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ORIGINAL RESEARCH

Factors associated with β-blocker initiation and discontinuation in a population-based cohort of seniors newly diagnosed with heart failure

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Purpose: β-Blockers (bisoprolol, carvedilol, and metoprolol) are the cornerstone of heart failure (HF) management. The incidence rate of β-blocker initiation and discontinuation and their associated factors among seniors with a first HF diagnosis were assessed.

Methods: A population-based inception cohort study that included all individuals aged ≥65 years with a first HF diagnosis in Quebec was conducted. β-Blockers initiation among 91,131 patients who were not using β-blockers at the time of HF diagnosis and discontinuation among those who initiated a β-blocker after HF diagnosis were assessed. Stepwise Cox regression analyses were used to calculate hazard ratios (HR) and to identify factors associated with β-blocker initiation and discontinuation.

Results: After HF diagnosis, 32,989 (36.2%) individuals initiated a β-blocker. Of these, 15,408 (46.7%) discontinued their β-blocker during the follow-up. Individuals more likely to initiate a β-blocker were those diagnosed in a recent calendar year (2009: HR, 2.11; 95% confidence interval [CI], 2.00–2.23) and diagnosed by a cardiologist (HR, 1.38; 95% CI, 1.34–1.42). Individuals less likely to initiate were those aged ≥90 years (HR, 0.65; 95% CI, 0.61–0.68) and those with chronic obstructive pulmonary disease (HR, 0.66; 95% CI, 0.64–0.68). Individuals more likely to discontinue were those with more than nine medical consultations (HR, 1.14; 95% CI, 1.10–1.18) and those with dementia (HR, 1.13; 95% CI, 1.01–1.27). Individuals less likely to discontinue were those diagnosed in a recent calendar year (2009: HR 0.74; 95% CI, 0.65–0.82) and those exposed to another β-blocker before HF diagnosis (HR, 0.88; 95% CI, 0.85–0.91).

Conclusion: Quebec seniors seem to be underexposed to β-blocker following HF diagnosis. Among those who initiate β-blocker use, discontinuation is high. Better understanding of the underlying causes is needed to help target interventions to improve the management of HF.

Keywords: heart failure, β-blocker initiation, β-blocker discontinuation, cohort study, drug use

Introduction

Heart failure (HF) is the main cause of hospitalization among seniors.[1] The risk of dying is 3.6 times greater among people with HF than in the general population[2] and an estimated 12.6% of individuals will die in the year following HF diagnosis.[3]

Effective drug regimen can reduce both HF-related morbidity and mortality. According to clinical guidelines,[4,5] patients with HF should be treated with one of the three β-blockers: carvedilol, bisoprolol, or metoprolol (referred to as β-blockers). Guidelines also recommend combining the β-blocker with an angiotensin-converting enzyme inhibitor (ACEi), or an angiotensin receptor blocker (ARB), if an ACEi cannot be tolerated. If ACEi and ARB cannot be tolerated, hydralazine combined with isosorbide dinitrate can also be used.[4,6] In selected patients with moderate to severe

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symptoms, digoxin and/or an aldosterone antagonist may be added.[4,6]

Unfortunately, patients with HF appear to underuse β-blockers.[7–9] It has been reported that patients with HF are less likely to be exposed to a β-blocker as they age,[8,10,11] if they use treatments such as aspirin and nonspecific vasodilators,[10] and as the number of HF symptoms increases.[8,10] However, studies on that issue are difficult to interpret since they included established HF cases rather than newly diagnosed patients.[8,10,11]

Little is known about the timing of β-blocker treatment initiation and the factors associated with its initiation. Among those who start β-blocker treatment, it is unclear to what extent the β-blocker treatment is later discontinued. In two studies in which β-blocker treatment discontinuation was studied,[12,13] the follow-up was limited to a maximum of 3 months, which is too brief for a disease necessitating long-term treatment.

We assessed the incidence rate of β-blocker initiation among seniors newly diagnosed with HF but not using a β-blocker at the time of HF diagnosis and the factors associated with β-blocker initiation. We also assessed the incidence rate of β-blocker treatment discontinuation and its associated factors.

Methods

We conducted a population-based inception cohort study using data administered by the Quebec Health Insurance Board (Régie de l'assurance maladie du Québec [RAMQ]) and the Institut de la statistique du Québec. These data include information on patient demographics, vital status, in-hospital and outpatient medical diagnoses, and on the use of medical services by all permanent residents of Canadian Quebec province. The RAMQ drug plan database is known to be accurate for prescription claims.[14] It contains information on prescription drugs for Quebec residents not covered by a private drug insurance group plan, welfare recipients, and seniors aged 65 years and older. The Research Ethics Committee of the Centre Hospitalier Affilié Universitaire de Québec approved this study. As this study was an administrative denominalized data analysis patient consent was not required by the Research Ethics Committee of the Centre Hospitalier Affilié Universitaire de Québec.

