2:30 p.m.

821-3 Evaluation of Beta-Blocker Dose in Community-Based Treatment of Heart Failure

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Background: Randomized clinical trials (RCT) are performed in a very different environment from community practice. Heart failure patients in the community tend to be older, have more comorbidities and are not cared for by the teams of heart failure specialists who recruit patients into RCT, which may be especially important when beta-adrenergic blocking drugs are prescribed to patients with heart failure.
Methods: In order to explore these prescribing effects we determined the dose of carvedilol at end-titration in 4,113 patients in the practice setting and related this to physician type (cardiologists vs. non-cardiologists), heart failure severity, and the risks of hospitalization and death.
Results: Dose achieved was not related to patients' age, sex, race, history of diabetes or other major demographic/clinical factors. The table shows factors that are influenced by dose.

Patient Characteristics and Outcomes	Carvedilol dose at end-titration (mg bid)					
	0 mg	3.125 mg	6.25 mg	12.5 mg	25 mg	50 mg
No. Patients	386	416	722	759	1672	158
Dose distribution in NYHA I patients (n=445)	7%	7%	17%	17%	46%	5%
Dose distribution in NYHA II patients (n=2099)	9%	9%	16%	18%	43%	4%
Dose distribution in NYHA III patients (n=1390)	11%	11%	18%	19%	38%	3%
Dose distribution in NYHA IV patients (n=131)	5%	18%	30%	21%	23%	4%
Dose distribution in cardiologists' patients (n=2994)	10%	8%	14%	17%	47%	4%
Dose distribution in non-cardiologists' patients (n=1119)	7%	17%	27%	21%	24%	4%
HF hospitalizations per dose group	22%	17%	14%	11%	9%	8%
Odds ratio of HF hospitalizations (95% CI)	ref	0.71 (0.48-1.06)p=0.0974	0.59 (0.42-0.85)p=0.0043	0.47 (0.33-0.68)p<0.0001	0.44 (0.32-0.62)p<0.0001	0.42 (0.21-0.84)p=0.0137
KM rate per dose group	17%	11%	10%	7%	5%	5%
Hazard ratio for death (95% CI)	ref	0.66 (0.42-1.05)p=0.0780	0.55 (0.36-0.84)p=0.0060	0.35 (0.22-0.54)p<0.0001	0.25 (0.18-0.39)p<0.0001	0.38 (0.16-0.93)p=0.034

ref = referent group for Odds Ratio and Hazard Ratio is the 0 mg dose group
KM rate = Kaplan-Meier rate for all-cause mortality

Conclusions: Carvedilol dose in the community appears lower than in RCT, is influenced by NYHA functional class and tends to be higher when prescribed by cardiologists. At all doses, patients taking carvedilol have a lower incidence of death and heart failure hospitalization than those not receiving drug. This study demonstrates the utility of beta-blocker therapy in the community and also confirms the RCT findings that lower doses of carvedilol can also provide clinical benefit in the usual care setting.

2:45 p.m.

821-4 Beta-Blockers Reduce Heart Failure Mortality Regardless of the Initial Heart Rate: Data From the ICONS Study

Jonathan G. Howlett, David E. Johnstone, Jafna L. Cox, Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada

Background: The role of heart rate reduction as a mechanism of beta blockade (BB) effect in reduction of heart failure (HF) mortality is unknown. We sought to determine whether the mortality effect of BB was related to initial heart rate in hospitalized HF patients.
Methods: We utilized a prospective registry-based disease management database, the Improving Cardiovascular Outcomes in Nova Scotia (ICONS) study, to identify individuals with a discharge diagnosis of HF from any Nova Scotia hospital between October 15, 1997 and July 1, 2000. Patients were stratified according to their admission heart rate quintiles in beats/min, (> 115, 100-115, 86-99, 72-85,<72). Variables were recorded prospectively and censored at 2 years.
Results: There were 4888 unique patients, with average age of 76 years; 52% were female. Patients prescribed BB were younger (age 74 vs. 77), with lower creatinine (133 vs. 143 umol/L) and higher EF (43% vs. 38%). After adjustment for co-morbid conditions, hazard ratios for mortality with BB at two years were determined:

