Journal of Geriatric Cardiology (2019) 16: 320–328

Research Article · **Open Access** ·

Clinical characteristics, treatment and prognosis of patients with idiopathic dilated cardiomyopathy: a tertiary center experience

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Abstract

Background Contemporary heart failure medications have led to considerable improvement in the survival of patients with heart failure. However, limited evidence is available regarding the effect of those medications in patients with idiopathic dilated cardiomyopathy (IDCM), particularly in China. We sought to analyze the trends in clinical characteristics and the prescription rate of recommended therapies and its prognostic impact in patients with IDCM. **Methods** From 2009 to 2016, 1441 consecutive patients (age: 55±14 years, 68% men, LVEF: 33% ± 12%) fulfilling World Health Organization criteria for IDCM were enrolled in the current retrospective cohort study. Temporal trends of baseline clinical characteristics, treatment and prognosis were analyzed, and potential influential factors were explored. **Results** Rates of patients receiving angiotensin-converting enzyme inhibitors/angiotensin II receptors blockers, β-blockers, aldosterone receptor antagonists and diuretics increased from 55%, 45%, 58%, 51% in 2009 to 67%, 69%, 71%, 64% in 2016, respectively ($P < 0.05$); whereas, the proportion of patients receiving digoxin decreased from 39% in 2009 to 28% in 2016 ($P < 0.05$). The overall proportion of patients with optimal guideline-directed medical therapy (GDMT) was 44.6%; however, that rate increased from 33% in 2009 to 41%, 49% and 56% in 2012, 2014 and 2016 respectively ($P < 0.05$). Patients with optimal GDMT had a better outcome than those without, but there was no temporal trend toward improvement in the overall long-term prognosis of IDCM patients with the years. There was a trend towards admission of patients with milder disease and toward increased admission to a cardiology ward with the years. **Conclusions** An improvement in prescription rates of guideline-recommended medications in IDCM patients was observed. However, it remains suboptimal, and there is still some room for improvement. The prognosis of patients with optimal GDMT was better than those without. Moreover, the following patient category also had an improved prognosis: patients with LVEF ≥ 40%, with device therapy, and those admitted to a cardiology ward.

J Geriatr Cardiol 2019; 16: 320–328. doi:10.11909/j.issn.1671-5411.2019.04.004

Keywords: Dilated cardiomyopathy; Heart failure; Medications; Prognosis

1 Introduction

Idiopathic dilated cardiomyopathy (IDCM) is a primary heart muscle disease characterized by dilatation and systolic dysfunction of the left or both ventricles.[1,2] IDCM represents a frequent cause of heart failure (HF), in most multicenter randomized controlled trials (RCTs) and registries in HF, around 20% to 40% of enrolled patients have DCM.[3–6] Several RCTs have shown a favorable effect of angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptors blockers (ARB), β-blockers and aldosterone receptor antagonists on the prognosis of HF patients including those with IDCM, and hence became the background therapy in IDCM.[3,4,6,7] Similarly, several observational studies reported that an evidence-based therapeutic approach has improved the long-term prognosis of IDCM.[8–10] However, previous HF surveys have identified an apparent gap between clinical trials and daily practice characterized by suboptimal use of recommended medications, ACEIs and β-blockers in particular.[11,12] In China, there is limited evidence concerning the current status of the treatment and prognosis of patients with IDCM following the emergence of recent trial evidence and updated international guidelines. The purpose of the present study was to analyze the temporal trends in baseline clinical characteristics, treatment and prognosis of a considerable cohort of consecutively hospitalized and angiographically negative patients with IDCM, and to identify the factors that may impact the implementation of optimal guideline-directed medical therapy (GDMT) and factors that may influence survival. The results indicated that the prescription rates of guideline-recommended medications are increasing and improving the prognosis in

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Received: October 29, 2018 **Revised:** February 20, 2019
Accepted: March 10, 2019 **Published online:** April 28, 2019

IDCM patients, but it remains suboptimal, and a standardized therapeutic platform should be implemented to guide the treatment.