The source population is based on all Quebec residents aged 18 years or older who received a first HF diagnosis from January 1, 2000, to December 31, 2009, inclusively. RAMQ identified every person eligible for the public health insurance plan, with at least one HF diagnosis (International Classification of Diseases [ICD]-9 code: 428; ICD-10 code: i50). From this population, RAMQ removed all individuals who had not been continuously eligible for the provincial drug plan in the year before their first HF diagnosis. For the source population, RAMQ provided the data recorded in the databases until December 31, 2009, death or end of eligibility for the drug plan.

We excluded individuals with only one HF diagnosis, unless this diagnosis was made in hospital. Such a procedure was shown to be valid at identifying cases of HF using administrative data.[15] Where there was more than one HF diagnosis, the date of the first recorded one determined the HF diagnosis baseline date. We then excluded individuals aged <65 years at HF diagnosis, those who died on the HF diagnosis date or during the hospital stay in which HF was diagnosed, and all those who received no follow-up. Next, we excluded individuals who had used a β-blocker in the year before HF diagnosis but had stopped their treatment before their HF diagnosis. We assessed the use of β-blockers at the time of HF diagnosis in the remainder of our population. To estimate the rate of β-blocker initiation, we settled on a β-blocker-naïve cohort by excluding individuals who had taken a β-blocker before or who were taking one at the time of HF diagnosis. β-Blocker treatment discontinuation was assessed among patients who initiated a β-blocker after HF diagnosis.

Individuals with a claim of taking carvedilol, bisoprolol, or metoprolol in the year before or at HF diagnosis were regarded as using a β-blocker before or at HF diagnosis. Then, to cover the claim duration and to take into account less-than-optimal adherence to treatment, we added 1.5 times the number of days' supply to the date of the most recent claim in that period. Because no information on drug exposure during hospitalization was available, we excluded hospital days from the calculation. If this time period included the date of HF diagnosis, the patient was assumed to be using the drug at the time of HF diagnosis.

β-blocker-naïve individuals were deemed to have initiated a β-blocker if they had at least one β-blocker claim between the HF diagnosis date and the end of their follow-up. We followed up patients until the study end (December 31, 2009), loss of eligibility for the public drug plan, or death. In assessing β-blocker treatment discontinuation among those who initiated a β-blocker after HF diagnosis, we looked for the first gap in refills that was equal to twice the days' supply of a claim after β-blocker initiation. Hospital days were excluded from the calculation of this "permissible gap" requirement for treatment discontinuation. The discontinuation date was the date of the last claim plus its number of days' supply.

Analyses were conducted on many variables. We first took into account the calendar year at HF diagnosis. Next,

we reviewed patient characteristics known to influence drug prescription in the elderly: age,[10,16] sex,[17] and socioeconomic status[10] at HF diagnosis. We considered the use of health services (number of hospitalizations, medical visits, and specialty of the physicians consulted), presence of a pacemaker, comorbidities, and drug use in the year before HF diagnosis. Concerning comorbidities, we took into account both evidence-based contraindications (asthma, bradycardia without a pacemaker) and chronic obstructive pulmonary disease (COPD), which is perceived but not supported by evidence, as well as conditions requiring close β-blocker monitoring (orthostatic hypotension, chronic kidney disease, hepatic failure, diabetes, peripheral atherosclerotic disease, and depression) and diseases for which β-blockers are indicated independently of HF (ischemic heart disease, atrial fibrillation, and arterial hypertension). We also looked for diseases that may reduce life expectancy (dementia, non-skin neoplasia). For each condition, we searched for a diagnosis either outpatient or inpatient recorded during the year before HF diagnosis. For diabetes and dementia, we also looked for a claim for an antidiabetic drug and for cholinesterase inhibitors or memantine, respectively. In addition, we took into account the use of other β-blockers, other recommended drugs for treatment of HF (ACEi, ARB, or a combination of hydralazine and isosorbide dinitrate; digoxin and spironolactone), other cardiovascular drugs (aspirin, clopidogrel, and oral anticoagulants), and potentially inappropriate treatment with drugs contraindicated in patients with HF (nonsteroidal anti-inflammatory drugs, thiazolidinediones, calcium channel blockers [non-dihydropyridines and nifedipine], and class I antiarrhythmics).[6]

Statistical analysis

Proportions, medians, and means were used to describe the study population according to the use or not of a β-blocker before HF diagnosis. Proportions and medians were compared using chi-square and Satterthwaite tests, respectively. Kaplan–Meier survival curves were used to analyze the time to β-blocker initiation and time to β-blocker discontinuation, with time 0 being HF diagnosis and β-blocker initiation, respectively. Stepwise Cox multivariate regression analyses were used to assess the association between potential factors and β-blocker initiation and discontinuation. The input threshold was set at P-value ≤ 0.1. Only statistically significant variables (P-value < 0.05) were retained in the final model. Analyses were performed using SAS® (Version 9.3; SAS Institute Inc., Cary, NC, USA).

