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Research paper

Prescription in patients with chronic heart failure and multimorbidity attended in primary care

Eva Frigola-Capell MSc
Scientific Institute for Quality of Healthcare, Radboud University Nijmegen Medical Centre, The Netherlands; Instituto Universitario Avedis Donabedian, Spain; Universitat Autònoma de Barcelona, Spain; Red de Investigación en Servicios de Salud en Enfermedades Crónicas (REDISSEC), Spain.

Jose M Verdú-Rotellar PhD MD
Instituto Catalán de la Salud, Barcelona, Spain

Josep Comin-Colet PhD MD
Departamento de Cardiología, Hospital del Mar, Barcelona, Spain

Josep Davins-Miralles PhD MD
Subdirecció General de Serveis Sanitaris, Departament de Salut, Generalitat de Catalunya, Spain

Eduardo Hermosilla
Statistician, Primary Care University Research Institute (IDIAP Jordi Gol), Spain

Michel Wensing PhD
Professor, Scientific Institute for Quality of Healthcare, Radboud University Nijmegen Medical Centre, The Netherlands

Rosa Suñol PhD MD
Professor, Instituto Universitario Avedis Donabedian, Spain; Universitat Autònoma de Barcelona, Spain; Red de Investigación en Servicios de Salud en Enfermedades Crónicas (REDISSEC), Spain

ABSTRACT

Background Multimorbidity and polypharmacy pose challenges to improving the quality of care.
Objectives To determine the association between prescription of recommended treatment in ambulatory patients with chronic heart failure and multiple comorbidities and hospitalisation events.
Design A population-based retrospective cohort study in Catalonia (north-east Spain).
Participants We included 7173 newly registered patients with chronic heart failure (59% women; mean [SD] age 76.3 [10.7] years). Patients were selected from the electronic patient records of primary care practices and followed for three years.
Outcome measures Prescription of angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs) and beta-blockers (BBs).
Results Prescription of ACEI/ARBs in patients managed in primary care without a hospitalisation event during the follow-up rose from 50.8 to 83.5% for 0 and $\geq$ 4 comorbidities, respectively, and for ACEI/ARBs and BB from 13.1 to 30.6% for 0 and $\geq$ 4 comorbidities respectively. Patients with a hospitalisation event were treated more often (ACEI/ARBs or 1.47 [1.17 to 1.85]; ACEI/ARBs and BB or 1.41 [1.17 to 1.69]). Comorbid conditions receiving more treatment were hypertension (ACEI/ARBs or 3.75 [3.33 to 4.22]; ACEI/ARBs and BB or 1.40 [1.23 to 1.59]), diabetes mellitus (ACEI/ARBs or 1.79 [1.57 to 2.04]; ACEI/ARBs and BB or 1.33 [1.18 to 1.49]) and ischaemic heart disease (ACEI/ARBs or 1.25 [1.10 to 1.42]; ACEI/ARBs and BB or 3.01 [2.68 to 3.38]).
Conclusion Prescription of recommended treatment in patients with chronic heart failure increased as the number of comorbidities increased. Family physicians can provide equivalent care to more complex patients and those less complex, according to the number of comorbidities.

Keywords: comorbidity, health services, heart failure, prescription, primary healthcare

How this fits in with quality in primary care

What do we know?
The literature reports that lack of confidence for initiating treatment with angiotensin-converting enzyme inhibitors (ACEIs) in patients who are often elderly and frail, with comorbidity and polypharmacy may generate an increase of referrals to specialist care who are more likely to prescribe in chronic heart failure (CHF) patients.

What does this paper add?
Our study showed that prescription by family practitioners (FPs) of recommended treatment in CHF patients increased as the number of comorbidities increased, which suggests that FPs can provide equivalent care to more complex compared to less complex patients, as measured by the number of comorbidities.