2 Methods

2.1 Study population

The comprehensive referral center for cardiomyopathies has been well-established for more than a decade in West China Hospital of Sichuan University, a large multispecialty tertiary hospital with > 4000 beds. This is a retrospective study of 2044 consecutive patients who presented with signs and symptoms of decompensated chronic or a mixture of both acute and chronic HF and were hospitalized at West China Hospital of Sichuan University from January 2009 to May 2016 with a discharge diagnosis of IDCM. In 603 patients, the cause of DCM was found to be secondary to ischemic heart disease, hypertension, valvular heart disease, congenital heart diseases, diabetes mellitus, heavy alcohol consumption, chemotherapy, or other cardiac or systemic diseases. The remaining 1441 were classified as IDCM, according to the World Health Organization criteria and on the basis of negative coronary angiography. Enrolled patients presented with left ventricular ejection fraction (LVEF) < 50% at baseline in the absence of chronic increased afterload (*i.e.*, aortic stenosis or hypertension), or volume overload (*i.e.*, primary mitral regurgitation or congenital heart disease), and the absence of significant coronary artery disease sufficient to cause global systolic dysfunction, advanced systemic disease, pericardial diseases, active myocarditis, and congenital heart diseases. Patients were also excluded if they had other forms of cardiomyopathy (*i.e.*, hypertrophic cardiomyopathy) and patients with transplanted heart; or if they were aged less than 18 years.

Data were derived from the hospital electronic medical record system and the following data were retrospectively abstracted: patients' demographic data (age, sex, body weight and height), clinical status during admission [vital signs, routine laboratory tests, electrocardiography, echocardiography, coronary angiography, New York Heart Association (NYHA) functional class, the primary diagnosis, type of hospital ward and date of admission], the clinical status at discharge (discharge medications, device therapy and discharge diagnosis). The temporal trends in the prescription rate of pharmacological and device therapy, and whether they meet the guideline recommendations were analyzed based on the year of admission from 2009 through 2016. Patients were then divided into two groups, 617 (44.6%) patients with optimal GDMT, and 766 (55.4%) patients with non-optimal GDMT, and the two groups were compared in terms of prognosis. Optimal GDMT was defined as the prescription of ACEI/ARB, β-blockers, and aldosterone receptor antagonist (three drugs) for all IDCM patients with LVEF of ≤ 35%, and ACEI/ARB plus β-blockers (two drugs) for those with LVEF > 35%. Non-optimal GDMT was considered if the above conditions were not met.[13–15]

In our institution, device therapy including implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy (CRT) implantation has been performed prior to the beginning of the current study and practiced according to guidelines regarding this issue.

All procedures performed in the present study were in accordance with the ethical standards of the institutional research committee of West China Hospital of Sichuan University. Informed consent was taken from all the patients at the time of admission to the hospital.

2.2 Follow-up

Endpoint of the study was all-cause mortality. The mean follow-up was 35.2 months. The follow-up data were obtained by regular visits to our hospital, chart reviews, and telephone contact with the patients or their families. Out of 1441 patients, 58 died in the hospital, and 241 were lost to follow-up. Finally, 1383 patients were included for the treatment analysis and 1142 for the prognosis evaluation. The study closed in May 2016. In patients who died, end of follow-up was considered as the time of death.

2.3 Statistical analysis

The quantitative variables with normal distribution were presented as mean ± standard deviation (SD), median was used for quantitative variables with skewed distribution and the number (percentage) for categorical variables. Baseline comparisons between groups were made using Shapiro-Wilk tests to assess the normality of distribution and homogeneity of variance for quantitative variables. To compare groups, Student's *t*-test or two-way analysis of variance (ANOVA) for continuous and discrete variables with normal distribution were applied. Student-Newman-Keuls method was used for multiple comparisons. The Wilcoxon rank sum test was used to assess quantitative data of skewed distribution or non-homogenous variance. For categorical variables, chi-square test or Fisher's exact test as appropriate was applied for comparisons. Survival estimates curves were obtained using Kaplan–Meier method. The multivariate Cox proportional hazards model was used to analyze the relationship between survival and prognostic indices. The following variables were included in the multivariable

analysis: sex, age ≥ 50 years, optimal GDMT, device therapy, LVEF ≥ 40%, systolic blood pressure (SBP) < 100 mmHg, diastolic blood pressure (DBP) < 60 mmHg, Heart rate (HR) < 60 beats per minute (bpm), moderate to severe mitral regurgitation (MR), NYHA class III–IV, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), admission to cardiology ward, IDCM as the primary diagnosis, left bundle-branch block (LBBB), atrioventricular block (AVB), admission to intensive coronary care unit (ICCU), intravenous (IV) inotropic therapy, permanent atrial fibrillation (AF). A two-tailed *P*-value of < 0.05 was required for statistical significance. All analyses were conducted using SPSS 20.0 (SPSS, Inc., Chicago, Illinois) statistical package.

3 Results

3.1 Patient characteristics

Baseline characteristics are shown in Table 1. A total of

Table 1. Characteristics of the study population according to treatment-defined groups.