Results

Table 1 shows the characteristics of our study population and of the individuals excluded because they were on a β-blocker at the time of HF diagnosis. Of the 91,131 β-blocker-naïve individuals who made our study population (Figure 1), 32,989 (36.2%) initiated a β-blocker during the follow-up (incidence rate: 17.7 per 100 person-years). Figure 2 shows the Kaplan–Meier curve displaying the probability of initiating a β-blocker during the follow-up period. Median time between HF diagnosis date and β-blocker initiation date was 51 days (minimum: 1 day; maximum: 3,615 days). Adjusted hazard ratios (HRs) describing factors associated with β-blocker initiation after HF diagnosis are presented in Table 2.

Finally, we assessed β-blocker treatment discontinuation among the 32,989 individuals who initiated a β-blocker treatment after HF diagnosis. Of these, 15,408 (46.7%) stopped using β-blockers during the follow-up (incidence rate: 27.3 per 100 people per year). Figure 3 shows the Kaplan–Meier curve displaying the probability of stopping β-blocker use during the follow-up period. Median time between β-blocker initiation date and discontinuation date was 197 days (minimum: 1 day; maximum: 3,550 days). Table 3 shows adjusted HRs for factors associated with β-blocker discontinuation.

Discussion

Important findings emerge from this study. First, of the 119,184 seniors who survived after a first HF diagnosis, >75% had not been exposed to a β-blocker before or at the time of diagnosis (Table 1). More importantly, since the proportion of patients not exposed to a β-blocker at the time of HF diagnosis and who later initiated a β-blocker, was low (36.2%), it would appear that seniors are underexposed to β-blockers after HF diagnosis.

Several factors might be related to the decision to prescribe a β-blocker, or not, to newly diagnosed HF individuals. β-blockers were significantly less likely to be initiated by individuals whom prescribers might perceive as being more complicated to manage (older patients with comorbidities) and who were diagnosed not by cardiologists, but by general practitioners or geriatricians outside of a hospital setting. For many patients, the HF diagnosis represents an opportunity to prescribe them a first-time β-blocker, knowing these drugs have a demonstrated effect on mortality reduction[18,19] and hospitalization.[19] At least two other studies[7,8] have evaluated exposure to a β-blocker after HF diagnosis. Comparing our results with those of these studies is difficult since the populations studied and designs used

Table 1 Characteristics of individuals according to the use of a β-blocker (bisoprolol, carvedilol, or metoprolol) at the time of HF diagnosis (n=119,184)

Characteristics	Had a β-blocker at the time of HF diagnosis				*P*-value
	Yes		No		
	28,053 (n)	23.5 (%)	91,131 (n)	76.5 (%)	
Age (years)					
Mean (SD)	78.3	(7.2)	78.90	(7.5)	<0.0001
65–69	3,657	13.0	11,338	12.4	<0.0001
70–74	5,406	19.3	16,786	18.4	
75–79	6,677	23.8	20,694	22.7	
80–84	6,416	22.9	20,038	22.0	
85–89	4,037	14.4	14,193	15.6	
≥90	1,860	6.6	8,082	8.9	
Sex					<0.0001
Men	13,095	46.7	41,283	45.3	
Women	14,958	53.3	49,848	54.7	
Socioeconomic status					<0.0001
No GIS	11,699	41.7	36,623	40.2	
Partial GIS	13,979	49.8	46,067	50.6	
Welfare or maximum GIS	2,375	8.5	8,441	3	
Calendar year at HF diagnosis					<0.0001
2000	2,687	9.6	16,719	18.4	
2001	2,789	9.9	13,438	14.8	
2002	2,478	8.8	10,355	11.4	
2003	2,626	9.4	8,833	9.7	
2004	2,763	9.9	8,228	9.0	
2005	2,679	9.6	7,355	8.1	
2006	2,786	9.9	6,890	7.6	
2007	3,072	11.0	6,693	7.3	
2008	3,247	11.6	6,533	7.2	
2009	2,926	10.4	6,087	6.7	
Specialty of physician who diagnosed HF					<0.0001
Cardiologist	10,757	4	29,841	32.8	
Internist	3,674	13.1	12,145	13.3	
Geriatrician	141	0.5	652	0.7	
General practitioner	11,862	42.3	42,234	46.3	
Hospitalized at the time of HF diagnosis	17,068	60.8	58,208	63.9	<0.0001
Number of hospitalization days in the year before HF diagnosis (median: 25th–75th percentile)	6	(0–16)	3	(0–13)	<0.0001
Number of medical consultations in the year prior to HF diagnosis (median: 25th–75th percentile)	13	(7–22)	9	(7–17)	<0.0001
Seen by (in the year prior to HF diagnosis)					
Cardiologist	14,163	50.5	28,154	30.9	<0.0001
Internist	7,632	27.2	18,750	20.6	<0.0001
Geriatrician	380	1.4	1,190	1.3	0.5
General practitioner	23,310	83.1	71,015	77.9	<0.0001
Drugs used in the year prior to HF diagnosis					
HF drugs					
ACEi or ARB or a combination of hydralazine and isosorbide dinitrate	19,223	68.5	45,133	49.5	<0.0001
Digoxin	3,902	13.9	11,942	13.1	0.0005
Spironolactone	869	3.1	2,107	2.3	<0.0001
Other cardiovascular drugs					
Aspirin/clopidogrel	19,717	70.3	42,381	46.5	<0.0001
Oral anticoagulants	8,178	29.2	15,321	16.8	<0.0001
β-blocker other than bisoprolol, carvedilol, or metoprolol	2,288	8.2	19,138	21.0	<0.0001
Potentially inappropriate treatment	9,316	33.2	32,221	35.4	<0.0001

