CARDIOVASCULAR MEDICINE

Effect of a community heart failure clinic on uptake of β blockers by patients with obstructive airways disease and heart failure

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Objective: To determine the pattern of β blocker prescribing over one year in a heart failure clinic with a structured approach towards initiation and dose titration and to give a real life perspective on β blocker use, compliance, and target dose achievement.
Methods: Data were retrospectively analysed on 513 consecutive patients regularly attending a community heart failure clinic over a year. Systolic dysfunction was determined from two dimensional echocardiography (left ventricular ejection fraction $\leqslant$ 40%) and lung function was assessed by spirometry. All patients were considered for β blocker initiation and dose up titration.
Results: Within one year 157 patients died. 143 patients started β blockers resulting in 315 (88%) patients taking β blockers at one year; 38% were taking the target dose. 124 had evidence of airways obstruction at baseline, 100 (81%) of whom were taking β blockers at one year. Forced expiratory volume in one second (1.1 *v* 1.5 l, $p < 0.01$) and forced vital capacity (2.3 *v* 2.5 l/min, $p = 0.2$) were not reduced in patients with airways obstruction who received β blockers. Daily doses of β blockers at one year did not differ statistically between patients with obstructive and patients with non-obstructive spirometry results. 12 patients discontinued β blockers and 14 required dose reduction due to side effects.
Conclusion: The majority of patients with heart failure and obstructive airways disease can safely tolerate low dose initiation and gradual up titration of β blockers.

Heart failure is a serious health problem that is becoming increasingly more common in both men and women.[1] In 1995, an estimated one million patients had chronic heart failure in the UK, accounting for approximately 1.9% of annual National Health Service expenditure.[2]

β Blockers, along with angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers, and aldosterone antagonists, reduce morbidity, hospitalisations, and mortality in patients with heart failure.[3–5] Despite national and international guidelines recommending this evidence based treatment, a significant proportion of patients do not receive these drugs.[6 7] Only 36.9% of the 11 016 participants in the European Society of Cardiology heart failure survey in 2003 were prescribed β blockers.[8]

Several obstacles to β blocker use in chronic heart failure have been reported.[9] Long term β blocker compliance data suggests significant discontinuation rates, together with poor target dose achievement.[10 11] Randomised controlled trials of β blockers in heart failure achieve target doses in up to 80% of patients[12] with discontinuation rates up to 32%.[13] Whether this is representative of or indeed achievable by patients encountered in a clinical setting is unclear.

Our objectives were to determine the pattern of β blocker prescribing (over a year) in a heart failure clinic with a structured approach towards initiation and dose titration and to give a real life perspective on β blocker use, compliance, and target dose achievement.

METHODS

We studied 356 consecutive patients with diagnosed chronic heart failure assessed and treated in a heart failure clinic for the first time between September 2001 and July 2003 who were followed up for a minimum of one year. Left ventricular systolic dysfunction was defined as a left ventricular ejection fraction of $\leqslant$40% determined by two dimensional echocardiography and the modified Simpson's rule. In cases where an accurate quantitative measurement was not possible, a qualitative assessment was used. Patients with at least moderate impairment of systolic function were included.

Patients were referred to the clinic by their primary health care physician (72%) or by other hospital physicians (28%) once heart failure had been diagnosed. The heart failure service has no exclusion criteria for attendance.

At the baseline visit, a thorough medical history (including documentation of cardiac medication) and examination were performed together with spirometry (with a handheld Vitalograph 2120 device, with the patient supine; Vitalograph Ltd), 12 lead ECG, and two dimensional echocardiography. Patients with heart failure then entered a structured follow up programme to allow β blocker and ACE inhibitor initiation and titration. Both doctors and specialist heart failure nurses participate in the programme, with patients being reviewed initially every two to four weeks. The strategy is to achieve optimal heart failure treatment for all patients. All patients were considered for β blockers unless contraindicated. The only contraindications to β blockade were asthma (requiring regular inhaled steroids and bronchodilators), significant bradycardia (heart rate < 45 beats/min), or high grade atrioventricular block in the absence of a permanent pacemaker. Obstructive airways

