤35% and LBBB with QRS width ≥120 ms.\(^\text{16, 17, 29}\) Although the mortality was low post-CRT implant in our study, it was still 4.5% at 1 year. CRT is an expensive therapy. Given the limited resources in New Zealand and the high upfront costs of CRT devices, identifying appropriate patients with HF most likely to benefit from a CRT device is essential.

**Limitations**

This was a single-centre, retrospective observational study with relatively low sample size. We have recently published trends of CRT therapy use for eligible patients with HF in New Zealand and the data suggests that there is a significant unmet clinical need for CRT implantation in the Northern Region.\(^\text{30}\) Affordability and capacity are of concern in this region. Considering current workforce, funding constraints and the conservative approach taken, the published 2010 New Zealand guidelines (box 1) have more restrictive recommendations for CRT. This could all result in the low sample size. Our data do not provide specific information on the type of hospitalisation (HF-related vs non-HF-related) prior and post CRT implantation and on the different aspects of non-hospital HF management such as outpatient HF clinics or the use of pharmacotherapy after discharge.

Our study has not included comparison between CRT-responders versus non-responders. There are a significant number of current issues that exist when assessing CRT response. Firstly, the CRT response definition is highly dependent on the criteria used to define the response.\(^\text{31}\) The response rates tend to be higher when clinical measures, such as subjective measurements, i.e, NYHA class, are used but are much lower when remodelling or outcome measurements are used.\(^\text{32}\) There is no consensus on the optimal timeline to assess response in clinical trials that involved CRT. Secondly, response criteria may vary greatly among investigators in different trials. Thirdly, multiple different factors between individual patients can affect the CRT response. In addition, it is unknown which CRT response definition, i.e, improvement in clinical symptoms or LV reverse modelling will result in overall improved survival.

Another limitation is the short follow-up period used in our study (1 year). Boriani et al reported in a study on ICD and CRT-D implantations with a follow-up of minimum 3 years and maximum 8 years has suggested that studies with even longer follow-up could beneficially use DAOH and themselves advocate the calculation of DAOH ‘from administrative databases with full coverage of long follow-up periods’.\(^\text{15}\) Although the results of some studies indicate gradual improvement in the QoL up to 2 years after CRT, others have reported high fluctuations (improvement and deterioration over the course of several months) in the first year after CRT.\(^\text{33, 34}\) Huynh et al reported the results of 382 patients with HF (61% male, median age 75 years) from the MARATHON study in Australia that compare predictors of 30 day readmission or death with those of an alternative outcome in HF, DAOH within 12 months of discharge, which incorporates mortality and all hospitalisations into a single measure.\(^\text{35}\) The study showed that median DAOH within 12 months was 350 days (IQR 302–363). The final predictive model of DAOH included NYHA classification (r=-0.29, p<0.001), LV volume index (r=-0.27, p<0.001), LA volume index (r=-0.26, p<0.001), presence of CKD (r=-0.22, p=0.007), cognitive function using Montreal Cognitive Assessment (MoCA) score (r=0.21, p<0.001) and presence of life-threatening arrhythmia (r=-0.16, p=0.002) and this model of DAOH was more predictive than the risk score of 30 day readmission or death.\(^\text{35}\) Therefore, DAOH provides a valuable tool to estimate longevity and QoL in HF even the follow-up duration was short. In our study, patients implanted in ‘real world’ clinical practice with...
CRT device have, a relatively favourable improvement within a year of the implant. It is also difficult to compare patients before and after CRT implant as most of our patients would be hospitalised with their index event leading causing HF in the year prior to the implantation. The main strength of our study was the ability to assess the global burden of hospitalisation during follow-up, combining data with DAOH summarising the overall impact of CRT on HF mortality and morbidity.

CONCLUSION

Patients with HF implanted with CRT have greater DAOH within 1-year follow-up. The use of DAOH provides an alternative method for measuring the overall positive impact of CRT on HF mortality and morbidity. This technique may have more utility in assessing treatment within 1-year follow-up. The use of DAOH provides an

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