(*Continued*)

Table 1 (*Continued*)

Characteristics	Had a β-blocker at the time of HF diagnosis				*P*-value
	Yes		No		
	28,053 (n)	23.5 (%)	91,131 (n)	76.5 (%)	
Comorbidities					
Contraindication for β-blocker (real or perceived)					
Asthma	1,310	4.7	7,044	7.7	<0.0001
Conduction disorder without a pacemaker	722	2.6	1,609	1.8	<0.0001
COPD	4,446	15.9	21,557	23.7	<0.0001
Associated with precautions					
Chronic kidney disease	4,519	16.1	8,709	9.6	<0.0001
Depression	1,256	4.5	4,594	5.0	0.0001
Diabetes	9,969	35.5	24,812	27.23	<0.0001
Hepatic failure	232	0.8	923	1.0	0.0055
Orthostatic hypotension	381	1.4	909	1.0	<0.0001
Peripheral atherosclerotic disease	3,967	14.1	8,193	8.99	<0.0001
Other indication for β-blocker use					
Atrial fibrillation	8,128	29.0	17,013	18.7	<0.0001
Arterial hypertension	15,499	55.3	38,620	42.4	<0.0001
Ischemic heart disease	20,765	74.0	47,288	51.9	<0.0001
Reduced life expectancy					
Non-skin neoplasia	4,916	17.5	15,443	17.0	0.02
Dementia	1,218	4.3	3,964	4.4	0.95
Presence of a pacemaker	2,671	9.5	5,367	5.9	<0.0001

Note: Otherwise indicated, values are numbers and percentages.
Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; COPD, chronic obstructive pulmonary disease; GIS, guaranteed income supplement; HF, heart failure; SD, standard deviation.

