Heart failure clinics improve use of evidence-based heart failure therapies in patients with reduced ejection fraction following acute coronary syndrome (ANZACS-QI 48)

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ABSTRACT

AIMS: To describe the use of evidence-based heart failure therapies in patients with reduced left ventricular ejection fraction (LVEF) following acute coronary syndrome (ACS).

METHODS: Patients with ACS and LVEF ≤40% were identified from the All New Zealand Acute Coronary Syndrome Quality Improvement (ANZACS-QI) registry between June 2017 and May 2018. Data was obtained from retrospective review of clinical records. Dispensed medications were identified from pharmacy dispensing records and compared with target doses recommended in guidelines.

RESULTS: Of 292 patients, 28% were seen in cardiology heart failure (HF) clinic, 54% seen in general cardiology clinic and 17% were not seen in cardiology clinic. At one year post-discharge, 52% and 39% were dispensed ≥50% target dose of angiotensin converting enzyme inhibitor (ACEi)/ angiotensin receptor blocker (ARB), and beta-blockers respectively. Seventy-one percent and 68% of patients were on maximally tolerated doses of ACEi/ARB and beta-blockers respectively. The highest rates of medication up-titration occurred in those seen in cardiology HF clinics. Seventy-four percent and 59% were dispensed ≥50% target dose of ACEi/ARB and beta-blocker respectively. Ninety-five percent and 89% were on maximally tolerated doses of ACEi/ARB and beta-blockers respectively. Thirteen percent were potentially eligible for primary prevention implantable cardiac defibrillator; however, only 24% of these eligible patients had one implanted by one year post-discharge.

CONCLUSIONS: Evidence-based HF therapies were underutilised in this regional cohort of patients with reduced LVEF post-ACS. Strategies to improve use of these therapies should focus on increasing the number of patients seen by HF clinics and reducing clinic waiting times.

Heart failure (HF) and reduced ejection fraction associated with an acute coronary syndrome (ACS) is associated with adverse prognosis.[1–3] While clinical HF may occur in the setting of an ACS hospitalisation, asymptomatic LV systolic dysfunction carries substantial risk of subsequent development of clinical heart failure. Current clinical guidelines have given a class I recommendation for the use of angiotensin converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), beta-blockers and mineralocorticoid receptor antagonists (MRA) following ACS with

HF and/or reduced left ventricular ejection fraction (LVEF) of <40%.[4,5] These medications often need to be initiated at a low dose during hospitalisation for ACS because of the presence of HF and/or borderline haemodynamic observations. Ideally these medications need to be up-titrated prior to discharge or in the early outpatient setting, to target doses that were shown to have clinical benefit in randomised controlled trials. Nurse-led medication up-titration clinics have an established role for patients with HF with reduced ejection fraction to achieve maximum tolerated doses of ACEi, ARB, beta-blockers and MRAs and are recommended in local guidelines.[6]

Our previous study of a New Zealand-wide cohort of patients with ACS showed that rates of evidence-based HF therapies in those with reduced LVEF were low at one-year post discharge, with only 34% and 35% received ≥50% target doses of ACEi/ARB and beta-blockers respectively.[7] While very few patients had documented contraindication or intolerance to these medications at baseline, the observational nature of this national cohort precluded understanding of potential reasons why target dosages of these medications were not achieved.

Implantable cardiac defibrillators (ICDs) are indicated for primary prevention of sudden cardiac death in patients with reduced LVEF following myocardial infarction.[4,5] Previous international studies have demonstrated suboptimal rates of primary prevention ICD implantation at one year post-myocardial infarction.[8,9] The current use of primary prevention ICD following acute coronary syndromes in New Zealand is unknown.

The aim of this study was to describe the use of evidence-based heart failure therapies in a population of patients with reduced LVEF following ACS.

Methods

Study population

Patients from the Auckland Region (defined as those residing in Waitemata, Auckland or Counties Manukau District Health Boards (DHBs)) were identified from the All New Zealand Acute Coronary Syndrome Quality Improvement (ANZACS-QI) registry. This web-based registry records a mandatory dataset for almost all patients who are admitted to a New Zealand public hospital with an ACS and have coronary angiography. Further details regarding this registry have been previously reported.[10] Patients with confirmed ACS, who underwent coronary angiography between the dates of 1 June 2017 and 31 May 2018, and who had LVEF measured by echocardiogram during their index admission of less than 40% were included in this study. Patients were excluded from this study if they were a non-New Zealand resident, moved outside of the Auckland region within one year of index admission or if they died or received palliative care within three months of index admission. Patients were also excluded if there were discrepancies between the clinical record and that in ANZACS-QI.