Introduction

Chronic heart failure (CHF) is a prevalent and costly condition. In many industrialised countries, costs represent between 1 and 2% of total healthcare expenditure, and up to two thirds of costs are related to hospitalisations.[1,2] Because the prevalence of CHF increases with age and the elderly population is growing it is expected to be a heavier burden in future.[3,4] Appropriate treatment of heart failure effectively improves survival and quality of life.[5] International guidelines recommend widespread use of both angiotensin-converting enzyme inhibitors (ACEIs) and beta-blockers (BBs) to improve symptoms and survival unless a specific contraindication exists.[6,7] Despite these recommendations treatment of patients with CHF remains suboptimal.[8,9]

CHF is mostly managed in primary care, where the diagnosis is often initiated[8,10] and the condition followed up. Several studies using qualitative methods have reported that the complexity of these patients, because of ageing, comorbidities and uncertainty about diagnosis, are self-reported by family physicians (FPs) to be barriers to the use of recommended treatments.[11,12] Whether this is consistent with FPs' real clinical performance has not yet been reported in large community studies. Previous trials showed that specialist care increases the probability of receiving the recommended treatment for CHF when compared with usual care by FPs, but the complexity of these patients in terms of comorbidities was not considered.[13,14] The aim of this study was to determine the association between prescription of recommended treatments in ambulatory patients with CHF and concomitant comorbidities, with or without hospitalisation events, in Catalonia (north-east Spain).

Methods

Study design and setting

We conducted a population-based retrospective cohort study using the data collected in a project published in the Clinical Trials database (NCT00792402). Briefly, this project used a non-equivalent controlled before and after quasi-experimental design with a population-based approach to evaluate the impact of a clinical practice guideline on CHF in two regions of Catalonia (a Spanish region with a population of 7 210 508).[15] For this study, we combined data from both arms, including intervention (urban) and control (rural) regions. Despite urbanisation differences, both regions shared the same organisational features (Table 1).[16]

Participants

We selected patients newly registered with a diagnosis of CHF (codes I11.0, I13.0, I13.2, I50, I50.0, I50.0, I50.1, I50.9 and P29.0 according to the *International Classification of Diseases Tenth Revision* used in primary care) during the study follow-up (January 2005 to December 2007). Registration of the diagnosis was done by FPs using electronic patient records. We included patients over 30 years old because we did not have younger patients fulfilling the inclusion criteria. We only included patients with information recorded in their electronic patient records for all measures that we analysed. At practice level, we included all primary care practices (PCPs) in the rural area. In the urban area, we included just those PCPs participating in the project described above (half of all the PCPs in the urban area), which were selected from a previous randomisation process.

Table 1 Organisational features of participating primary care practices

Features	
Healthcare provider	Catalan Health Institute care provider for the 80% of the population in the Autonomous Community of Catalonia (population of 7 210 508) and belongs to the Spanish National Health System
Coverage	Universal coverage for either primary and secondary care
Funding	State funded through general taxes. Coexistence with private sector
Access to care	Every citizen is registered with a family physician who acts as a gatekeeper to specialised care
Medical records	Electronic patient records system
Provision of care	Network of practices that behave as geographical and administrative units in which physicians are part of the staff (from 4 to 36 physicians per practice depending on the population attended)
	Single healthcare centres (urban regions); single healthcare centres and satellite offices (rural regions)
Diagnosis process/ integrated care	Cardiologists and other specialised services attending practices weekly since 1990, to support physicians on the diagnosis process, management and training

Measures

Our primary measures were patients with a prescription of ACEI or ARBs; or alternatively ACEI or ARBs with BB if a diagnosis of asthma was not present. We collected this information at the end of each year of the follow-up period. Our primary predictors were the total number of conditions affecting each patient and recorded hospital events due to cardiovascular causes. We selected those comorbidities recorded in the primary care electronic patient record associated with worsening CHF prognosis.[17] We defined these on the basis of the *International Classification of Diseases Tenth Revision* codes used in our primary care setting including hypercholesterolemia, hypertension, diabetes mellitus, ischaemic heart disease, chronic obstructive pulmonary disease (COPD) and chronic kidney disease (CKD) codes recorded either before or during the period of our study. We considered any hospital events due to cardiovascular causes as a primary diagnosis at discharge during the period of follow-up (codes 398–39899, 402–40291, 428–4289, 9971, 40390–40391, 404–40493, 411–41189, 414–4149 and V173 according to the *International Classification of Diseases Ninth Revision* used in hospital databases). Other covariates considered were patient age, gender and region. We obtained age by calculating the difference between the initial date of our study (1 January 2005) and date of birth. CHF diagnosis was recorded by FPs, which in Catalonia is usually done after consultation with a cardiologist (Table 1) or after hospital admission, although the source of the diagnosis was not registered in the electronic patient record. We also collected patients with diuretics prescription in each group. We also considered mortality from any cause.