Initial Heart Rate (beats/min)	Hazard Ratio	95% CI	p Value
> 115 (n=990)	0.54	0.42- 0.71	0.0001
100-115 (n=1006)	0.62	0.47- 0.80	0.0003
86-99 (n=977)	0.57	0.44 - 0.75	0.0001
72-85 (n=1015)	0.61	0.47-0.79	0.0002
< 72 (n=900)	0.69	0.52- 0.92	0.002

Beta blocker prescription at discharge was associated with 37% lower two year mortality (31% vs. 42%). This finding was consistent regardless of heart rate quintile. The hazard ratio for BB in those with heart rate <65 bpm was 0.71, p= 0.09.
Conclusion: Beta blockers reduce mortality in unselected patients discharged from hospital with HF regardless of their admission heart rate. Further data is required in those with severe bradycardia.

3:00 p.m.

821-5 Risks of Death and Hospitalization in Heart Failure Patients Receiving Carvedilol Versus Metoprolol Tartrate: A Retrospective Claims-Based Study

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Background: The Carvedilol or Metoprolol European Trial (COMET) demonstrated improved survival with carvedilol (C) versus metoprolol tartrate (MT) in patients with heart failure. The benefits of C versus MT in heart failure patients in typical US clinical practice are unknown.
Methods: Using a large US health-insurance claims database linked to mortality information from the US Social Security Administration, we compared the risks of death and hospitalization and the costs of inpatient care in heart failure patients receiving C versus MT. Subjects included all persons with ≥1 prescription for either C or MT (but not both) from 9/97-8/00 who, within 12 months of their first prescription for C or MT, had: (1) ≥1 medical encounter with a primary diagnosis of heart failure; (2) ≥1 prescription for a loop diuretic; (3) ≥1 prescription for an angiotensin-converting enzyme inhibitor; (4) no prescriptions for a beta-blocker; and (5) continuous eligibility for health benefits.
Results: A total of 887 C patients and (coincidentally) an equal number of MT patients met all criteria for inclusion in the study. Mean follow-up was 11 months (maximum, 36 months). Mean dose prescribed (mg/day supplied) was 24 for C and 70 for MT; mean dose received (mg/day of follow-up) was only 14 for C and 44 for MT. C patients were younger, more likely to be men, seen by a cardiologist, and prescribed digoxin; they also had higher pretreatment heart failure costs. However, they were less likely to have hypertension or other cardiovascular disease, and also had lower pretreatment cardiovascular costs. Controlling for these differences using Cox proportional hazards regression, receipt of C versus MT was associated with reduced risk of all-cause mortality (hazard ratio .78; 95% CI .61-.99) and all-cause hospitalization (hazard ratio .76; 95% CI .66-.89). In a propensity-matched sample of C and MT patients (n=562 each), expected costs of cardiovascular inpatient care at 36 months were $6,164 lower for C than MT (95% CI $1,330-$10,714).
Conclusion: Consistent with findings from COMET, our results suggest that C improves survival and reduces costs of care compared with MT in heart failure patients in typical US clinical practice.

3:15 p.m.

821-6 Beta-Blocker Utilization in Patients With Heart Failure: A Single-Center, Two-Year Follow-Up

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Background: The longitudinal pattern of beta-blocker (BB) utilization in a heart failure (HF) practice setting has not been explored. Studies have not addressed the use of BB over time to determine the "target" rates of use and reasons for discontinuation.
Methods: We reviewed consecutive patients with a clinical diagnosis of HF seen in a specialized HF clinic between 3/01-5/01, and determined the pattern of BB utilization and clinical outcomes over a subsequent 2-year period.
Results: From a cohort of 496 patients (mean age 61±14 years, 60% male, 53% with ischemic etiology, mean LVEF 28±15%), 75% had a trial with a BB. On follow-up at 6, 12, and 24 months, BB utilization rates were maintained at 69%, 70% and 67%, respectively. Of the 120 non-BB users, 28 (23%) were subsequently initiated on BB, despite known relative contraindications in 53% of patients. In 2 years, the discontinuation rate was 10%, and the most common reason for discontinuation was failure to restart BB following hospitalization (31%). In this non-randomized cohort, the 2-year all-cause mortality was comparable among different BBs (Figure).
Conclusion: Utilization rates of BB in our HF clinic remain constant (67-70%) throughout a 2-year follow-up and likely represents a reasonable "target". Of those who discontinued