Clinical variables

All data was collected via retrospective review of electronic clinical records by two authors (DC and JK). Baseline characteristics including demographics, comorbidities, ACS presentation and management in hospital were obtained from the discharge summary. Outpatient clinic follow-up within one year of discharge was recorded to be either in cardiology HF clinic, general cardiology clinic or no cardiology clinic. Cardiology HF clinics are nurse-led outpatient clinics under the supervision of a cardiologist, with goals including heart failure education and medication up-titration. General cardiology clinics may have been with either a cardiologist, registrar or nurse practitioner without involvement of specific HF services. Patients with no cardiology clinic follow-up may have been seen by other services (eg, renal medicine) during the follow-up period. Time to first clinical outpatient clinic follow up was recorded. New York Heart Association (NYHA) symptom class and cardiac rhythm was recorded at the last clinical encounter within one year post-discharge.

Echocardiogram reports from the index admission were reviewed for LVEF and the presence of moderate or severe right ventricular systolic impairment; at least one moderate or greater regurgitant or stenotic valvular lesion; and moderate or severe pulmonary hypertension. Time to first repeat echocardiogram after discharge, and LVEF recorded on the that echocardiogram were recorded if it occurred within one year of discharge.

Medications

Medication dispensing was identified from Test Safe community dispensing records, which captures virtually all dispensing of subsided medications from community pharmacies in New Zealand. Medications were deemed to be in patient possession if there was dispensing of a sufficient supply of medications to last until a pre-defined time point: at discharge, three months post-discharge and 12 months post-discharge. For example a patient would have been in possession of a medication at 12 months post-discharge, if a 30 day supply was dispensed at 11 months post-discharge, but not if dispensed at 10 months post-discharge.

Three classes of medications were investigated in this study; ACEi/ARBs, beta-blockers and MRAs. Sacubitril with valsartan (Entresto) was approved for use in New Zealand during the follow-up period in this study and was included under the ACEi/ARB medication class. Target doses of medications were used to standardise comparison of medications within the same class. Target doses of ACEi/ARB, beta-blockers and MRAs were based upon the 2016 ESC guidelines for the diagnosis and treatment of acute and chronic HF.[6,11] Doses of medications were either classified as low dose (<50% of target dose), 50–99% of target dose or target dose (see Appendix Table 1).

Patients were defined to be on a maximally tolerated dose of a specific drug class if they were either dispensed ≥50% target dose, or if they had a documented reason why this medication could not be up-titrated further. Patients not on maximally tolerated doses could potentially have had their evidence-based HF therapy up-titrated further. Potential reasons for failure to up-titrate medications to ≥50% target doses were identified from review of all available hospital discharge summaries, outpatient clinic letters and laboratory results, up to one year post-discharge or death (whichever occurred first).

Possible reasons why target doses of medications are not achieved are based upon the European and New Zealand HF guidelines.[6,11] Reasons for failure to achieve ≥50% target doses of ACEi/ARB were defined as renal impairment (sustained rise in creatinine >50%, creatinine >221μmol/L or eGFR <30mL/min/1.73m^2), hyperkalaemia (>5.0mmol/L), hypotension (systolic blood pressure <90mmHg), allergy or other drug intolerance. Reasons for failure to achieve ≥50% target doses of beta-blockers were defined as bradycardia (HR <60bpm), high-degree AV block, hypotension (systolic blood pressure <90 mmHg), allergy or other drug intolerance. Reasons for failure to achieve ≥50% target doses of MRAs were the same as for ACEi/ARB. Additionally MRAs were documented to not be indicated in some patients—MRAs are clinically indicated post-ACS if LVEF is ≤40% with HF or diabetes;[4] and if LVEF ≤35% with NYHA II-IV symptoms.[11]

Implantable cardiac defibrillators

Primary prevention ICDs were defined to be potentially clinically indicated in patients with NYHA class II–III symptoms and LVEF≤35% or NYHA class I and LVEF ≤30%, according to current clinical guidelines.[4,5,12] Patients were deemed ineligible for primary prevention ICD if they were ≥75 years of age or if they had a condition associated with a reduced life expectancy of <18 months (eg, chronic kidney disease on renal replacement therapy, advanced malignancy, cognitive impairment, poor functional status requiring assistance with activities of daily living) consistent with New Zealand guidelines.[13] Clinical records were reviewed for documentation of a primary prevention ICD (or cardiac resynchronisation therapy with defibrillator) implant, within one year of discharge. Patients with an ICD prior to index admission or who received a secondary prevention ICD were excluded.

Ethics

This study was deemed not to be within the scope of the Health and Disability Ethics Committee (HDEC) review and further ethics approval was not required. This study received locality approval from the respective DHB research offices.

Statistics

Categorical data are presented as frequency and percentage. Continuous variables are presented as mean ± standard deviation or median and interquartile range.