Data sources

The central database of the Catalan Health Institute supplied us with all patient information required for this study, as recorded by FPs in electronic patient records. Patient information related to hospital admissions was collected from the Division of Demand and Activity Registries (Minimum Basic Data Set for Acute Care Hospitals; MBDS), of the Catalan Health Service, where Catalan hospitals are committed to send in their data for reimbursement. Information on mortality was provided by the Mortality Register of Catalonia and we combined this information with the FPs mortality register on patient status. We were able to link all data from the three database sources because every Catalan citizen has a unique and anonymous identification number for healthcare use. The informatics officers responsible for data abstraction did not participate in the subsequent data analysis.

Statistical methods

Descriptive data for age, gender and prevalence of relevant variables were calculated for all patients and

according to hospitalisation events. Chi-square and Pearson tests, for categorical and continuous variables, respectively, were used to conduct bivariate analysis comparing patients with and without a hospitalisation event. The probability of the total number of comorbidities and hospitalisation events associated with primary measures (ACEI/ARBs, ACEI/ARBs and BB) was reported using multivariable and multilevel logistic regression models. For this purpose, we merged the six comorbidities included in our study into four categories (one, two, three and four or more comorbidities) to increase the power of the analysis because some of the categories did not have enough patients; we considered this variable as categorical. Primary measures were converted into two dichotomous variables for the whole follow-up period (prescription of ACEI or ARBs at any time during the follow-up; or ACEI/ARBs and BB at any time during the follow-up).

Because patients were selected from PCPs, we established those as random units to control for the variability associated with primary care clinical practice. Next, we established a conditional basal model with the covariates region and hospitalisation. Using a step-forward method we introduced each candidate variable (the number of comorbidities and hospitalisation) into the basal model and compared the two models using the likelihood ratio test. The final multivariate regression model included the basal model together with the significant candidate variables. All tests were two-tailed and significant at 5% level ($\alpha = 0.05$). Patients with missing values for any of the relevant variables were excluded from the analysis. We also calculated the probability of each comorbidity receiving treatment. All analyses included all patients (including deceased) and those who survived the study period; we did not find significant differences in prescriptions.

Missing values were calculated (0.3% of our final sample) and found to be not relevant for the results of our analysis.

All analyses were undertaken with use of StataCorp. 2009 (Stata Statistical Software: Release 11, StataCorp LP, College Station, TX, USA).

Results

Initially, we identified 20 576 potentially eligible patients with a diagnosis of CHF from 68 PCPs, covering a population of 1 522 564 listed citizens. According to our sampling and inclusion criteria, we did not study cases from 25 urban PCPs, and we excluded patients diagnosed before our study period (3591), those with an unknown diagnosis registration date (2221), and 23 patients for whom there was no information on the relevant variables. Our final sample included 4735 patients from urban areas (covering 558 515 inhabitants) and 2438 patients from rural areas (covering 480 827 inhabitants).

Patient characteristics and comparison according to hospitalisation event are presented in Table 2. Overall, patients without hospital events had a lower prevalence of comorbidities. The group with hospital events during the follow-up period had significantly more patients on diuretics ($P < 0.001$), ACEI/ARBs ($P < 0.001$) and ACEI/ARBs and BB ($P < 0.001$). We did not find significant differences related to age and gender.

