Influence of carvedilol on hospitalizations in heart failure: incidence, resource utilization and costs


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
A strategy of adding carvedilol to current treatment regimes for patients with heart failure was evaluated. Current treatment regimes included diuretics, digoxin and angiotensin-converting enzyme (ACE) inhibitors. Patients tolerating open-label carvedilol (6.25 unspecified units, twice daily) for 2 weeks underwent treatment with either carvedilol or placebo, and were then uptitrated and maintained on regimens of target doses (up to 25 to 50 mg, twice daily) for up to 15 months.

Type of intervention
Treatment and secondary prevention.

Economic study type
Cost-effectiveness analysis (cost-consequences).

Study population
The study population comprised patients with systolic dysfunction (a left ventricular ejection fraction of less than 0.35), and who were in the New York Heart Association (NYHA) class II to IV despite drug therapy.

Setting
The setting was secondary care. The economic study was conducted in several states on the east and west coasts of the United States.

Dates to which data relate
The inclusion of patients into the trial programme commenced in 1993 and ended in early 1995. All prices were adjusted to 1994 prices.

Source of effectiveness data
The effectiveness data were derived from a single study (see Other Publications of Related Interest). The trial programme consisted of four studies that evaluated carvedilol in heart failure. Data on the patients in all four studies were pooled in this analysis.

Link between effectiveness and cost data
The resource use and data on clinical consequences were obtained from the same patients in one trial programme.

Study sample
Details of power calculations or sample selection were not provided in the economic paper. A total of 1,197 patients
entered a pre-study, open-label, run-in phases of the trial programme, of which 1,094 patients were randomised to double-blind treatment. A total of 398 patients were randomised to placebo and 696 to carvedilol.

Study design
The trial programme consisted of four multi-centre, double-blind, randomised studies. The duration of the treatment ranged from 1 day to 15.1 months (median: 6.5 months). Eighty-five per cent of the placebo-treated patients, and 89% of the carvedilol-treated patients, continued with the study medication until the end of the trial. The patients were followed-up for 15 months.

Analysis of effectiveness
The authors stated that the analysis was conducted on an intention to treat basis. The authors also reported that the pre-treatment characteristics were similar in the two groups. The risk of hospitalisation due to congestive heart failure, myocardial infarction, intermediate coronary syndrome, or other reasons, was recorded in the study. Differences in the hospitalisation risk were plotted using Kaplan-Meier methods, and tested using a Cox proportional hazards regression model.

Effectiveness results
Carvedilol reduced the risk of being hospitalised at least once for any reason by 29% (95% confidence interval, CI: 8 - 46, p=0.034). Similarly, carvedilol reduced the risk of hospitalisation by 28% (95% CI: 2 - 46) for cardiovascular causes and by 38% (95% CI: 2 - 61) for heart failure. Carvedilol also reduced the mean number of hospitalisations per patient for any reason by 25% (p=0.003).

Clinical conclusions
The authors stated that carvedilol both reduced the risk of clinical deterioration in patients with heart failure, and lessened the severity of illness among those patients who were hospitalised.

Modelling
Models were used to assign costs to the types of hospitalisation that were evaluated in the trial. These cost-prediction models used data from routinely collected hospitalisation records in acute-care hospitals in the USA.

Measure of benefits used in the economic analysis
No summary measure of benefit was used in the paper. The analysis therefore used a cost-consequences approach.

Direct costs
The cost per hospitalisation was estimated using cost-prediction models developed using a hospital administrative database. The costs included the time spent in various hospital units, the services used, and the total hospitalisation costs. The authors selected a master sample of hospital admissions for heart failure using International Classification of Diseases (ICD-9) codes for heart failure in the database. The ICD-9 codes were also used to develop cost prediction models for four different hospitalisation diagnoses. These were "congestive heart failure", "myocardial infarction", "intermediate coronary syndrome" and "other or unspecified angina pectoris". These modes were applied to the resource use identified in the trial programme. All the costs were adjusted to 1994 levels. The costs were, appropriately, not discounted because discounting was irrelevant.

Statistical analysis of costs
The difference in resource use between treatment with carvedilol or placebo was analysed using the Wilcoxon rank sum test. Cost-variance analyses were used to evaluate whether the reduction in the hospital costs was due to fewer admissions or to a reduced cost per stay.
Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was not carried out.

Estimated benefits used in the economic analysis
Not applicable due to the cost-consequences approach adopted. See the 'Effectiveness Results' section.

Cost results
The average cost of hospitalisation for cardiovascular admissions was $1,912 per patient for carvedilol patients, and $4,463 per patient for those receiving placebo. This was a difference of 57% (p=0.016). Carvedilol reduced the cost for heart failure admissions by 81%. The cost was $452 for the carvedilol group versus $2,338 for the placebo group, (p=0.022). The authors also identified a 43% reduction in the cost of each hospital stay for cardiovascular causes, and a 63% reduction for heart failure causes.

Synthesis of costs and benefits
The costs and the benefits were not combined.

Authors' conclusions
Many hospitalisations for heart failure, and associated costs, may be prevented by the addition of carvedilol to drug treatment for patients with heart failure.

CRD COMMENTARY - Selection of comparators
The authors compared 'current treatment', with and without the addition of carvedilol, for the treatment of heart failure. Current treatment may include diuretics, digoxin and ACE inhibitors. Comparing the intervention with current treatment, and leaving some influence of the treatment decision to the treating physician, may increase the generalisability of these results from the trial setting to clinical practice settings.

Validity of estimate of measure of effectiveness
The effectiveness estimate for this study used a large prospective, randomised, double-blind trial that was published in a well-respected journal. The study design and patient sample were both appropriate for the hypothesis, and the data were analysed using appropriate methods. The validity of the results should, therefore, be high.

Validity of estimate of measure of benefit
The authors adopted a cost-consequences approach for their analysis, which was appropriate for the intervention and patient domain. As such, outcomes were left disaggregated.

Validity of estimate of costs
The cost-prediction models developed in an observational database were applied to the actual resource use in the trial. The authors pointed to a study that has validated such an approach to costing, but emphasised that caution should be
exercised in the interpretation of these data. The authors also pointed out that only inpatient costs were included in the analysis and that the other costs were excluded. For example, the cost of carvedilol and associated monitoring costs. The costs were appropriately analysed using a non-parametric test. However, the paper would have benefited from presenting confidence intervals around the estimated differences in the average costs.

**Other issues**

The study included an appropriate patient sample. In addition, it measured relevant outcomes and applied appropriate analysis techniques. In terms of comparisons with other studies, the authors stated that the results from this study confirmed the findings of other studies of carvedilol in heart failure. Patients from several centres in several states were included in the study. Thus, the results are likely to be generalisable to patients in NYHA classes II to IV in the USA. The results are also likely to be generalisable to patients with similar characteristics in other settings, where heart failure is treated in a similar fashion.

**Implications of the study**

The authors commented that beta-blockade with carvedilol, in conjunction with ACE inhibition, should be used in order to reduce hospitalisation frequency of patients with heart failure.

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**Other publications of related interest**


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