Results

Three hundred and fifty-nine patients were identified from the ANZACS-QI registry with an ACS, reduced LVEF and whom reside in one of the three Auckland region DHBs between 1 June 2017 and 31 May 2018. Sixty-seven patients (18.7%) were excluded from further analysis—27 died within three months of discharge, 25 did not have an LVEF >40% documented during their index admission, 12 did not reside in an Auckland region DHB and on review three did not have a diagnosis of ACS during index admission. The remaining 292 patients were included in the study. They all had at least one year of follow-up available. One hundred and twenty-three patients (42%) were from Waitemata DHB, 52 (18%) from Auckland DHB and 117 (40%) from Counties Manukau DHB.

Baseline characteristics and clinical follow-up (Table 1)

Eighty-three patients (28%) were seen at least once in cardiology HF clinic, 159 patients (54%) were seen in cardiology clinic and 50 patients (17%) had no cardiology clinic follow-up. Seventy-two percent of patients seen in nurse-led cardiology HF clinics were also seen by a cardiologist at a separate appointment. Median time to first outpatient clinic follow-up was shorter for those seen in cardiology HF clinics compared to general cardiology clinics (43 vs 75 days).

Patients seen in cardiology HF clinics were on average younger, more likely to be male and of New Zealand Māori or Asian ethnicity. They were also more likely to have diabetes, clinical heart failure (Killip Class ≥II) and have more severe LV impairment (LVEF ≤30%) on presentation. Median length of stay during the index admission was longer in those seen in cardiology HF clinics. In contrast patients with no cardiology clinic follow-up were older, more likely to be female and of European ethnicity. They were also more likely to have prior cardiovascular disease or renal disease, and less likely to receive revascularisation.

Only 156 patients (53%) had a repeat echocardiogram to reassess LVEF within one year of discharge. Rates were highest in those seen in cardiology HF clinics (72%) and lowest in those with no cardiology clinic follow-up (26%). However, patients seen in cardiology HF clinics had the longest median time to their first repeat echocardiogram (195 days).

Target doses of medications (Figure 1 and Appendix Tables 2–S4)

Rates of ACEi/ARB and beta-blocker dispensing on discharge were relatively high, 83% and 87% respectively. However, the number of patients discharged on ≥50% target doses of an ACEi/ARB were only 35% and 31% respectively. Only 18% of patients were dispensed a MRA on discharge.

At one year post-discharge, overall dispensing rates of ACEi/ARB, beta-blocker and MRA were similar to those at discharge—83%, 82% and 23% respectively. Dispensing rates were highest in those seen in cardiology HF clinics—92% on ACEi/ARB, 90% on beta-blockers and 41% on MRA. Rates were lowest in those with no cardiology clinic follow-up—64% on ACEi/ARB, 70% on beta-blockers, 10% on MRA. Dispensing rates were intermediate for those seen in general cardiology clinics

More patients were dispensed ≥50% target dose of ACEi/ARB and beta-blockers at one year post-discharge—52% and 39% respectively. The highest medication up-titration was in patients seen in cardiology HF clinics—29% were dispensed ≥50% target dose of ACEi/ARB at discharge, increasing to 74% at one year. Thirty-three percent were dispensed ≥50% target dose of beta-blockers at discharge, increasing to 59% at one year. Less up-titration occurred in patients seen in general cardiology clinics, with only 48% and 34% achieving ≥50% target doses of ACEi/ARB and beta-blockers respectively at one year. No significant up-titration occurred in patients with no cardiology clinic follow-up.

Maximally tolerated doses of medications (Table 2 and Figure 2)

Seventeen percent of patients had a documented reason why their ACEi/ARB dose could not be dispensed or up-titrated. The most common reason was renal impairment or hyperkalaemia (8%). When taking this into account, 71% were on a maximally tolerated dose of ACEi/ARB at one year post-discharge or at time of death. Ninety-five percent of patients seen in cardiology HF clinic were on a maximally tolerated

Table 1: Baseline characteristics.