Abbreviations: ACE, angiotensin converting enzyme; CI, confidence interval; COMET, carvedilol or metoprolol European trial; COPD, chronic obstructive pulmonary disease; COPERNICUS, carvedilol prospective randomised cumulative survival; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; IMPACT-HF, initiation management predischarge process for assessment of carvedilol therapy for heart failure; MERIT-HF, metoprolol CR/XL randomised intervention trial in congestive heart failure; NYHA, New York Heart Association; OR, odds ratio

disease without evidence of reversibility was not an absolute contraindication to β blockade. Wherever possible, patients began taking ACE inhibitors before β blockers were considered.

In accordance with National Institute for Health and Clinical Excellence guidelines,[14] β blockers of choice for heart failure were carvedilol and bisoprolol. Both were initiated at low dose (carvedilol 3.125 mg twice daily and bisoprolol 1.25 mg once daily), with gradual titration over a period of months towards a target dose of 25 mg twice daily for carvedilol and 10 mg once daily for bisoprolol. Patients' doses were up titrated at each clinic visit unless symptoms or clinical findings determined otherwise. Clinics were staffed by both physicians and nurse specialists. All decisions to adjust medication or dose were made by a physician. During the titration process, attempts were made to switch patients taking unlicensed β blockers to either bisoprolol or carvedilol. In addition, patients were informed that a transient period of worsening symptoms may result from an increase in dose. Patients with significant dyspnoea or oedema at baseline were stabilised with diuretics and ACE inhibitors before β blockers were initiated.

To determine the efficacy of this approach towards β blockade for heart failure, data collected at baseline was compared with data at one year.

Table 1 Baseline clinical characteristics

Characteristic	Patient group: All	Airways obstruction*	No airways obstruction
Number	356	124	232
Age (years)	70.7 (9.6)	71.8 (8.9)	70.1 (9.9)
⩾70	213 (59.8%)	82 (66.1%)	131 (56.5%)
Men	256 (71.9%)	74 (59.7%)	182 (78.4%)
IHD†	254 (71.3%)	86 (69.4%)	168 (72.4%)
Smoking history	238 (66.8%)	94 (75.8%)	144 (62.1%)
Hypertension	123 (34.6%)	37 (29.8%)	86 (37.1%)
Diabetes	71 (19.9%)	20 (16.1%)	51 (22.0%)
Atrial fibrillation	75 (21.1%)	26 (21%)	49 (21.1%)
NYHA class			
I	36 (10.1%)	9 (7.3%)	27 (11.6%)
II	226 (63.5%)	83 (66.9%)	144 (62.7%)
III	88 (24.7%)	31 (25.0%)	57 (24.6%)
IV	5 (1.4%)	1 (0.8%)	4 (1.7%)
β Blockers	172 (48.3%)	54 (43.5%)	118 (50.9%)
Aspirin	180 (50.6%)	56 (45.3%)	124 (53.4%)
Warfarin	80 (22.5%)	28 (22.6%)	52 (22.4%)
Diuretic	257 (72.2%)	93 (75%)	164 (70.7%)
Spironolactone	71 (19.9%)	18 (14.5%)	53 (22.8%)
Digoxin	61 (17.1%)	25 (20.2%)	36 (15.5%)
ACE inhibitor	269 (75.6%)	94 (75.8%)	175 (75.4%)
ARB	16 (4.5%)	5 (4.0%)	11 (4.7%)
Statin	153 (43.0%)	51 (41.1%)	102 (44%)
LVEF (%)	32.0 (7.5)	31.7 (6.9)	32.2 (7.8)
LVEDD (cm)	6.2 (1.0)	6.2 (1.1)	6.2 (1.0)
Resting HR (beats/min)	75.7 (19.6)	77.1 (19.8)	74.9 (19.5)
PR interval (ms)	172.8 (32.6)	172.0 (24.9)	172.5 (35.6)
QRS duration (ms)	113.4 (30.2)	112.3 (31.8)	114 (29.3)
FEV_1 (l)	1.7 (0.8)	1.1 (0.4)	2.1 (0.7)
FVC (l/min)	2.6 (1.0)	2.3 (0.8)	2.8 (1.0)
BMI (kg/m^2)	26.3 (5.6)	25.0 (5.7)	27.0 (5.5)
Creatinine (μmol/l)	114.8 (39.6)	111.5 (40.8)	116.6 (38.9)