Variable	Optimal guideline-directed medical therapy group (*n* = 617)	Non-optimal guideline-directed medical therapy group (*n* = 766)	*P*-value
Male	421 (68.2%)	516 (67.4%)	0.39
Age, yrs	54.76 ± 13.6	56.24 ± 14.7	0.05
Year of admission			< 0.01
2009–2010	108 (17.5%)	221 (28.8%)	
2011–2012	140 (22.6%)	198 (25.8%)	
2013–2014	214 (34.7%)	224 (29.3%)	
2015–2016	155 (25.2%)	123 (16.1%)	
Admission to cardiology ward	554 (89.8%)	509 (66.4%)	< 0.01
CKD	10 (1.6%)	31 (4.3%)	< 0.01
COPD	40 (6.5%)	91 (11.9%)	< 0.01
LBBB	124 (20.1%)	481 (10.6%)	< 0.01
AF	123 (19.9%)	179 (23.4%)	0.07
AVB	40 (6.5%)	50 (6.5%)	0.53
Moderate to severe MR	269 (43.6%)	342 (44.6%)	0.36
SBP on admission, mmHg	116.0 ± 16.2	112.1 ± 17.1	< 0.01
DBP on admission, mmHg	74.8 ± 12.0	71.7 ± 11.9	< 0.01
HR on admission, bpm (*n* = 1367)	86.0 ± 21.7	84.8 ± 21.5	0.08
LVEF (*n* = 1109)	32.7% ± 11.3%	34.4% ± 13.7%	0.02
LVEDD, mm (*n* = 1054)	66.1 ± 9.2	64.9 ± 9.9	0.04
LAD, mm (*n* = 1034)	44.5 ± 7.8	44.8 ± 8.5	0.52
NYHA III–IV	421 (68.2%)	526 (68.7%)	0.45
SBP < 100 mmHg (*n* = 1369)	82 (13.3%)	171 (22.7%)	< 0.01
DBP < 60 mmHg (*n* = 1369)	35 (5.7%)	83 (11.0%)	< 0.01
HR < 60 bpm (*n* = 1367)	42 (6.8%)	73 (9.7%)	0.03
In-hospital stay, day	9.76 ± 5.0	10.75 ± 7.3	< 0.01
IDCM as the primary diagnosis	503 (81.5%)	498 (65.0%)	< 0.01
Admission to ICCU	83 (13.5%)	108 (14.1%)	0.39
Medications (*n* = 1383)			
ACEI/ARB	617 (100%)	219 (28.6%)	< 0.01
β-blockers	617 (100%)	205 (26.7%)	< 0.01
Aldosterone receptor antagonists	482 (78.2%)	440 (57.4%)	< 0.01
Loop diuretics	410 (66.6%)	375 (49.3%)	< 0.01
Digitalis	264 (43%)	259 (33.8%)	< 0.01
Intravenous Inotropic therapy	66 (10.7%)	103 (13.4%)	0.07
Device therapy	129 (20.9%)	66 (8.6%)	< 0.01

Data are presented as means ± SD or *n* (%). ACEI: angiotensin-converting enzyme inhibitor; AF: atrial fibrillation; ARB: angiotensin receptor blocker; AVB: atrioventricular block; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DBP: diastolic blood pressure; HR: heart rate; ICCU: intensive coronary care unit; IDCM: idiopathic dilated cardiomyopathy; LAD: left atrial diameter; LBBB: left bundle-branch block; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; NYHA: New York Heart Association; SBP: systolic blood pressure.

1441 IDCM patients were enrolled, 68% were men, and the average age was 55 ± 14 years. Mean left ventricular end-diastolic diameter (LVEDD) was 65.6 ± 9.7 mm, LVEF was 33.4% ± 12.5%, and mean left atrial diameter was 44.8 ± 8.3 mm; moderate to severe MR was diagnosed in 633 patients (44%) and NYHA III–IV accounted for the majority (70%) of patients, according to the NYHA functional classification system. Patients with concomitant AF, LBBB and AVB were 22%, 14.5%, and 5.7%, respectively. The majority of patients (76%) were admitted to the cardiology ward. The average length of hospital stay was 10.2 ± 6.5 days. Admission to ICCU was required in 15% of patients during their hospital stay. IV inotropic therapy was indicated in 13% of patients. In-hospital mortality rate was around 4%.

From 2009 to 2016, the incidences of the following patient categories increased: patients who were admitted to the cardiology ward, who required intravenous inotropic therapy and those with moderate to severe MR, AF and LBBB. While the proportion of patient with NYHA III–IV class and those who were rescued in ICCU decreased (Table 2).

3.2 IDCM therapies and its temporal trends

Prescription rates of guideline-recommended drugs and devices in IDCM patients during the study period are presented in Figure 1. The prescription rate of the following

Table 2. Baseline characteristics of IDCM patients categorized by the year of admission.