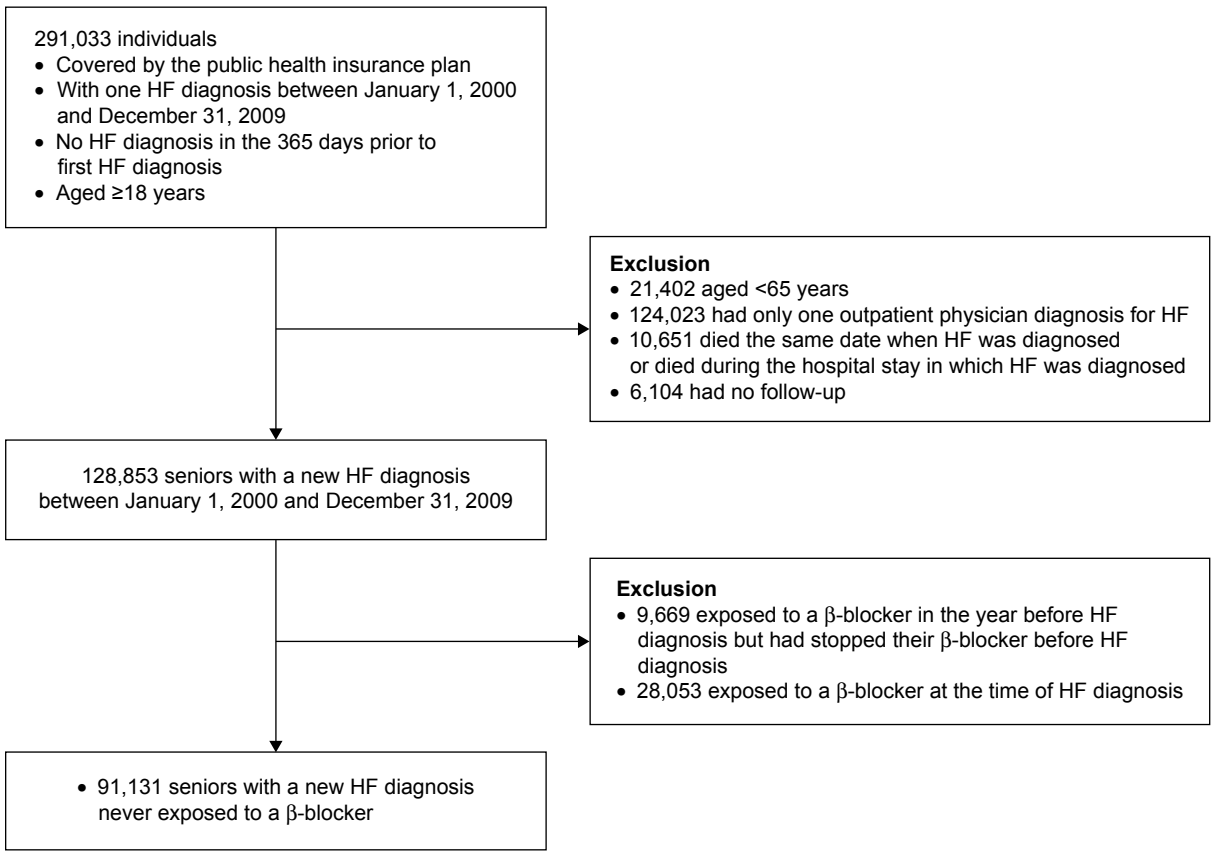

Figure 1 Selection of the study population.
Abbreviation: HF, heart failure.

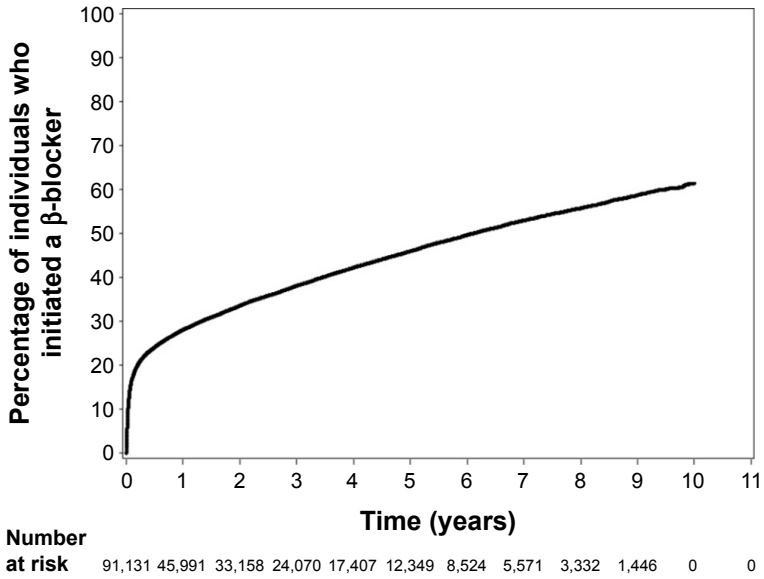

Figure 2 Probability of β-blocker initiation after heart failure diagnosis among those not exposed to a β-blocker at time of heart failure diagnosis.

Table 2 Factors associated with β-blocker (bisoprolol, carvedilol, or metoprolol) initiation after HF diagnosis among those who did not use a β-blocker before (n=91,131)

Characteristics	Adjusted HR	95% CI	*P*-value
Age (years)			
65–69	1.00	Ref	
70–74	0.95	0.92–0.98	0.005
75–79	0.90	0.87–0.94	<0.0001
80–84	0.85	0.82–0.88	<0.0001
85–89	0.77	0.73–0.80	<0.0001
≥90	0.65	0.61–0.68	<0.0001
Sex			
Men	1.09	1.07–1.12	<0.0001
Women	1.00	Ref	
Socioeconomic status			
No GIS	1.00	Ref	
Partial GIS	0.98	0.95–1.00	0.03
Welfare or maximum GIS	0.90	0.87–0.94	<0.0001
Calendar year at HF diagnosis			
2000	1.00	Ref	
2001	1.22	1.17–1.27	<0.0001
2002	1.37	1.31–1.43	<0.0001
2003	1.47	1.41–1.53	<0.0001
2004	1.57	1.50–1.64	<0.0001
2005	1.71	1.63–1.79	<0.0001
2006	1.73	1.65–1.82	<0.0001
2007	1.81	1.72–1.90	<0.0001
2008	1.93	1.83–2.03	<0.0001
2009	2.11	2.00–2.23	<0.0001
Specialty of physician who diagnosed HF			
Cardiologist	1.38	1.34–1.42	<0.0001
Geriatrician	0.74	0.62–0.89	0.001
General practitioner	1.00	Ref	
Hospitalized at the time of HF diagnosis	1.31	1.27–1.34	<0.0001
Number of hospitalization days in the year before HF diagnosis			
≤ median (3 days)	1.00	Ref	
> median	0.72	0.70–0.74	<0.0001