	All n=292	**Cardiology heart failure clinic** n=83	**General cardiology clinic** n=159	**No cardiology clinic** n=50
Age (years), mean ± SD	66.4±11.4	64.4±10.8	66.5±11.7	69.6±10.6
Male	232 (79.5)	70 (84.3)	128 (80.5)	34 (68.0)
Ethnic group				
NZ Māori	28 (9.6)	11 (13.3)	14 (8.8)	3 (6.0)
Pacific	54 (18.5)	12 (14.5)	32 (20.1)	10 (20.0)
Asian	51 (17.5)	20 (24.1)	26 (16.4)	5 (10.0)
European/Other	159 (54.5)	40 (48.2)	87 (54.7)	32 (64.0)
Prior CVD	108 (37.0)	24 (28.9)	64 (40.3)	20 (40.0)
Prior heart failure	24 (8.2)	8 (8.4)	13 (8.2)	4 (8.0)
Diabetes	121 (41.4)	42 (50.6)	59 (37.1)	20 (40.0)
eGFR (ml/min/1.73m^2)				
<30	24 (8.2)	2 (2.4)	14 (8.8)	8 (16.0)
30–<60	66 (22.6)	15 (18.1)	39 (24.5)	12 (24.0)
≥60	202 (69.2)	66 (79.5)	106 (66.7)	30 (60.0)
Killip Class				
I	198 (67.8)	45 (54.2)	117 (73.6)	36 (72.0)
II–IV	94 (32.2)	38 (45.8)	42 (26.4)	14 (28.0)
GRACE Score				
<1%	21 (7.2)	4 (4.8)	16 (10.1)	1 (2.0)
1–3%	107 (36.6)	29 (34.9)	56 (35.2)	22 (44.0)
≥3%	164 (56.2)	50 (60.2)	87 (54.7)	27 (54.0)
Type of ACS				
STEMI	112 (38.4)	34 (41.0)	61 (38.4)	17 (34.0)
NSTE-ACS	180 (61.6)	49 (59.0)	98 (61.6)	33 (66.0)
Revascularisation				
PCI	163 (55.8)	48 (57.8)	90 (56.6)	25 (50.0)
CABG	57 (19.5)	19 (22.9)	31 (19.5)	7 (14.0)
Left ventricular ejection fraction				
35–40%	132 (45.2)	17 (20.5)	87 (54.7)	28 (56.0)
30–35%	68 (23.3)	22 (26.5)	31 (19.5)	15 (30.0)
25–30%	55 (18.8)	26 (31.3)	26 (16.4)	3 (6.0)
< 25%	37 (12.7)	18 (21.7)	15 (9.4)	4 (8.0)
Echocardiography variables				
≥ moderate RV impairment	54 (18.5)	16 (19.3)	31 (19.5)	7 (14.0)
≥ moderate valvular disease	44 (15.1)	10 (12.0)	24 (15.1)	10 (20.0)
≥ moderate pulmonary HTN	23 (7.9)	4 (4.8)	12 (7.5)	7 (14.0)
Length of stay (days), median (IQR)	7 (4–13)	8 (4–15)	7 (4–12)	5 (3–13)

NB: All values are frequency (%) unless otherwise specified.
CVD = cardiovascular disease; eGFR = glomerular filtration rate estimated by the Chronic Kidney Disease Epidemiology Collaboration equation; STEMI = ST elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; RV=right ventricular; HTN = hypertension.

Figure 1: Achievement of target doses at discharge, three months and a year.

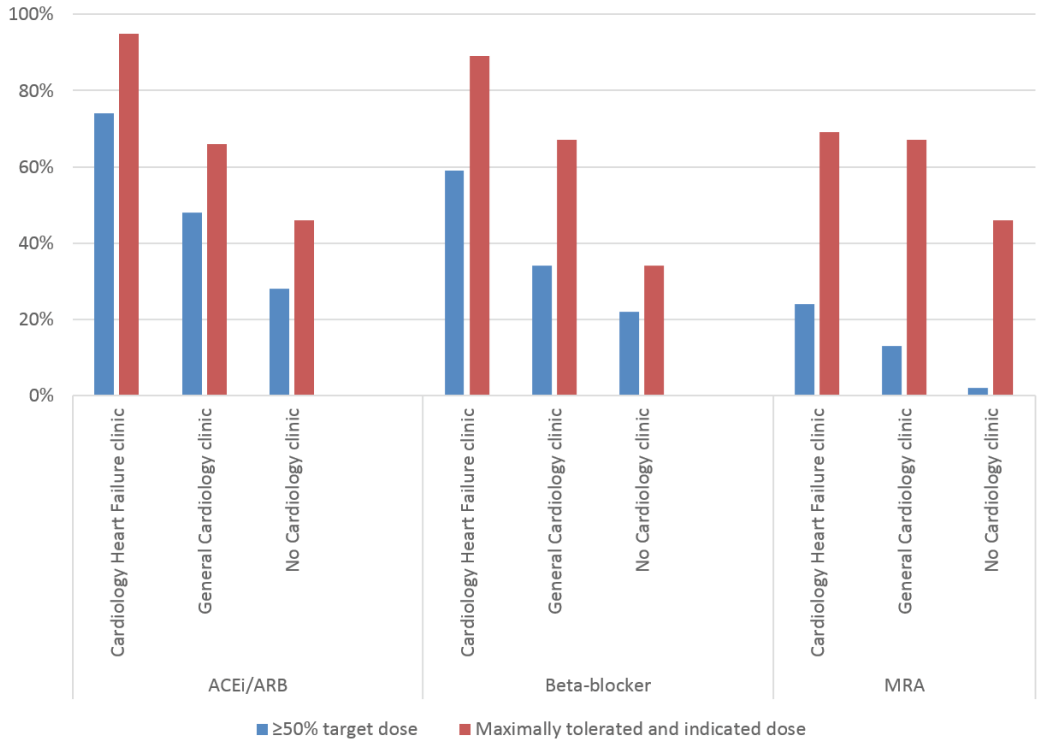
NZMJ 12 June 2020, Vol 133 No 1516
ISSN 1175-8716
www.nzma.org.nz/journal

Table 2: Reasons why target doses of medications were not achieved.