Variable	2009–2010 (*n* = 351)	2011–2012 (*n* = 353)	2013–2014 (*n* = 450)	2015–2016 (*n* = 287)	*P*-value
Male	243 (69.2%)	233 (66.0%)	312 (69.3%)	187 (65.2%)	0.52
Age, yrs	56.81 ± 14.7	54.62 ± 14.2	55.30 ± 14.4	55.92 ± 13.8	0.2
Admission to cardiology ward	244 (69.5%)	283 (80.2%)	342 (76.0%)	231 (80.5%)	< 0.01
LVEDD, mm	65.7 ± 9.7	64.4 ± 8.8	65.9 ± 10.0	66.2 ± 9.9	0.13
LVEF	33.1% ± 11.3%	34.1% ± 12.6%	33.2% ± 12.8%	33.4% ± 12.9%	0.75
LAD, mm	46.0 ± 9.3	45.0 ± 7.9	44.4 ± 8.4	44.5 ± 8.1	0.22
AF	49 (14.0%)	106 (30.0%)	95 (21.1%)	70 (24.4%)	< 0.01
SBP on admission, mmHg	114.0 ± 16.3	113.1 ± 17.1	114.2 ± 17.2	112.7 ± 16.9	0.60
DBP on admission, mmHg	73.0 ± 11.7	72.9 ± 12.2	73.2 ± 12.3	72.1 ± 12.4	0.66
HR on admission, bpm	85.9 ± 21.7	86.7 ± 23.9	84.5 ± 21.4	83.5 ± 19.1	0.23
LBBB	22 (6.3%)	51 (14.4%)	82 (18.2%)	54 (18.8%)	< 0.01
LVEF ≥ 40%	38 (10.8%)	66 (18.7%)	98 (21.8%)	69 (24.0%)	< 0.01
Moderate to severe MR	136 (38.7%)	156 (44.2%)	189 (42.0%)	152 (53.0%)	0.03
NYHA III–IV	269 (79.4%)	260 (73.9%)	299 (66.9%)	173 (60.7%)	< 0.01
In-hospital stay, day	9.6 ± 6.6	10.1 ± 6.3	10.2 ± 6.1	11.2 ± 7.1	0.02
Admission to ICCU	73 (20.8%)	66 (18.7%)	52 (11.6%)	26 (9.1%)	< 0.01
Intravenous inotropic therapy	27 (7.7%)	53 (15.0%)	60 (13.3%)	53 (18.5%)	< 0.01

Data are presented as means ± SD or *n* (%). AF: atrial fibrillation; DBP: diastolic blood pressure; HR: heart rate; ICCU: intensive coronary care unit; IDCM: idiopathic dilated cardiomyopathy; LAD: left atrial diameter; LBBB: left bundle-branch block; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; NYHA: New York Heart Association; SBP: systolic blood pressure.

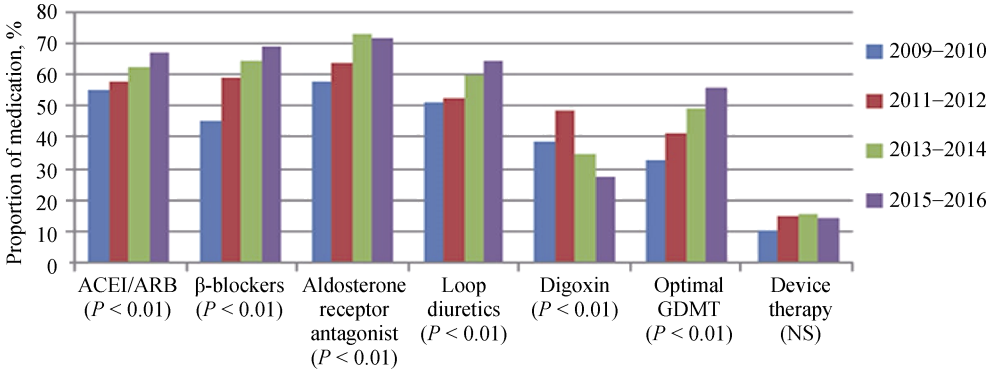

Figure 1. The implementation rate of pharmacological and device therapy based on the year of admission. From 2009 to 2016, the prescription rate of ACEI/ARB, β-blockers, aldosterone receptor antagonist and diuretics increased, whereas the prescription rate of digoxin decreased and device therapy remained constant. ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; AVB: atrioventricular block; GDMT: guideline-directed medical therapy; NS: non-significant.

drugs increased: ACEI/ARB, β-blockers, aldosterone receptor antagonist, and diuretics, whereas the prescription rate of digoxin decreased. For instance, ACEI/ARB prescription rate increased significantly from 55% in 2009 to around 57%, 62% and 67% in 2012, 2014 and 2016 respectively ($P < 0.01$). The most obvious trend was observed in β-blockers use, where it increased from 45% in 2009 to 69% in 2016 ($P < 0.01$). The overall proportion of patients with optimal GDMT was around 45%. However, that rate increased progressively throughout the study period from around 33% in 2009 to approximately 41%, 49% and 56% in 2012, 2014 and 2016 respectively ($P < 0.01$). Implantation rate of ICD and CRT remained stable from 2009 to 2016 (14.1% *vs.*14.4%).