(*Continued*)

Table 2 (*Continued*)

Characteristics	Adjusted HR	95% CI	*P*-value
Number of medical consultations in the year prior to HF diagnosis			
≤ median (9 consultations)	1.00	Ref	
> median	0.91	0.89–0.93	<0.0001
Seen by (in the year before HF diagnosis)[a]			
Cardiologist	1.07	1.04–1.10	<0.0001
Drugs used in the year before HF diagnosis[a]			
HF drugs			
ACEi or ARB or a combination of hydralazine and isosorbide dinitrate	1.03	1.01–1.06	0.01
Spironolactone	0.84	0.77–0.91	<0.0001
Other cardiovascular drugs			
Aspirin/clopidogrel	0.97	0.94–0.99	0.005
Oral anticoagulants	0.86	0.83–0.89	<0.0001
β-blocker other than bisoprolol, carvedilol, or metoprolol	0.87	0.85–0.90	<0.0001
Comorbidities[a]			
Contraindication for β-blocker (real or perceived)			
Asthma	0.73	0.70–0.77	<0.0001
COPD	0.66	0.64–0.68	<0.0001
Associated with precautions			
Chronic kidney disease	1.06	1.02–1.10	0.004
Depression	0.91	0.86–0.96	0.0005
Diabetes	1.19	1.16–1.22	<0.0001
Hepatic failure	0.72	0.63–0.82	<0.0001
Peripheral atherosclerotic disease	1.17	1.13–1.22	<0.0001
Other indication for β-blocker use			
Atrial fibrillation	1.09	1.06–1.13	<0.0001
Arterial hypertension	1.07	1.04–1.09	<0.0001
Ischemic heart disease	1.34	1.31–1.37	<0.0001
Reduced life expectancy			
Non-skin neoplasia	0.91	0.88–0.93	<0.0001
Dementia	0.76	0.71–0.82	<0.0001
Presence of a pacemaker	0.94	0.90–0.99	0.02

Note: [a]Individuals in the reference groups are those without the characteristics.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CI, confidence interval; Ref, reference; COPD, chronic obstructive pulmonary disease; GIS, guaranteed income supplement; HF, heart failure; HR, hazard ratio.

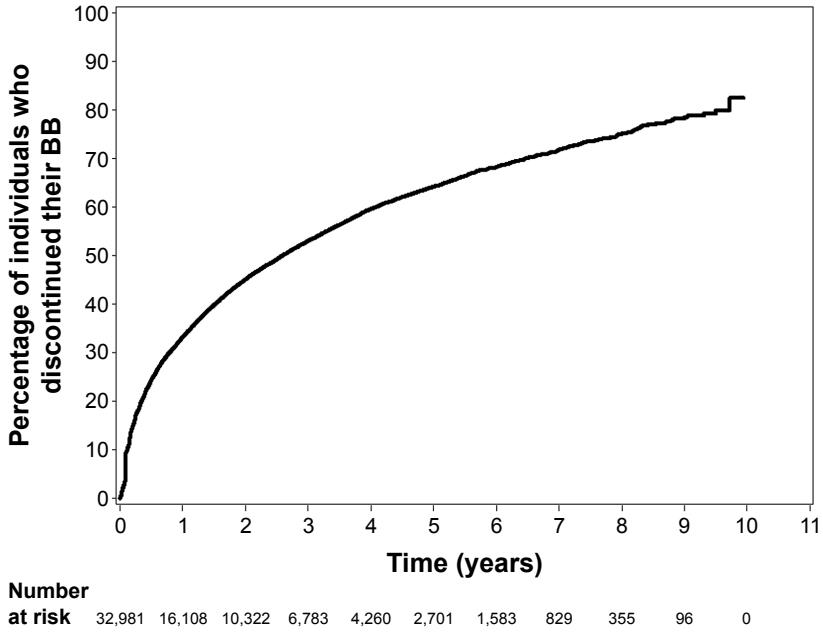

Figure 3 Probability of β-blocker discontinuation among patients who initiated a β-blocker after heart failure diagnosis.
Abbreviation: BB, β-blocker.