Data are mean (SD) or number (%).
*Defined as forced expiratory volume in one second (FEV_1) to forced vital capacity (FVC) ratio <70% plus FEV_1 <60% predicted; †defined as any of angina, myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft, regional wall motion abnormalities, or the presence of pathological Q waves on ECG.
ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; BMI, body mass index; HR, heart rate; IHD, ischaemic heart disease; LVEDD, left ventricular end diastolic dimension; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Statistical analysis

Discrete variables are expressed as frequency counts and percentages and continuous variables are expressed as mean (SD). Standard descriptive statistics including frequency distributions are used to summarise group characteristics. The χ^2 test was used to determine differences in rates of use of β blockers by subgroups. Differences in lung function at one year compared with baseline were established by the paired samples *t* test.

Relations between β blocker use at one year and baseline variables were explored by calculating odds ratios (ORs) with 95% confidence intervals (CIs) where the OR is an approximation to the relative risk.[15 16] For missing data an extra category was calculated that allowed us to assess bias. ORs were calculated by using the GLIM4 statistical computer package.[17] A nominal level of 5% significance was assumed (two tailed).

β Blocker analysis

Only two β blockers are licensed for use in heart failure within the UK (carvedilol and bisoprolol). Therefore, analysis of β blocker use is based on initiating and achieving target doses of either carvedilol or bisoprolol. All other β blockers are included for analysis within the ''unlicensed β blocker'' category.

RESULTS

Over a period of 29 months (September 2001 to July 2004), heart failure was diagnosed in 513 patients. Within one year of follow up 157 of these patients died (all cause mortality) leaving 356 patients with a minimum of one year follow up. Deaths were determined by local clarification. All surviving patients attended one year follow up. The majority of patients were elderly white men with systolic dysfunction of ischaemic aetiology and New York Heart Association (NYHA) class II symptoms. Table 1 shows clinical characteristics.

β Blocker use

At first attendance 172 (48.3%) patients were taking a β blocker; 27 (15.7%) were taking an optimal dose (that is, bisoprolol 10 mg once daily or carvedilol 25 mg twice daily). Carvedilol was the most commonly prescribed (n = 66 or 38.4% of patients taking β blockers), followed by bisoprolol (57 (33.1%)), with mean daily doses of 24.1 (16.9) mg and 4.9 (3.0) mg, respectively. β Blockers not licensed in the UK for use in heart failure accounted for 28.5% (n = 49), predominantly atenolol. At the time of initial assessment 184

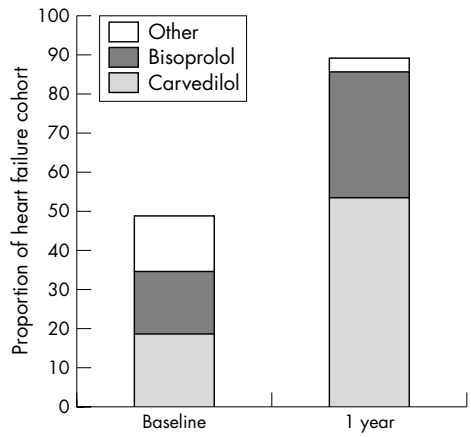

Figure 1 Comparison of β blocker prescribing over one year.