3.3 Factors affecting drug prescription in IDCM patients

Logistic regression analysis showed that admission to cardiology ward and device therapy were predictors of better implementation of guideline-directed drug therapy. While older age, SBP < 100 mmHg, HR < 60 bpm, LVEF ≥ 40%, CKD, COPD, IV inotropic therapy, admission to ICCU, and NYHA class IV were predictors of under-prescription of guideline-recommended drugs (Table 3).

3.4 Prognosis of IDCM patients and its affecting factors

The mean follow-up was 35.2 months. All-cause mortality rate was around 31.4%. Multivariate Cox proportional hazards regression model and Kaplan–Meier analysis showed that patients with optimal GDMT had a longer survival than those without (Table 4, Figure 2). However, there was no temporal trend toward improvement in the overall long-term prognosis of IDCM patients throughout the study period (Figure 3). Furthermore, LVEF ≥ 40%, device therapy, and admission to a cardiology ward were independently associated with a better prognosis (Table 4, Figure 2). On the other hand, age ≥ 50 years, SBP < 100 mmHg, NYHA class III–IV, IV inotropic therapy, and AF were shown to be independent predictors of poor prognosis (Table 4). Of note, analysis of baseline characteristics of patients lost to follow-up and those with frequent follow-up revealed that there were few differences between the two groups. Compared to patients with frequent follow-up, those lost to follow-up were younger (53 ± 14 *vs.* 56 ± 14) with slightly worse left ventricular function (31.7 ± 11.5 *vs.* 33.9 ± 12.8), moderately less chances to be admitted to a cardiology ward (71% *vs.*78.%) and higher AF occurrence rate (22.9% *vs.*17%). However, other features were similar in both patient groups (Table 5).

Table 3. Multivariate cox regression analysis of factors affecting the prescription rate of guideline-recommended drugs.

Variable	Hazard Ratio (95% CI)	*P*-value
SBP < 100 mmHg	0.418 (0.589–0.418)	< 0.001
HR < 60 bpm	0.573 (0.924–0.356)	0.022
LVEF ≥ 40%	0.713 (0.992–0.512)	0.045
COPD	0.628 (0.987–0.399)	0.044
CKD	0.367 (0.827–0.163)	0.016
Admission to ICCU	0.585 (0.863–0.397)	0.007
Intravenous inotropic therapy	0.656 (0.982–0.438)	0.041
NYHA IV	0.587 (0.800–0.431)	0.001
Admission to cardiology ward	4.530 (6.449–3.182)	< 0.001
Device therapy	2.091 (3.063–1.427)	< 0.001

CI: confidence interval; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; HR: heart rate; ICCU: intensive coronary care unit; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; SBP: systolic blood pressure.

4 Discussion

The present study describes the temporal trends in the baseline characteristics and the prescription rate of guideline-recommended drugs, and its impact on the prognosis in patients with IDCM. The results of the present study identify an improvement in the prescription rates for guideline-recommended drugs, including ACEI/ARB, β-blockers, and aldosterone receptor antagonists. The study also demonstrates that the following patient category had an improved prognosis: patients with optimal GDMT, with LVEF ≥ 40%, with device therapy, and those admitted to a cardiology ward.

Heart failure treatment is continuously evolving and has led to incredible achievements during the past decades. The

Table 4. Multivariate cox regression analysis of prognostic factors affecting all-cause mortality in IDCM patients.

Variable	Hazard Ratio (95% CI)	*P*-value
Age > 50 yrs	1.353 (1.695–1.080)	0.08
AF	1.401 (1.783–1.101)	0.006
SBP < 100 mmHg	1.434 (1.848–1.113)	0.05
NYHA III–IV	1.607 (2.138–1.208)	< 0.001
Intravenous inotropic therapy	2.398 (3.155–1.823)	< 0.001
LVEF ≥ 40%	0.676 (0.935–0.488)	0.018
Optimal GDMT	0.564 (0.710–0.449)	< 0.001
Device therapy	0.666 (0.947–0.468)	0.024
Admission to cardiology ward	0.704 (0.909–0.545)	0.007

AF: atrial fibrillation; CI: confidence interval; GDMT: guideline-directed medical therapy; IDCM: idiopathic dilated cardiomyopathy; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; NYHA: New York Heart Association; SBP: systolic blood pressure.