		All n=292	**Cardiology heart failure clinic** n=83	**General cardiology clinic** n=159	**No cardiology clinic** n=50
ACEi/ARB	Maximal tolerated dose	207 (70.9)	79 (95.2)	105 (66.0)	23 (46.0)
	CKD/hyperkalaemia Hypotension Allergy/intolerance Unknown	22 (7.5) 19 (6.5) 9 (3.1) 85 (29.1)	5 (6.0) 7 (8.4) 4 (4.8) 4 (4.8)	11 (6.9) 12 (7.5) 4 (2.5) 54 (34.0)	6 (12.0) 0 (0.0) 1 (2.0) 27 (54.0)
Beta-blockers	Maximal tolerated dose	197 (67.5)	74 (89.2)	106 (66.7)	17 (34.0)
	Bradycardia Hypotension Allergy/intolerance Unknown	58 (19.9) 6 (2.1) 15 (5.1) 95 (32.5)	19 (22.9) 1 (1.2) 4 (4.8) 9 (10.8)	37 (23.3) 4 (2.5) 11 (6.9) 53 (33.3)	2 (4.0) 1 (2.0) 0 (0.0) 33 (66.0)
MRA	Maximal tolerated and indicated dose	186 (63.7)	57 (68.7)	106 (66.7)	23 (46.0)
	Not indicated	101 (34.6)	25 (30.1)	61 (38.4)	15 (30.0)
	CKD/hyperkalaemia Allergy/intolerance Unknown	32 (11.0) 10 (3.4) 106 (36.3)	7 (8.4) 4 (4.8) 26 (31.3)	19 (11.9) 6 (3.8) 53 (33.3)	6 (12.0) 0 (0.0) 27 (54.0)

NB: All values are frequency (%) unless otherwise specified.
ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; CKD = chronic kidney disease.

Figure 2: Heart failure medication doses at 12 months post-discharge.



NZMJ 12 June 2020, Vol 133 No 1516
ISSN 1175-8716
www.nzma.org.nz/journal

dose of ACEi/ARB, compared to 66% seen in general cardiology clinic and 46% not seen in cardiology clinic.

Twenty-seven percent of patients had a documented reason why their beta-blocker dose could not be dispensed or uptitrated. The most common reason for inability to up-titrate beta-blockers was bradycardia (20%). When taking this into account, 68% were on a maximally tolerated dose of beta-blocker at one year post-discharge or at time of death. Eighty-nine percent of patients seen in cardiology HF clinic were on the maximally tolerated dose of beta-blocker, compared to 67% seen in general cardiology clinic and 34% not seen in cardiology clinic.

Fourteen percent of patients had a documented reason why a MRA could not be dispensed or up-titrated. MRAs were not indicated in 35% of patients in this study. When taking this into account, 64% of patients received a maximally tolerated and indicated dose of MRAs.

Primary prevention implantable cardiac defibrillator (Table 3)

Very few patients (13%) were eligible for primary prevention ICD implantation. The most common reasons for ineligibility were not meeting clinical indications (66%), age ≥75 years (32%) or life-limiting condition (17%). Seventeen patients received a secondary prevention ICD within one year of their index admission. Only nine patients (24% of potentially eligible patients) received a primary prevention ICD within one year of their index admission. The large majority of these patients were seen in Cardiology HF clinics (seven patients), the remaining were seen in general cardiology clinic.

Discussion

In a regional cohort of patients with ACS and reduced LVEF, there was underutilisation of evidence-based therapies for treatment and prevention of clinical heart failure. Proportions of patients dispensed ≥50% target dose of ACEi/ARB or beta-blockers at one year post-discharge were low (52% and 39% respectively), although these proportions were somewhat higher for those considered to be receiving maximally tolerated dosages of these medications (71% and 68% respectively). Importantly, those patients who attended a cardiology HF clinic rather than a general cardiology clinic were more likely to achieve ≥50% target dose of ACEi/ARB or beta-blockers. Furthermore, around 90% attending cardiology HF clinics achieved the maximum tolerated dose of both compared with only two-thirds in general cardiology clinics. Only 3% received an ICD implant for primary prevention within one year of discharge.

Table 3: Eligibility for ICD.