As shown in Table 3, the prescription of recommended treatment in CHF patients increased as the number of chronic conditions increased. For patients managed in primary care without attending hospital, prescription of ACEI/ARBs rose from 50.8 to 83.5% for 0 and ≥ 4 comorbidities, respectively, and for ACEI/ARBs and BB from 13.1 to 30.6% for 0 and ≥ 4 comorbidities, respectively. In patients with hospitalisation events during the follow-up period, prescription of ACEI/ARBs rose from 66.0 to 86.9% for 0 and ≥ 4 comorbidities, respectively, and for ACEI/ARBs and BB from 19.1 to 39.4% for 0 and ≥ 4 comorbidities, respectively.

The multivariable analysis (Table 4) confirmed that patients receiving more treatments were patients with 3 comorbidities (odds ratio [OR] 5.10 [4.12–6.28] for ACEI/ARBs treatment and OR 2.67 [2.10–3.38] for ACEI/ARBs and BB), and ≥ 4 comorbidities (OR 4.90 [3.72–6.47] for ACEI/ARBs treatment and OR 2.95 [2.24–3.89] for ACEI/ARBs and BB), and patients with a hospital event during the follow-up (OR 1.47 [1.17–1.85]) for ACEI/ARBs treatment and OR 1.41 [1.17–1.69] for ACEI/ARBs and BB).

The univariate analysis (Table 5) showed that comorbidities with higher numbers of ACEI/ARBs prescriptions were hypertension (OR 3.75 [3.33–4.22]), diabetes mellitus (OR 1.79 [1.57–2.04]), ischaemic heart disease (OR 1.25 [1.10–1.42]), hypercholesterolemia (OR 1.27 [1.04–1.56]) and CKD (OR 1.17 [1.00–1.37]). Those comorbidities with more ACEI/ARBs and BB prescriptions were ischaemic heart disease (OR 3.01 [2.68–3.38]), hypertension (OR 1.40 [1.23–1.59]), diabetes mellitus (OR 1.33 [1.18–1.49]) and hypercholesterolemia (OR 1.58 [1.32–1.89]).

No significant changes were found when removing deceased patients from the analysis.

Cluster analysis reported 0.5% (95% confidence interval [CI] 0.2–0.7) variability on prescription between PCPs.

Table 2 Patient characteristics

	Overall ($n = 7173$)	No hospital event ($n = 6528$)	Hospital event ($n = 645$)	*P*-value (Pearson)
Age (mean, SD)	76.5 (10.5)	76.5 (10.5)	77.1 (10.4)	0.134
Gender [*n* (%) women]	4202 (58.6)	3835 (58.7)	367 (56.9)	0.193
Hypercholesterolemia *n* (%)	675 (9.4)	614 (9.4)	61 (9.5)	0.944
High blood pressure *n* (%)	5129 (71.5)	4646 (71.2)	483 (74.9)	0.049
Diabetes mellitus *n* (%)	2275 (31.7)	2010 (30.8)	265 (41.1)	< 0.001
Ischaemic heart disease *n* (%)	2023 (28.2)	1757 (26.9)	266 (41.2)	< 0.001
CKD *n* (%)	1132 (15.8)	972 (14.9)	160 (24.8)	< 0.001
COPD *n* (%)	1136 (15.8)	1004 (15.4)	132 (20.5)	0.001
Rural *n* (%)	2438 (34)	2247 (34.4)	191 (29.6)	0.007
Urban *n* (%)	4735 (66)	4281 (65.6)	454 (70.4)	0.007
Patients on diuretics *n* (%)	5654 (78.8)	5069 (77.6)	585 (90.7)	< 0.001
ACE/ARBs in 2005–2007 *n* (%)	5533 (77.1)	4990 (76.4)	543 (84.2)	< 0.001
ACE/ARBs + BB in 2005–2007 *n* (%)	1635 (22.8)	1438 (22)	197 (30.5)	< 0.001
Comorbidities per patient. Median (interquartile range)	2 (1,2)	2 (1,2)	2 (1,2)	–

Table 3 Prescription according to the number of comorbidities and hospitalisation event