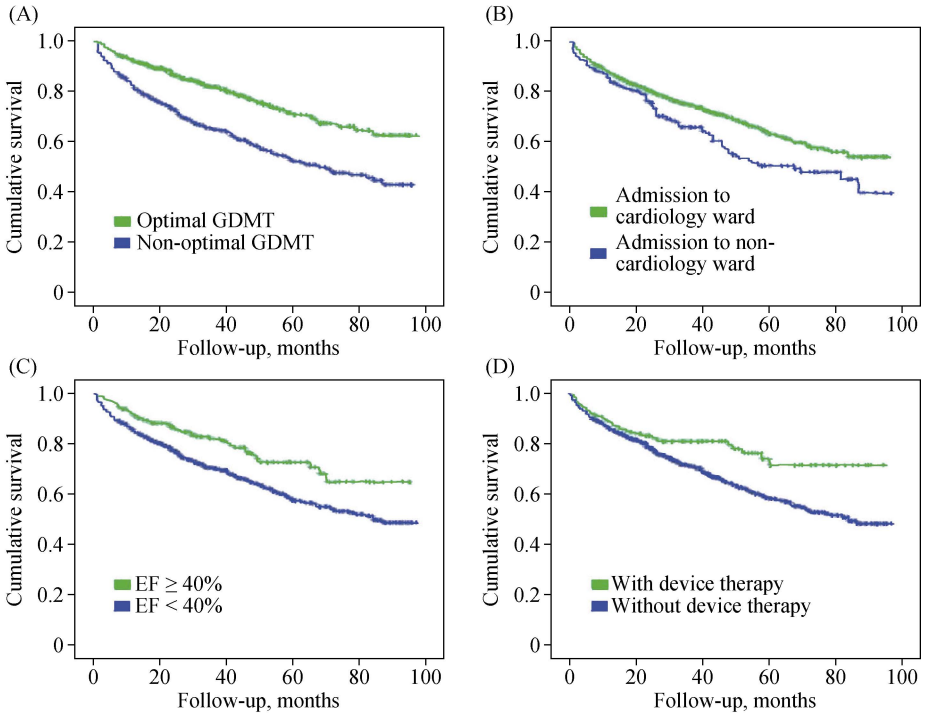

Figure 2. Kaplan-Meier curve of cumulative survival free of all-cause mortality according to (A): with optimal GDMT and non-optimal GDMT groups; (B): admission to cardiology and non-cardiology ward groups; (C): EF < 40% and EF ≥ 40% groups; and (D) the presence and absence of device therapy groups. Patient with optimal GDMT, admitted to cardiology ward, with EF ≥ 40% and those with device therapy had better survival. EF: ejection fraction; GDMT: guideline-directed medical therapy.

Table 5. Comparison of baseline characteristics of patients lost to follow-up and those with frequent follow-up.

Variable	Lost to follow-up group (n = 241)	Frequent follow-up group (n = 1142)	P-value
Male	166 (68.9%)	771 (67.5%)	0.68
Age, yrs	53 ± 14.4	56.24 ± 13.9	0.002
Admission to cardiology ward	171 (71.0%)	892 (78.1%)	0.012
CKD	6 (2.5%)	37 (3.2%)	0.54
COPD	27 (11.2%)	104 (9.1%)	0.31
AF	41 (17.0%)	261 (22.9%)	0.04
Moderate to severe MR	101 (41.9%)	510 (44.7%)	0.43
SBP on admission, mmHg	114.0 ± 17.4	113.8 ± 16.7	0.85
DBP on admission, mmHg	73.5 ± 12.5	73.7 ± 11.9	0.56
HR on admission, bpm (n = 1367)	86.5 ± 22.8	84.6 ± 21.4	0.22
LVEF (n = 1109)	31.7% ± 11.5%	33.9% ± 12.8%	0.039
LVEDD, mm (n = 1054)	65.6 ± 9.4	65.5 ± 9.6	0.89
LAD, mm (n = 1034)	45.9 ± 8.7	44.5 ± 8.1	0.61
NYHA III–IV	163 (67.6%)	784 (68.7%)	0.75
SBP < 100 mmHg (n = 1369)	47 (20.0%)	206 (18.2%)	0.51
DBP < 60 mmHg (n = 1369)	20 (8.5%)	98 (8.6%)	0.94
HR < 60 bpm (n = 1367)	19 (8.2%)	96 (8.5%)	0.87
In-hospital stay, day	10.4 ± 7.7	10.2 ± 6.1	0.71
IDCM as the primary diagnosis	167 (69.3%)	834 (73.0%)	0.23
Admission to ICCU	36 (14.9%)	155 (13.6%)	0.57