Table 3 Factors associated with β-blocker (bisoprolol, carvedilol, or metoprolol) discontinuation among those who initiated a β-blocker after HF diagnosis (n=32,989)

Characteristics	Adjusted HR[a]	95% CI	*P*-value
Socioeconomic status			
No GIS	1.00	Ref	
Partial GIS	0.93	0.90–0.96	<0.0001
Calendar year at HF diagnosis			
2000	1	Ref	
2001	0.98	0.93–1.03	0.5
2002	0.91	0.86–0.96	0.001
2003	0.87	0.82–0.92	<0.0001
2004	0.84	0.79–0.89	<0.0001
2005	0.83	0.78–0.89	<0.0001
2006	0.80	0.75–0.86	<0.0001
2007	0.84	0.78–0.91	<0.0001
2008	0.76	0.70–0.83	<0.0001
2009	0.73	0.65–0.82	<0.0001
Specialty of physician who diagnosed HF			
Internist	1.07	1.01–1.13	0.01
General practitioner	1	Ref	
Hospitalized at the time of HF diagnosis	0.88	0.85–0.91	<0.0001
Number of medical consultations in the year prior to HF diagnosis			
≤ median (9 consultations)	1	Ref	
> median	1.14	1.10–1.18	<0.0001
Seen by (in the year before HF diagnosis)[b]			
Cardiologist	1.05	1.02–1.10	0.004
Internist	1.04	1.00–1.09	0.05
Drugs used in the year before HF diagnosis[b]			
HF drugs			
Digoxin	1.08	1.03–1.14	0.001
β-blocker other than bisoprolol, carvedilol, or metoprolol	0.88	0.85–0.91	<0.0001
Comorbidities[b,c]			
Contraindication to β-blocker (real or perceived)			
Asthma	1.09	1.02–1.17	0.008
COPD	1.08	1.04–1.13	0.0003
Associated with precautions			
Diabetes[d]	0.90	0.87–0.94	<0.0001
Reduced life expectancy			
Non-skin neoplasia	1.05	1.00–1.10	0.04
Dementia[e]	1.13	1.01–1.27	0.03
Presence of a pacemaker	0.90	0.84–0.97	0.003

Notes: [a]Variables presented in the multivariate analysis were selected in a stepwise fashion with an input threshold set at a *P*-value of ≤0.1 and an output threshold set at ≥0.05. [b]Individuals in the reference groups are those without the characteristics. [c]Presence of a disease (for all but dementia, diabetes, and ischemic heart disease) was defined based on a diagnosis recorded in the medical services database or in the hospitalization registry during the time period beginning 365 days before the HF diagnosis. [d]Diabetes was defined based on a diagnosis of diabetes recorded in the RAMQ medical services database, or in the hospitalization registry, or claim for insulin or an oral antidiabetes drug in the RAMQ drug plan database. [e]Dementia was defined based on a diagnosis of dementia recorded in the RAMQ medical services database, or in the hospitalization registry, or a claim for donepezil, galantamine, rivastigmine, or memantine in the RAMQ drug plan database.

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; GIS, guaranteed income supplement; Ref, reference; HF, heart failure; HR, hazard ratio; RAMQ, Régie de l'assurance maladie du Québec.

were different. For example, Maison et al[7] observed that only 19% of individuals aged 75 years and older used a β-blocker; a lower proportion than what we observed in this same age category (32.9%). This is probably because Maison et al assessed exposure to β-blocker at a single point in time (hospital discharge), whereas our exposure assessment period was from HF diagnosis to the end of follow-up. de Groote et al[8] conducted a chart review of patients with HF in a cardiology clinic. They observed that 57% of patients aged 75 years and older were being exposed to a β-blocker, which is a larger proportion than we observed. However, they included only individuals treated by cardiologists, whereas our study population comprised all HF-diagnosed individuals, irrespective of the diagnosing physician's specialty. This could explain the higher proportion observed by de Groote et al,[8] especially in light of our observation that individuals

diagnosed by cardiologists rather than general practitioners are 1.38 times more likely to receive a β-blocker.

We observed a 24% decrease in the likelihood of β-blocker initiation in those suffering from dementia. This result is in line with the findings of a study, where patients with dementia were less likely to be exposed to cardiovascular treatment.[20] Physicians might fear seniors with dementia are at higher risk of adverse reactions and so may perceive the β-blocker benefit/risk ratio as unfavorable. Further research is needed to better understand the issues surrounding cardioprotective pharmacotherapy for patients with dementia.

Given increased age is not a contraindication for β-blocker use, its association with a higher likelihood of initiating β-blockers is surprising. However, this result corresponds to what others have reported. For example, Shah et al[17] observed that patients aged between 65 years and 69 years had a threefold greater probability of being exposed to a β-blocker than those aged 85 years and older, even though dementia was not considered in the analysis. By contrast, once a β-blocker has been initiated, increased age is not a factor associated with its discontinuation, which suggests that tolerance to β-blockers is similar among all patients. This result is not in accord with the results of two studies where a 1-year increase in age was associated with a 1%[13] and 2%[21] increase in β-blocker discontinuation. However, in the first study,[13] the association between increased age and β-blocker discontinuation was not statistically significant when controlling for potential confounders, while results in the other[21] were not adjusted for confounders such as comorbidities and use of health services.