Number of comorbidities		Patients taking ACE/ARBs *n* (%)	Patients taking ACE/ARBs and BB *n* (%)
0 ($n = 820$)	No hospital event ($n = 773$)	393 (50.8)	101 (13.1)
	Hospital event ($n = 47$)	31 (66.0)	9 (19.1)
1 ($n = 2314$)	No hospital event ($n = 2149$)	1625 (75.6)	391 (18.2)
	Hospital event ($n = 165$)	131 (79.4)	43 (26.1)
2 ($n = 2299$)	No hospital event ($n = 2122$)	1725 (81.3)	509 (24.0)
	Hospital event ($n = 177$)	158 (89.3)	52 (29.4)
3 ($n = 1223$)	No hospital event ($n = 1066$)	898 (84.2)	309 (29.0)
	Hospital event ($n = 157$)	137 (87.3)	54 (34.4)
≥ 4 ($n = 517$)	No hospital event ($n = 418$)	349 (83.5)	128 (30.6)
	Hospital event ($n = 99$)	86 (86.9)	39 (39.4)

Table includes just patients with a drug prescription. Patients without a prescription are not included.

Table 4 Modelling analysis of the prescription of treatment

	ACE/ARBs in the overall sample	ACE/ARBs and BB in the overall sample
$n = 7173$	OR (95% CI)	OR (95% CI)
1 Comorbidity	2.96 (2.50–3.50)	1.49 (1.18–1.86)
2 Comorbidities	4.27 (3.58–5.08)	2.07 (1.66–2.59)
3 Comorbidities	5.10 (4.12–6.28)	2.67 (2.10–3.38)
4 Comorbidities	4.90 (3.72–6.47)	2.95 (2.24–3.89)
Hospital event	1.47 (1.17–1.85)	1.41 (1.17–1.69)

Table shows that the odds of receiving drug treatment in a multivariable analysis increase as the number of comorbidities increases. Having a hospitalisation event also increases the odds.

Table 5 Prescription for each condition (univariate model)

	OR (95% CI)	*P*-value (LR* test)
ACE/ARBs		
Age	0.99 (0.99–0.10)	0.003
Gender (male)	1,02 (0.91–1.14)	0.705
Hypercholesterolemia	1.27 (1.04–1.56)	0.019
Hypertension	3.75 (3.33–4.22)	< 0.001
Diabetes mellitus	1.79 (1.57–2.04)	< 0.001
Ischemic heart disease	1.25 (1.10–1.42)	0.001
CKD	1.17 (1.00–1.37)	0.049
COPD	0.91 (0.78–1.06)	0.229
Region	0.94 (0.77–1.15)	0.528
Hospital event	1.65 (1.32–2.06)	< 0.001
ACE/ARBs + BB		
Age	0.96 (0.95–0.96)	< 0.001
Gender (male)	1.62 (1.45–1.82)	< 0.001
Hypercholesterolemia	1.58 (1.32–1.89)	< 0.001
Hypertension	1.40 (1.23–1.59)	< 0.001
Diabetes mellitus	1.33 (1.18–1.49)	< 0.001
Ischemic heart disease	3.01 (2.68–3.38)	< 0.001
CKD	1.12 (0.96–1.30)	0.139
COPD	0.63 (0.53–0.74)	< 0.001
Region	0.93 (0.81–1.06)	0.290
Hospital event	1.56 (1.30–1.86)	< 0.001

* Likelihood ratio.
Gender, COPD, and region have no effect on the odds of receiving ACE/ARBs. CKD and region have no effect on the odds of receiving ACE/ARBs and BB. For the rest, in a univariate analysis, having a specific condition increased the odds of a drug prescription.

Discussion

In our cohort of patients from PCPs registered with the diagnosis of CHF, we found that the prescription of ACEI/ARBs and ACE/ARBs with BB increased as the number of comorbidities increased. These prescriptions were also more prevalent in patients who had attended hospital. Hypertension, diabetes mellitus and ischaemic heart disease were comorbid conditions significantly more associated with higher rates of prescribing.