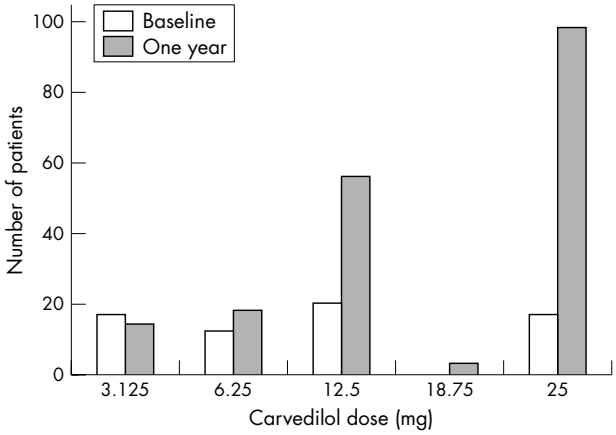

Figure 2 Comparison between baseline and one year carvedilol prescribing.

(51.7%) patients with systolic dysfunction were not taking β blockers.

At one year 315 patients (88.5%) were taking β blockers, carvedilol and bisoprolol accounting for 303 (96.2%) prescribed β blockers. Figure 1 shows a comparison between β blocker use at baseline and at one year.

β Blocker initiation

Of the 184 patients not taking β blockers at baseline 155 (84.2%) attempted initiation. Twelve patients discontinued treatment as a result of side effects (see below), resulting in the vast majority (315 (88.5%)) of patients taking β blockers at one year. Twenty nine patients did not attempt β blocker initiation, all of whom were receiving regular inhaled bronchodilators for either chronic obstructive pulmonary disease (COPD) or asthma.

β Blocker titration

Of the 329 patients who successfully started treatment, who were taking a suboptimal β blocker dose at baseline, or who were taking unlicensed β blockers, 100 achieved target dose carvedilol or bisoprolol after titration. Thus, 119 (37.8% of patients taking β blockers) were at the target dose at one year, 19 of whom were taking the target dose at baseline. The target dose was achieved by 51.8% of patients receiving carvedilol and 18.4% receiving bisoprolol.

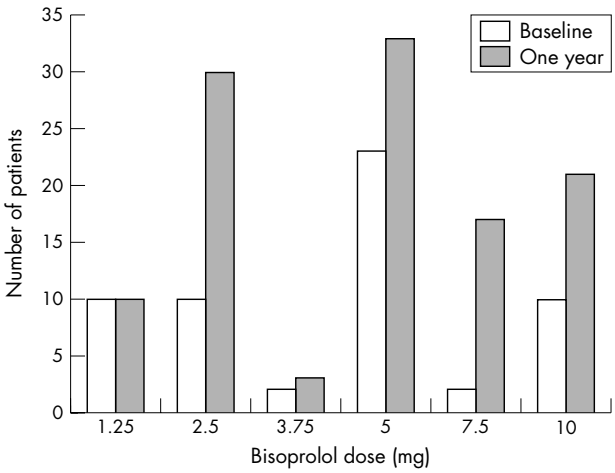

Figure 3 Comparison between baseline and one year bisoprolol prescribing.

Fourteen patients taking β blockers required dose down titration due to side effects (see below). During follow up 39 of the 49 patients taking unlicensed medication were changed from their baseline β blocker to carvedilol or bisoprolol. Mean daily dose of carvedilol (n = 189) at one year was significantly increased from baseline (24.1 (16.9) *v* 37.4 (20.0) mg, $p < 0.01$) (fig 2). The mean daily dose of bisoprolol at one year and at baseline did not differ (4.9 (3.0) *v* 5.3 (2.9) mg, respectively, p = 0.3), although the number of patients prescribed bisoprolol doubled (n = 114; fig 3).

β Blocker discontinuation

Few (n = 12 or 3.7% of those either starting β blockers or taking β blockers at baseline) patients discontinued β blocker as a result of intolerable side effects or worsening symptoms. At one year 41 (11.5%) patients were not taking β blockers, 58.5% of whom had evidence of airways obstruction. The predominant reason for discontinuation was worsening dyspnoea related either to heart failure decompensation or to exacerbation of obstructive airways disease. Figure 4 shows reasons for discontinuation or down titration.