Since β-blockers are contraindicated in asthma,[22] the observed 27% decrease in the likelihood of initiating β-blocker is quite reassuring. We observed that COPD was also associated with a reduced likelihood of β-blocker initiation. There are reports that physicians, other than cardiologists, overestimate the respiratory risks of β-blockers and so are underprescribing them.[23] COPD and asthma are often considered together as possible contraindications to β-blockers. Komajda et al[11] reported a 65% reduced probability of exposure to a β-blocker among those suffering from any respiratory/pulmonary disease. However, exposure to a β-blocker among patients with COPD has been shown a safe and effective means of reducing mortality.[24] Nevertheless, Shah et al[17] observed that asthma and COPD were each associated with a 63% decrease in exposure to a β-blocker. In our study, we found that, among individuals who initiated a β-blocker, patients who had COPD, and patients who had asthma in the year before HF diagnosis, were more likely to discontinue. Although statistically significant, the increase in the risk of discontinuation was very low: 8% for patients with COPD and 9% for patients with asthma.

The likelihood of β-blocker initiation has risen over the years. Among exposed individuals, those diagnosed after 2001 are less likely to discontinue their use of β-blockers, although the magnitude of the likelihood remains stable for individuals diagnosed between 2002 and 2009. These results probably reflect the increased evidence for the benefits of β-blockers in patients with HF in the last 10 years and physicians' gradual adoption of clinical practice guidelines.[17]

Being exposed to a β-blocker other than bisoprolol, carvedilol, or metoprolol in the year before HF diagnosis was associated with a decreased likelihood of initiation of one of these three drugs. We hypothesize that because β-blockers can be used before HF diagnosis to treat diseases other than HF, clinicians may choose to continue the same drug after HF diagnosis and so do not switch to an evidence-based HF β-blocker. Two studies[8,17] observed that around 12% of patients exposed to a β-blocker after HF diagnosis are exposed to a β-blocker other than one of the three recommended by clinical guidelines. As specified in clinical guidelines, the beneficial effect of exposure to any β-blocker should not be considered a class effect and so the recommendation is to switch patients to an evidence-based β-blocker. Finally, we also observed that exposure to a non-evidence-based β-blocker in the year before HF diagnosis is associated with a decreased probability of discontinuation of the evidence-based β-blocker.

These results suggest that in real-life clinical practice, despite long-established clinical practice guidelines with clear directions for β-blocker usage, clinicians, and in particular general practitioners, might judge the risk/benefit profile of β-blockers as unfavorable and therefore do not initiate β-blockers for most elderly individuals with HF due to their perceived frailty, the presence of various comorbidities, and a history of frequent hospitalizations before HF diagnosis.

Our study population accurately reflects the real-world population with HF and their exposure to cardiovascular medication. There are some limitations related to the absence of certain clinical data in administrative databases. First, we were unable to disentangle HF patients with preserved left ventricular ejection fraction (HFpEF) from those with decreased left ventricle ejection fraction. The prevalence of HFpEF in seniors with HF is estimated to vary between 34%[25] and 55%.[26] Although benefits of exposure to β-blockers have been shown for patients with HF with decreased left ventricle

ejection fraction, there is no clear evidence of benefits for those with HFpEF; yet, they could also be used in those patients to optimally manage blood pressure, heart rate, and myocardial ischemia.[6] Not surprisingly, in our study, having arterial hypertension and ischemic heart disease in the year before HF diagnosis were factors associated with an increased likelihood of initiating a β-blocker. Therefore, the low rate of β-blocker initiation we observed is probably underestimating the quality of drug use.

Finally, frailty is also a clinical variable not captured in the RAMQ database. As frailty increases with age, it could partly explain why many of the older patients do not initiate β-blocker treatment. Only the more resilient patients might begin and continue with β-blocker treatment. Further research is needed to better understand the role of frailty in the management of HF treatment in the elderly.

Before our study, factors associated with β-blocker initiation and discontinuation had never been assessed in an elderly population newly diagnosed with HF. As 97% of seniors in Quebec are covered by the RAMQ drug plan, this population-based study is highly generalizable. Using administrative data allowed us to look at a large population in current clinical practice over a long period (up to 10 years). It was also possible to take into account potential factors that are generally unavailable, such as dementia and medical services usage. These factors were found to have an important effect on seniors' exposure to a β-blocker.

To lessen the burden of HF, efforts should be made to reduce the need for health care service use among patients with HF. Since β-blockers have proved beneficial in reducing the use of health care services[27,28] even among seniors, exposing them to long-term, evidence-based β-blocker pharmacotherapy should be a priority. More work needs to be performed to examine clinicians' prescribing behavior. Better understanding of the underlying causes, including the gaps related to prescriber knowledge, attitude, belief, or health care system-related issues, will help to tailor the development of targeted interventions to improve the management of HF.

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Disclosure

The authors report no conflicts of interest in this work.

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