Data are presented as means ± SD or n (%). AF: atrial fibrillation; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DBP: diastolic blood pressure; HR: heart rate; ICCU: intensive coronary care unit; IDCM: idiopathic dilated cardiomyopathy; LAD: left atrial diameter; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; MR: mitral regurgitation; NYHA: New York Heart Association; SBP: systolic blood pressure.

use of ACEI/ARB, β-blockers and aldosterone receptor antagonists has been established during the past 3 decades, following major RCTs[3–7,16,17] and their subsequent impact on international HF guidelines.[13,15]

In our study, the prescription rates of guideline-recommended drugs increased significantly throughout the study period; this is probably related to improved awareness of the disease and better knowledge of international guidelines and the results of major clinical trials. Similar to some previously published studies,[18,19] we found that there is a marked increase in the rate of prescription of beta-blockers compared to other medications; this reflects the physicians' understanding of the important role of using beta blockers in HF management. Although prescription rates of recommended HF drugs have increased, the situation remained suboptimal for these drugs compared to the rates reported in landmark clinical trials. A HF team comprising cardiologists and well-trained HF nurses working under a standardized therapeutic and follow-up platform is mandatory for better implementation of guideline-recommended therapies. Several observational studies reported similar findings and demonstrated that the use of GDMT in the daily practice has not been consistent with the rates reported in major RCTs.[12,19,20] This finding, however, can be partially explained by the gaps that exist between the population characteristics of RCTs and daily practice HF populations.[20] Moreover, lower prescription rates of recommended therapies may be attributable to the adverse effects of HF medications and patients' co-morbidities, such as the higher hyperkalemia incidence that was reported after publication of the RALES study.[22] Nevertheless, physician-related factors cannot be excluded. A visit to a cardiologist, longer than 15 minutes has been reported to be associated with a better prescription of guideline-recommended HF medications.[20]

Our multivariate analyses demonstrate that old age was a predictor of under-prescription of guideline-recommended drugs. This result is consistent with previous studies that reported advanced age of HF patients as a major contributing factor in lack of adherence to guidelines.[12,19,23] Furthermore, the prescription rate of HF drugs was less in patients with LVEF ≥ 40%. Similarly, a previous cohort study has demonstrated that HF medications were prescribed less frequently as the LVEF was more preserved.[19] The negative impact of LVEF ≥ 40% on the prescription rate of HF drugs is probably due to the fact that these patients have HF and a mid-range EF (HFmrEF) and tend to be less symptomatic resembling to some extent the clinical characteristics of patients with HF and preserved ejection fraction (HFPEF) in which the contemporary HF drugs have not been shown to improve their outcome.[24,25] Moreover, our results, which are similar to many previous studies,[12,19,26] suggest that prescription of HF drugs is reduced in patients with SBP < 100 mmHg, HR < 60 beats/min, COPD, CKD as well as in old and frail patients. This can be partially explained by these co-morbidities being relative contraindications to HF medications. On the other hand, our results show that patients admitted to cardiology ward, and those with device therapy had better implementation of guideline-recommended medical therapy. Apparently, cardiologists are more enthusiastic in prescribing HF medications. Regarding device therapy, the ICD/CRT implantation rate remained steady throughout the study period; this is probably due to the lack of health insurance coverage of these devices and the underestimation of their role in the treatment of DCM patients.

The present study demonstrated that patients with optimal GDMT with ACEI/ARB, β-blockers, and aldosterone receptor antagonists showed better survival than those without (Figure 2). This finding is consistent with previous studies on Japanese and European patients; that patients managed with ACEI/ARBs and β-blockers showed a considerable relative risk reduction in cardiovascular mortality compared with those who were mainly treated with diuretics and digoxin.[8–10] Our results are also in agreement with other reports which have shown that adherence to HF medications significantly reduces mortality and re-admission rates to the hospital at 30 days.[27] Therefore, a better implementation of GDMT with the appropriate drug dosing is crucial for improving the survival of HF patients, including those with IDCM. Nevertheless, no temporal tends toward better prognosis was observed throughout the study period (Figure 3). This can be explained by the suboptimal overall implementation of recommended therapies, the relatively