Obstructive airways disease

At baseline assessment 238 patients (66.8% of total population) were either current (11.7%) or previous cigarette smokers (55.1%), with significantly more smokers not taking β blockers at one year (90% *v* 64%, $p < 0.01$). All patients underwent spirometry at baseline and at one year. Patients with spirometric abnormalities consistent with COPD of greater than mild severity (that is, forced expiratory volume in one second (FEV_1) to forced vital capacity (FVC) ratio < 70% and FEV_1 < 60% predicted) were analysed further.[18 19] According to the above criteria 124 (34.8%) patients had evidence of airways obstruction at baseline assessment, 54 of whom were taking β blockers, increasing to 100 (80.6%) at one year. Fifty nine were prescribed carvedilol (mean daily dose 35.5 (18.8) mg) and 40 bisoprolol (mean daily dose 5.5 (2.9) mg). The daily doses of carvedilol and bisoprolol at one year did not differ between patients with obstructive and patients with non-obstructive baseline spirometry. No reduction in mean FEV_1 (1.1 *v* 1.5 l, $p < 0.01$) or mean FVC (2.3 *v* 2.5 l/min, p = 0.2) was seen at one year in patients with airways obstruction who were started β blockers.

Patients not taking β blockers at one year had a trend towards worse lung function compared with those taking β blockers (FEV_1 1.4 (0.7) *v* 1.8 (1.4) l, p = 0.01; percentage predicted FVC 72.0 (21.0)% *v* 79.2 (22.0)%, p = 0.04). Paired *t* test for all 356 patients showed no difference between baseline and one year FEV_1 and FVC (1.7 (0.8) *v* 1.8 (0.8) l, p = 0.59 and 2.6 (1.0) *v* 2.7 (1.0) l/min, p = 0.84, respectively).

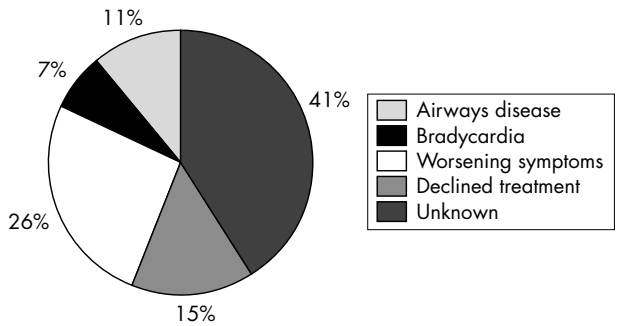

Figure 4 Reasons for β blocker discontinuation or down titration (n = 26).