	All n=292	**Cardiology heart failure clinic** n=83	**General cardiology clinic** n=159	**No cardiology clinic** n=50
Ineligible for primary prevention ICD	254 (87.0)	66 (79.5)	143 (89.9)	45 (90.0)
ICD prior to admission	6 (2.1)	0 (0.0)	5 (3.1)	1 (2.0)
Secondary prevention ICD	17 (5.8)	6 (7.2)	10 (6.3)	1 (2.0)
NYHA class ≥II and LVEF ≥35% OR NYHA class I and LVEF ≥30%	193 (66.1)	44 (53.0)	115 (72.3)	34 (68.0)
Life limiting condition	50 (17.1)	3 (3.6)	29 (18.2)	18 (36.0)
Age ≥75 years	92 (31.5)	18 (21.7)	54 (34.0)	20 (40.0)
Eligible for primary prevention ICD	38 (13.0)	17 (20.5)	16 (10.1)	5 (10.0)
Patients who received primary prevention ICD within one year of discharge*	9 (23.7)	7 (41.2)	2 (12.5)	0 (0.0)

NB: All values are frequency (%) unless otherwise specified.
* Frequency is of those who were eligible for primary prevention ICD.

Target doses versus maximally tolerated doses

Current clinical guidelines give a class I recommendation for the use of ACEi/ARB, beta-blockers and MRAs in patients with reduced LVEF following ACS, to reduce both morbidity and mortality.[4,5] This is based upon evidence from randomised clinical trials where the majority of patients were on target doses. For example, 79% of patients were on target doses of captopril in the SAVE trial,[14] 74% of patients were on target doses of carvedilol in the CAPRICORN trial[15] and the mean dose of eplerenone was 42.6mg (>80% target dose) in the EPHESUS trial.[16] However, an evidence-practice gap is seen in 'real-world' registries where few patients are able to achieve target doses. Only 34% and 35% of patients with reduced LVEF were on ≥50% target doses of ACEi/ARB and beta-blockers respectively one year post-ACS in a nationwide New Zealand cohort.[7] Similar findings are seen PREMIER/TRIUMPH ACS registries with only 32% of patients with LV dysfunction achieving goal doses of ACEi/ARB one year following ACS.[17] These findings are also seen in cohorts of patients with chronic HF.[18] Further medication up-titration may not been possible in patients due to comorbidities and drug intolerances. It may be unreasonable to aim for target doses of medications in all patients with reduced LVEF. In this study, 17% and 27% of patients had clear documented reasons why their ACEi/ARB and beta-blocker respectively, could not be up-titrated to ≥50% target doses.

In this retrospective study, the highest proportion of patients on target doses of evidence-based HF therapy were observed in patients seen in cardiology HF clinics. The majority of patients seen in cardiology HF clinics were on maximally tolerated doses of ACEi/ARB (95%) and beta-blockers (89%), however fewer patients in this group achieved ≥50% target dose of ACEi/ARB (74%) or beta-blocker (59%). This suggests that aiming for target doses of evidence-based HF therapies in all patients may not be achievable, even with intensive outpatient follow-up provided in cardiology HF clinics. It may be more reasonable to aim for all patients to be on maximally tolerated dose, rather than target doses of ACEi/ARB and beta-blockers.

Improving use of heart failure therapies via HF clinics

There is still room for improvement in the use of evidence-based HF therapies in patients with reduced LVEF post-ACS in this study. Patients not seen in cardiology HF clinic had lower rates of both patients on ≥50% target dose of ACEi/ARB or beta-blockers and patients on maximally tolerated doses of ACEi/ARB or beta-blockers. This study suggests that improved utilisation of evidence-based HF therapies could possibly be achieved by more patients being seen in cardiology HF clinics.

A multidisciplinary team (MDT) approach, including nurse-led HF clinics is considered the gold standard model for the delivery of HF care and is recommended by the European Society of Cardiology[11] and Cardiac Society of Australia and New Zealand.[6] Previous studies have demonstrated that patients seen in MDT HF clinics are more likely to reach target doses of beta-blockers[19] and achieve optimal cardiac medication therapy in shorter time periods.[20] MDT HF services also improve clinical outcomes. A local randomised controlled trial of integrated HF management improved quality of life and reduced total hospital admissions.[21] Planned referral to nurse-led HF clinics was associated with reduced mortality but not HF hospitalisation in the SwedeHF registry.[22] Reduction in both mortality and morbidity was observed in a Cochrane meta-analysis of nurse-led up-titration services.[23] It is unclear whether the clinical benefit of MDT HF services arises from improved medication up-titration, or from other interventions such as patient education, self-management, cardiac rehabilitation, more frequent clinical assessment and psychological support.[24]

However, cardiology HF clinics are a limited resource. In this study only 28% of patients were seen in cardiology HF clinics, however they appear to be appropriately utilised for patients with high-risk features such as more severe clinical heart failure and severe left ventricular systolic impairment. Although patients seen in cardiology HF clinics had shorter times to their first outpatient appointment, median time to first follow-up was still over seven weeks. Furthermore, a significant amount of medication up-titration appears to occur between 3 and 12 months post-discharge, suggesting

that there are barriers to quicker up-titration such as delays to repeat follow-up assessments. These delays to medication up-titration may result in adverse clinical outcomes. The patients included in this study were high-risk patients with reduced LVEF following ACS and it is reasonable that their medications should be up-titrated in the early outpatient setting, rather than primary care. Further resource allocation is required to reduce waiting times for outpatient follow-up, and to allow a greater proportion of patients to be seen in nurse-led HF clinics.