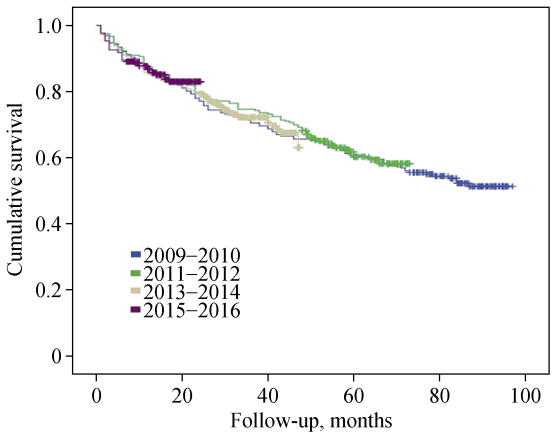

Figure 3. Kaplan-Meier curve of cumulative survival free of all-cause mortality according to the year of admission. The survival rate did not improve over time from 2009 to 2016.

short follow-up time and patients' frailty (the average LVEF was 33.4% ± 12.5%, and around 70% of enrolled patients were in NYHA III–IV functional class).

In multivariate Cox regression model, several IDCM patient subgroups had better survival. In particular, admission to cardiology ward was associated with improved prognosis. This can be explained by that admission to a cardiology ward is associated with better treatment implementation (Table 3). Furthermore, the improvement in prognosis was noted in patients with LVEF ≥ 40%. This finding is consistent with the previous studies which reported that improvement was observed in DCM patients with LVEF > 40%, but not in those with LVEF ≤ 40%,[10] and that in-hospital mortality was improved over time in HF patients with preserved LVEF, but not in those with reduced LVEF.[28] In addition to that, device therapy was also associated with better prognosis. In a previous meta-analysis of 6 randomized trials of device therapy for the treatment of HF, patients with ICDs alone and ICD+CRT had improved survival compared to no CRT-no ICD patients.[29] This is probably attributable to the positive impact of device therapy on improved implementation of pharmacological therapy in this patient group as shown in Table 3, and the role of CRT in reversing left ventricular (LV) remodeling and ICD in preventing sudden cardiac death.[30] On the other hand, age ≥ 50 years, SBP < 100 mmHg, NYHA class III–IV, IV inotropic therapy, and AF were shown to be independent predictors of poor prognosis. These factors are known indicators of worse cardiac function and limiting factors of treatment implementation, and subsequently poor prognosis.

Of note, most of the baseline characteristics were similar for both patients lost to follow-up and those with frequent follow-up (Table 5). However, few variations were noticed between the two patients groups; patients lost to follow were younger with slightly lower LVEF and lower rates of admission to a cardiology ward as well as higher AF occurrence rates. The relatively younger age of patients lost to follow up which is an indicator of a better prognosis can, to some extent, counterbalance the negative effect of other factors on the prognosis. Moreover, lower rates of admission to a cardiology ward in patients lost to follow-up group may be a cause of being lost to follow-up in this patient group rather than being only a negative prognostic indicator.

It is notable that there was a trend toward admission of patients with less severe cardiac dysfunction and lower NYHA class, and trends toward increased admission to a cardiology ward with the years. This trend presumably suggests an improved understanding of the relevant guidelines regarding IDCM diagnosis and management, increased awareness of the disease and enhanced guideline-driven triage of patients when seeking medical care.

4.1 Limitations

Our findings should be interpreted in the light of several considerations: First, our study is a retrospective observational study at one center in south-west China; we need to be cautious when extrapolating the present findings to other cohorts. Second, we evaluated IDCM treatment based on the discharge medications from data collected by the hospital electronic medical record system. This may introduce a selection bias. Third, as with all observational studies, there remain potential confounding factors that we could not account for in our examination of treatment and outcome. Fourth, the relatively short follow-up period requires cautious interpretation of our regression estimates. Fifth, the data regarding the levels of plasma brain natriuretic peptide, medication doses and cardiovascular-related mortality lacked for the majority of patients, therefore, were not included in the analysis. Finally, only IDCM patients were included in our study; therefore, the results should not be extended to patients with other causes of impaired left ventricular function.

4.2 Conclusion

The study demonstrates an improvement in prescription rates of guideline-recommended medications in IDCM patients. Nevertheless, it remains suboptimal, and there is still some room for improvement. Many factors including age, specialist therapy, co-morbidity, and type of HF influenced the rate of prescription of the recommended medications. The prognosis of patients with optimal GDMT was better than those without. However, the most obvious improvement was observed in patients with LVEF ≥ 40%, device therapy, and those admitted to a cardiology ward. There was a trend toward admission of patients with less severe cardiac dysfunction and lower NYHA class, and trends toward increased admission to a cardiology ward over the study period.

Acknowledgments

This study was supported by grants from the National Natural Science Foundation of China (No.81400267 & No.81370219) and the Sichuan Provincial Department of Science and Technology (2016FZ0084). The authors had no conflicts of interest to disclose.

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