Table 2 Relation between baseline variables and β blocker non-use at one year

Variable	Level	One year β blocker Yes	No	OR (95% CI)*	OR (95% CI)†
β Blocker at initial visit	No	150	34	1.0	
	Yes	165	7	0.2 (0.08 to 0.4)	
Age (years)	⩽65	85	8	1.0	1.0
	>65	230	33	1.5 (0.7 to 3.4)	1.7 (0.6 to 4.7)
Sex	Men	230	26	1.0	1.0
	Women	85	15	1.6 (0.8 to 3.1)	1.2 (0.6 to 2.7)
LVEF (%)	>35	92	11	1.0	1.0
	⩽35	133	28	1.2 (0.5 to 2.7)	1.1 (0.4 to 2.8)
	NK	42	11	2.7 (1.1 to 7.0)	3.4 (1.1 to 10.5)
NYHA class	I	35	1	1.0	1.0
	II	203	24	4.1 (0.6 to 28.8)	2.6 (0.3 to 19.8)
	III/IV	77	16	7.3 (0.9 to 56.7)	4.4 (0.6 to 34.9)
BMI (kg/m^2)	<24	47	8	1.6 (0.6 to 4.0)	1.6 (0.6 to 4.1)
	24–31	151	16	1.0	1.0
	>31	117	17	1.4 (0.7 to 2.5)	1.4 (0.6 to 3.3)
	<60	81	7	1.0	1.0
Resting HR (beats/min)	60–80	140	9	0.7 (0.3 to 2.1)	0.4 (0.1 to 1.6)
	>80	94	23	2.8 (1.1 to 6.9)	1.0 (0.3 to 3.4)
	⩽120	208	29	1.0	1.0
QRS duration (ms)	>120	101	9	0.6 (0.3 to 1.4)	0.7 (0.3 to 1.6)
	NK	6	3	3.6 (0.9 to 15.1)	4.2 (0.8 to 22.3)
LVEDD (cm)	⩽5.5	57	9	1.0	1.0
	>5.5	177	29	1.0 (0.5 to 2.3)	0.9 (0.4 to 2.3)
	NK	81	3	2.9 (0.06 to 0.9)	0.2 (0.04 to 1.1)
	⩽90	117	12	1.0	1.0
Mean blood pressure (mm Hg)	91–110	130	23	1.7 (0.8 to 3.6)	1.6 (0.7 to 3.7)
	>100	64	6	0.9 (0.3 to 2.6)	0.8 (0.2 to 2.5)
	NK	3	1	3.3 (0.3 to 33.9)	
	<120	196	29	1.0	1.0
Creatinine (μmol/l)	120–180	78	7	1.7 (0.7 to 3.9)	1.7 (0.6 to 4.5)
	>180	24	1	3.6 (0.5 to 27.3)	2.9 (0.4 to 23.9)
	NK	17	4	0.6 (0.2 to 2.0)	1.0 (0.3 to 3.8)
Anaemia‡	No	214	28	1.0	1.0
	Yes	76	12	1.2 (0.6 to 2.5)	1.3 (0.6 to 2.9)
	NK	25	1	0.3 (0.04 to 2.3)	0.3 (0.03 to 2.0)
IHD	No	89	13	1.0	1.0
	Yes	226	28	0.8 (0.4 to 1.7)	1.3 (0.6 to 2.9)
Hypertension	No	205	28	1.0	1.0
	Yes	110	13	0.9 (0.4 to 1.8)	1.2 (0.6 to 2.7)
Diabetes	No	249	36	1.0	1.0
	Yes	66	5	0.5 (0.2 to 1.4)	0.4 (0.1 to 1.2)
Obstructive airways disease	No	206	26	1.0	1.0
	Yes	109	15	1.1 (0.6 to 2.1)	0.9 (0.4 to 2.0)
Smoking	No	114	4	1.0	1.0
	Past	170	26	4.4 (1.5 to 12.8)	4.7 (1.4 to 16.6)
	Current	31	11	10.1(3.3 to 33.9)	10.6 (2.5 to 44.2)
Diuretics	No	88	11	1.0	1.0
	Yes	227	30	1.1 (0.5 to 2.2)	0.9 (0.3 to 2.9)
ACE inhibitors	No	72	15	1.0	1.0
	Yes	243	26	0.5 (0.3 to 1.0)	0.5 (0.2 to 1.0)
Spironolactone	No	251	34	1.0	1.0
	Yes	64	7	0.8 (0.3 to 1.9)	0.5 (0.2 to 1.9)
Digoxin	No	262	33	1.0	1.0
	Yes	53	8	1.2 (0.5 to 2.7)	1.1 (0.4 to 3.0)

*All data; †excluding patients who were taking β blockers at baseline; ‡defined as haemoglobin concentration <120 g/l for women and <130 g/l for men.
CI, confidence interval; NK, individual variables not known; OR, odds ratio.

β Blocker compliance was supported by a reduction in resting heart rate assessed by 12 lead ECG (75.8 (19.7) *v* 65.9 (14.6) beats/min, $p < 0.001$ at baseline and one year, respectively). Spirometry was assessed further in patients who started β blockers and who had a heart rate reduction of > 5 beats/min at one year (77.9% of those starting β blockers). No significant difference in FEV_1 or FVC was evident (1.7 (0.7) *v* 1.7 (0.7) litre and 2.5 (0.9) *v* 2.6 (0.9) l/min, respectively).

Inhaled bronchodilator use increased from 12.1% (n = 43) of patients at baseline to 14.9% (n = 53) of patients at one year assessment. Seven of the 10 patients who began bronchodilator treatment were taking β blockers, three of whom started β blockers during assessment and follow up.