Previous studies which have compared the clinical performance of FPs against cardiologists have found that hospitalisation and cardiologist care increased the odds of receiving ACEI and BB.[8,9,13,14,18] The justification self-reported by FPs includes difficulties with establishing a diagnosis and the lack of confidence in initiating treatment with ACEI, partly because of their adverse effects in patients who are often elderly and frail, with comorbidity and polypharmacy.[11] Nevertheless, our study showed that the relationship between FPs prescribing recommended treatments and the number of conditions remained positive, which suggests that FPs can provide equivalent care for more complex patients with greater comorbidities compared with less complex patients. Patients attending hospital had a higher probability of receiving treatment.

Similar trends were found in a previous study that focused on the quality of care for several chronic conditions rather than a single disease.[19] In this study, a positive relationship between quality of care and the number of chronic conditions was found, probably because these patients had more opportunities to receive care. Also, patients who had seen a relevant specialist received higher quality of care. Another trial focusing on patients with CHF managed in primary care reported no association between the number of comorbidities and the prescription of evidence-based pharmacotherapy.[18] These different results could be explained by differences in the comorbid conditions analysed and how these were measured.

Previous studies which have analysed the effect of comorbidities on prescribing have reported that a diagnosis of ischaemic heart disease increased the odds for prescription, whereas age and respiratory or pulmonary disease decreased it. [8,9,18] Our results were in line with this. We also reported a positive effect for hypertension and diabetes mellitus.

Prescription rates achieved in our study were higher than previously reported. In 2002, a European study involving FPs reported that in Spain prescription of diuretics was 63%, ACEI/ARBs was 51% and combined therapy with BB was 7%. In our study, prescription rose to 78.8% for diuretics, 77.1% for ACEI/ARBs and 22.8% for combined therapy with BB.[8] This showed that adherence to evidence-based pharmacotherapy had increased although there is still room for improvement.

Our study had some limitations. First, we used a simple count of comorbid conditions as one of our primary predictor variables. This method has been used previously with the disadvantage that it is a crude measure of complexity, because clinicians do not view all coexisting conditions as equivalent in complexity.[19] We identified CHF patients through their FPs' electronic patient records and did not formally validate the diagnosis of CHF because of resource constraints.

Furthermore, we did not have data to show how many patients had echocardiography performed, which would have confirmed the diagnosis and aetiology of CHF and helped in the interpretation of our results.

Therefore, those patients with no hospital event during study follow-up and without a prescription of diuretics (22.4%) may have had an uncertain diagnosis of CHF. Nevertheless our aim was to report on FPs' clinical performance when prescribing in patients with multiple comorbidities, including those with an uncertain diagnosis of CHF because this is what happens in real practice. Also, it is important to take into account our context in which FPs usually register a diagnosis of CHF after specialist confirmation. Specialists are also involved in the diagnosis and management of these patients in the community, and have provided support to FPs as part of an integrated care programme since 1990 (Table 1).[20] Nevertheless, we could not identify the source of diagnosis and could not exclude that the diagnosis of CHF was made by FPs using clinical means alone. Furthermore, we could not report on the severity of the illness, either for the CHF diagnosis or comorbidities, so we may have underestimated the total disease burden.

Despite not having access to those PCPs excluded in the urban region, we assumed that other ethnic or socio-economic difference affecting outcomes (in the urban area) were minimised by our selection process which began from a randomisation for a disease management intervention.

Conclusions

Prescription of recommended treatments in ambulatory patients with CHF increased as the number of comorbidities increased, regardless of hospitalisation events. This study suggests that FPs can provide care to more complex patients which is equivalent to those that are less complex, as determined by the number of comorbidities. Further research should explore patient experiences with drugs, including intolerance, contra-

indications and overall patient willingness to adhere to treatment. This may highlight other barriers which can help physicians and managers on delivering care.

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ETHICAL APPROVAL

The ethics committee of the Catalan Primary Care Research Institute 'IDIAP Jordi Gol', over sighted by the Spanish Ministry of Health approved this study.

PEER REVIEW

Not commissioned; externally peer reviewed.

CONFLICT OF INTEREST

None declared.

ADDRESS FOR CORRESPONDENCE

Eva Frigola-Capell, C/ Provença 293, pral. 08037 Barcelona, Spain. Email: eva.frigola@gmail.com

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