Implantable cardiac defibrillators

In this study, 13% of patients were eligible for, and only 3% received an ICD implantation for, primary prevention. This is comparable to other cohorts of patients with reduced LVEF following ACS. In the TRUIMPH registry of patients with acute myocardial infarction and LVEF <40%, only 2.4% of patients underwent ICD implantation by one year.[8] In a retrospective study of Medicare beneficiaries with an LVEF 35% post-myocardial infarction, the one-year ICD implantation rate was 8.1%.[9] In both studies earlier outpatient clinic follow-up was associated with a higher rate of ICD implantation. ICD implantation for primary prevention post-ACS with reduced LVEF is recommended 40 days after ACS to reduce mortality.[4,5] Median time to first clinic follow-up and reassessment of LVEF were beyond 40 days in this study, suggesting that there are potential missed opportunities to improve rates of primary prevention ICD implants in this population.

Strengths and limitations

This study was a retrospective analysis of hospital based electronic records of patients admitted with an ACS. This was a complete annual cohort of patients from three large metropolitan DHBs that provide care for approximately 35% of the total New Zealand population. Primary care records were not available and patients were not contacted, hence reasons why medications could not be up-titrated may be unreported in this study. In this observational study there are differences in the characteristics of the patients seen in each group and we can't be certain that some of the differences in attainment of target doses was not due to unrecorded reasons for not up-titrating medication. Nevertheless, the proportions of patients with definite reasons not to up-titrate were similar for the cardiology HF clinic and general cardiology clinic groups. Only medication dispensing was recorded and adherence to heart failure therapies was not obtainable. Lastly, the effect of medication up-titration on clinical outcomes was not recorded and outside of the scope of this study.

Conclusions

Evidence-based heart failure therapies were underutilised in this cohort of patients with reduced LVEF post-ACS with only half of patients being dispensed on ≥50% target doses of ACEi/ARB and few patients receiving primary prevention ICDs. However, the majority of patients seen in cardiology HF clinics were dispensed maximally tolerated doses of ACEi/ARB and beta-blockers. Strategies to improve use of these proven therapies should focus on increasing the number of patients seen in cardiology HF clinics and reducing clinic waiting times.

Appendix

Appendix Table 1: Guideline-recommended doses.

	Starting dose	≥50% target dose	Target dose
Angiotensin converting enzyme inhibitor/angiotensin receptor blocker			
Captopril	6.25mg tds	25mg tds	50mg tds
Enalapril	2.5mg bd	10mg bd	20mg bd
Lisinopril	2.5–5mg daily	10mg daily	20mg daily
Cilazapril	0.5mg daily	2.5mg daily	5mg daily
Quinapril	2.5mg bd	5mg bd	10mg bd
Perindopril	2mg daily	4mg daily	8mg daily
Candesartan	4–8mg daily	16mg daily	32mg daily
Losartan	12.5mg daily	50mg daily	100mg daily
Sacubitril with valsartan	24/26mg bd	49/51mg bd	97/103mg bd
Beta-blocker			
Metoprolol CR	23.75mg daily	95mg daily	190mg daily
Bisoprolol	1.25mg daily	5mg daily	10mg daily
Carvedilol	3.125mg bd	12.5mg bd	25mg bd
Mineralocorticoid receptor antagonist			
Spironolactone	12.5–25mg daily	25mg daily	50mg daily
Eplerenone	25mg daily	25mg daily	50mg daily

bd = twice daily, tds = three times daily.

Appendix Table 2: ACEi/ARB up-titration.

		All n=292	**Cardiology heart failure clinic** n=83	**General cardiology clinic** n=159	**No cardiology clinic** n=50
Discharge	Total, n (%)	243 (83.2)	72 (86.7)	133 (83.6)	38 (76.0)
	Doses, n (%)				
	- Nil	49 (16.8)	11 (13.3)	26 (16.4)	12 (24.0)
	- Low dose	140 (47.9)	48 (57.8)	73 (45.9)	19 (38.0)
	- 50–99% target dose	45 (15.4)	12 (14.5)	26 (16.4)	7 (14.0)
	- Target dose	58 (19.9)	12 (14.5)	34 (21.4)	12 (24.0)
3 months post discharge	Total, n (%)	260 (89.0)	80 (96.4)	140 (88.1)	40 (80.0)
	Doses, n (%)				
	- Nil	32 (11.0)	3 (3.6)	19 (11.9)	10 (20.0)
	- Low dose	121 (41.4)	30 (36.1)	72 (45.3)	19 (38.0)
	- 50–99% target dose	61 (20.9)	23 (27.8)	29 (18.2)	9 (18.0)
	- Target dose	78 (26.7)	27 (32.5)	39 (24.5)	12 (24.0)
12 months post discharge	Total, n (%)	242 (82.9)	76 (91.6)	134 (84.3)	32 (64.0)
	Doses, n (%)				
	- Nil	33 (11.3)	4 (4.8)	19 (11.9)	10 (20.0)
	- Low dose	91 (31.2)	15 (18.1)	58 (36.5)	18 (36.0)
	- 50–99% target dose	59 (20.2)	22 (26.5)	32 (20.1)	5 (10.0)
	- Target dose	92 (31.5)	39 (47.0)	44 (27.7)	9 (18.0)
	Deceased	17 (5.8)	3 (3.6)	6 (3.8)	8 (16.0)

Appendix Table 3: Beta-blocker up-titration.