Predictors of β blocker use

Table 2 presents baseline associations with β blocker use at one year. Demographic factors such as age, sex, and body mass index were not related to β blocker use at one year. However, there was a linear trend with NYHA class: as NYHA class became worse, the likelihood of taking a β blocker at one year was reduced. Similar trends were observed for FVC (percentage predicted), C reactive protein, and creatinine. Current or past smoking was less likely to result in taking a β blocker at one year. Diabetic patients and patients taking ACE inhibitors were more likely still to be taking β blockers at one year. Taking a β blocker at baseline was also associated with β blocker use at one year.

Table 2 also shows associations for patients taking β blockers at one year but not at baseline. These data indicate

that co-morbid conditions are likely to indicate non-β blocker use at one year, other than for patients with diabetes, who were more likely to continue taking β blockers.

Overall only two variables were independently related to β blocker non-use at one year. These were thiazide use (OR 5.8, 95% CI 2.0 to 17.2) and smoking (past smoking OR 4.4, 95% CI 1.5 to 12.8, and current smoking OR 10.1, 95% CI 3.3 to 33.9). β Blocker use at baseline was a predictor of one year β blocker use (OR 0.2, 95% CI 0.08 to 0.4). If we exclude β blocker use as a factor in the analysis, the OR for thiazides was 6.8 (95% CI 2.5 to 19.0), for past smoking 4.7 (95% CI 1.4 to 16.6), and for current smoking 10.6 (95% CI 2.5 to 44.2), where the OR is for not being prescribed a β blocker at one year. However, as only 11.5% of patients were not taking β blockers at one year, the large ORs may be explained by low numbers.

Permanent pacemaker insertion

During the one year follow up 14 patients (3.9%) required the insertion of a permanent pacemaker due to symptomatic bradycardias. Eight of these patients either were taking a β blocker at baseline or started taking a β blocker before pacemaker insertion. At one year 11 of the 14 patients with a pacemaker were taking β blockers.

DISCUSSION

The available randomised clinical trial data overwhelmingly support the use of β blockers (carvedilol, bisoprolol, and metoprolol CR/XL) for all severities of stable symptomatic heart failure. Guidelines recommend low dose initiation and titration towards a target dose, although β blocker doses below target levels have also shown clinical benefit.[20]

Despite the evidence for β blockers in heart failure many patients have relative contraindications to drugs or experience significant side effects, resulting in poor compliance or discontinuation.[10] Discontinuation rates from clinical trial data range from 13.9% (MERIT-HF (metoprolol CR/XL randomised intervention trial in congestive heart failure))[21] to 32% (COMET (carvedilol or metoprolol European trial)).[13] The main reasons for discontinuation are fatigue, dizziness, hypotension, worsening heart failure symptoms, and bradycardia. In a meta-analysis of all trials from 1966 to 2002, β blockers were associated with significant absolute annual increases in risks of hypotension (11 in 1000, 95% CI 0 to 22), dizziness (57 in 1000, 95% CI 11 to 104), and bradycardia (38 in 1000, 95% CI 21 to 54).[22]

Some obstacles have been reported to titration of β blockers outside of clinical trials,[9 23] and it is common for patients with heart failure to continue with low dose β blockers. Our results show that the vast majority of patients with heart failure can successfully start β blockers, with few patients discontinuing treatment because of side effects. Within a structured clinic setting, the target dose can be achieved by over one third of patients within a year.

Heart failure and COPD often coexist, with the prevalence of COPD in heart failure ranging from 23–33%.[24–26] The increase in life expectancy, together with improvement in cardiovascular disease survival, will inevitably result in a greater number of patients with both conditions. Patients with significant airways disease have largely been excluded from randomised controlled trials of β blockers in heart failure, primarily for safety reasons, based largely on case reports. However, a growing body of evidence supports the safe use and beneficial effect of β blockers on cardiovascular risk in patients with obstructive airways disease. Both selective and non-selective β blockers do not appear to adversely affect lung function (FEV_1, FVC, or bronchodilator response) in stable COPD, with low rates of discontinuation.[26–32]

Direct evidence for use of β blockers by patients with COPD and chronic heart failure is lacking. Whether the clinical benefits of β blockers seen in patients with heart failure alone apply to patients with COPD is not yet apparent. Comparisons have been made with post-myocardial infarction patients with COPD, who have been shown to benefit from β blockade. Analysis of over 200 000 post-myocardial infarction patients showed a relative risk of death after two years of 0.6 (95% CI 0.57 to 0.63) for patients with COPD taking β blockers compared with those who were not.[33] Current experience of β blocker use does not support the fear of inducing bronchoconstriction in these patients. In our experience β blocker treatment does not appear to be significantly influenced by the presence of stable obstructive airways disease, with no worsening of lung function evident at one year. Mean daily doses at one year were equal in patients with ''normal'' spirometry and those with ''obstructive'' results. All 29 patients who were not considered for β blockers had obstructive airways disease requiring regular bronchodilator treatment. No patient required hospitalisation due to decompensation of cardiac or pulmonary disease related to β blocker initiation or dose up titration.

Many strategies have been used to improve guideline implementation in heart failure, with active interventions being more successful than passive ones.[34 35] Such positive strategies include patient specific reminders, focused treatment objectives, patient involvement, and inpatient nurse facilitation. Our outpatient clinic allowed regular patient review, enabling physicians and nurse specialists to focus their efforts on β blocker use. The IMPACT-HF (initiation management predischarge process for assessment of carvedilol therapy for heart failure) study[36] examined whether the strategy of inpatient initiation improved β blocker use and adherence; patients were randomly assigned to inpatient or outpatient initiation. β Blocker use by those who started β blockers before discharge was significantly increased at 60 days ($p < 0.001$), without increasing side effects or length of stay. The COPERNICUS (carvedilol prospective randomised cumulative survival) study showed that patients with severe heart failure could safely tolerate inpatient initiation of β blockers.[37]

We have shown that a structured clinic programme with an aggressive approach to prescribing β blockers for patients with heart failure can result in significantly improved rates of use and adherence. Spirometry is a simple and useful tool for identifying and monitoring patients with respiratory disease who start β blocker treatment. Our experience of β blocker use by patients with (non-reversible) airways disease suggests that many patients with stable compensated cardiac failure can safely tolerate the careful introduction of β blockers without significant adverse effect.

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Use of nicotine replacement therapy and the risk of acute myocardial infarction, stroke, and death

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Please visit the *Heart* website [www.heartjnl.com] for a link to the full text of this article.

Objective: To determine whether nicotine replacement therapy (NRT) is associated with an increased risk of acute myocardial infarction, acute stroke, or death.
Design: Self control case series analysis of data from The Health Improvement Network (THIN) to estimate the relative incidence of myocardial infarction and stroke in four 14 day periods before and after the first prescription for NRT.
Setting: THIN is a computerised general practice database.
Subjects: Patients contributing data to THIN.
Interventions: Observational study of NRT.
Main outcomes: Acute myocardial infarction, acute stroke, and death.
Results: 33 247 individuals had been prescribed NRT, of whom 861 had had a myocardial infarction and 506 a stroke. There was a progressive increase in the incidence of first myocardial infarction in the 56 days leading up to the first NRT prescription (overall incidence ratio 5.55, 95% confidence interval (CI) 4.42 to 6.98), but the incidence fell after this time and was not increased in the 56 days after starting NRT (incidence ratio 1.27, 95% CI 0.82 to 1.97). The results were similar for second myocardial infarction and stroke, and for subgroups of people with pre-existing angina and hypertension. There were 960 deaths in our cohort during a mean follow up period of 2.6 years after starting NRT, with no evidence of an increased mortality in the 56 days after the NRT prescription (incidence ratio 0.86, 95% CI 0.60 to 1.23).
Conclusions: The use of NRT is not associated with any increase in the risk of myocardial infarction, stroke, or death.

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