		All n=292	**Cardiology heart failure clinic** n=83	**General cardiology clinic** n=159	**No cardiology clinic** n=50
Discharge	Total, n (%)	254 (87.0)	75 (90.4)	137 (86.2)	42 (84.0)
	Doses, n (%)				
	- Nil	38 (13.0)	8 (9.6)	22 (13.8)	8 (16.0)
	- Low dose	164 (56.2)	48 (57.8)	90 (56.6)	26 (54.0)
	- 50–99% target dose	68 (23.3)	23 (27.8)	35 (22.0)	10 (20.0)
	- Target dose	22 (7.5)	4 (4.8)	12 (7.5)	6 (12.0)
3 months post discharge	Total, n (%)	259 (88.7)	76 (91.6)	142 (89.3)	41 (82.0)
	Doses, n (%)				
	- Nil	33 (11.3)	7 (8.4)	17 (10.7)	9 (18.0)
	- Low dose	160 (54.8)	44 (53.0)	87 (54.7)	29 (58.0)
	- 50–99% target dose	71 (24.3)	23 (27.7)	41 (25.8)	7 (14.0)
	- Target dose	28 (9.6)	9 (10.8)	14 (8.8)	5 (10.0)
12 months post discharge	Total, n (%)	240 (82.2)	75 (90.4)	130 (81.8)	35 (70.0)
	Doses, n (%)				
	- Nil	35 (12.0)	5 (6.0)	23 (14.5)	7 (14.0)
	- Low dose	126 (43.2)	26 (31.3)	76 (47.8)	24 (48.0)
	- 50–99% target dose	76 (26.0)	32 (38.6)	38 (23.9)	6 (12.0)
	- Target dose	38 (13.0)	17 (20.5)	16 (10.1)	5 (10.0)
	Deceased	17 (5.8)	17 (5.8)	6 (3.8)	8 (16.0)

Appendix Table 4: Mineralocorticoid antagonist up-titration.

		All n=292	**Cardiology heart failure clinic** n=83	**General cardiology clinic** n=159	**No cardiology clinic** n=50
Discharge	Total, n (%)	53 (18.2)	19 (22.9)	28 (17.6)	6 (12.0)
	Doses, n (%)				
	- Nil	239 (81.8)	64 (77.1)	131 (82.4)	44 (88.0)
	- Low dose	23 (7.9)	6 (7.2)	12 (7.5)	5 (10.0)
	- 50–99% target dose	30 (10.3)	13 (15.7)	16 (10.1)	1 (2.0)
	- Target dose	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
3 months post discharge	Total, n (%)	66 (22.6)	28 (33.7)	32 (20.1)	6 (12.0)
	Doses, n (%)				
	- Nil	226 (77.4)	55 (66.3)	127 (79.9)	44 (88.0)
	- Low dose	28 (9.6)	12 (14.5)	11 (6.9)	5 (10.0)
	- 50–99% target dose	38 (13.0)	16 (19.3)	21 (13.2)	1 (2.0)
	- Target dose	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
12 months post discharge	Total, n (%)	68 (23.3)	34 (41.0)	29 (18.2)	5 (10.0)
	Doses, n (%)				
	- Nil	207 (70.8)	46 (55.4)	124 (78.0)	37 (74.0)
	- Low dose	26 (8.9)	14 (16.9)	8 (5.0)	4 (8.0)
	- 50–99% target dose	41 (14.0)	19 (22.9)	21 (13.2)	1 (2.0)
	- Target dose	1 (0.3)	1 (1.2)	0 (0.0)	0 (0.0)
	Deceased	17 (5.8)	17 (5.8)	6 (3.8)	8 (16.0)

Competing interests:
Dr Mazengarb and Dr Chan are supported by the Middlemore Hospital Cardiac Trust outside the submitted work; Dr Chan holds the AH Couch Research Scholarship; Dr Doughty holds the New Zealand Heart Foundation Chair of Heart Health.

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www.nzma.org.nz/journal-articles/heart-failure-clinics-improve-use-of-evidence-based-heart-failure-therapies-in-patients-with-reduced-ejection-fraction-following-acute-coronary-syndrome-anzacs-qi-48

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