

Clinical Outcomes in Patients With Congestive Heart Failure

The Age of Improvement

Congestive heart failure (CHF) is associated with significant morbidity and mortality rates. However, recent studies using linked patient databases have provided evidence that clinical outcomes are improving.

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Congestive heart failure (CHF) is a condition associated with significant morbidity and mortality. The natural history of CHF is characterised by a progressive course, that frequently includes repeated hospital admissions.¹ Accordingly, the principal goals of therapy in patients with CHF are not only to relieve symptoms, but also to improve clinical outcomes. These outcomes include mortality and hospitalisation for CHF. Fortunately, in the past decade there have been significant advances in the understanding of the pathophysiology of CHF.² This improved understanding is directly responsible for the development of contemporary pharmacologic therapy resulting in improved clinical outcomes in CHF patients. In this update, the evidence for improved clinical outcomes in patients with CHF, the potential reasons for these improvements and their implications for practising physicians will be discussed.

In this article:

1. What are the significant studies and clinical trials on congestive heart failure?
2. How are clinical outcomes explained?
3. What are the implications for GPs/FMs?

What are the landmark studies?

The mortality rate of patients diagnosed with CHF based on large-scale epidemiologic studies is shown in Table 1. In the population-based studies, the Framingham Heart Study followed over 600 subjects screened from 1948 to 1988 with new onset of CHF.³ The Rochester Epidemiology Project, conducted in Omsted County, Minnesota, followed 107 and 141 patients who presented with new onset CHF in 1981 and 1991, respectively.^{4,5}

Table 1

Mortality Rate Results from Epidemiologic Studies

Study	Mortality Rate			
	One-Year	Two-Year	Five-Year	10-Year
Population-Based Studies				
Framingham ³	17%	30%	56%	
Rochester ^{4,5}	24%	30%	65%	
NHANES ⁶				43%
Hospital-Based Studies				
Franciosa, et al. ⁸	34%	59%		
Wilson, et al. ⁹	48%	68%		
Brophy, et al. ⁷	33%			

The mortality rates of the Framingham and Rochester studies were similar. In both population surveillances, the five-year mortality rate was over 50%. According to the National Health and Nutrition Examination Survey (NHANES-1) Epidemiological Follow-Up Study, the 15-year mortality rate in patients 55 years of age and older was 40% for women and 72% for men.⁶

In the hospital-based studies, the sample size was typically smaller and the mortality rate was generally higher than those in population-based studies. This is conceivable, as these patients likely represented those with more advanced disease, including those who presented to the emergency department because of decompensation, or those referred to tertiary care centres because of intractable symptoms.⁷⁻⁹

About the author ...



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A recently published study employed the Canadian Institute for Health Information (CIHI) database to construct a retrospective cohort of over 38,000 patients in Ontario, who were hospitalised for CHF for the first time from April 1994 to March 1997.¹⁰ The CIHI database collected and collated data of all hospital discharges in Canada. Vital status was therefore determined through linkage with the Ontario Registered Person Database. Based on this analysis, the crude 30-day and one-year mortality rate after the first admission was 12% and 33%, respectively. These relatively high mortality rates may once again be related in part to the fact that only hospitalised patients were analyzed.

Some of the aforementioned large-scale epidemiologic studies have also attempted to examine changes in mortality rate over time. For example, the Framingham study reported no improvement in mortality from the 1948-1974 period to the 1975-1988 period.³ One possible explanation for the lack of improvement in the Framingham study was that the periods covered were prior to the widespread use of angiotensin-converting enzyme (ACE)

inhibitors. Indeed, results from the latest Framingham study, which covered time periods from 1950 to 1999, have suggested, for the first time, an improvement of survival rate after the onset of CHF of approximately 12% per decade.¹¹ The Rochester study compared the incidence of CHF and the survival in patients with CHF in 1981 with that observed in 1991.⁵ The incidence of CHF after adjustment for age and sex was not significantly different in the 1991 cohort compared with that in 1981. Likewise, the survival of patients newly diagnosed with CHF was similar in the two cohorts (one-year mortality rate of 28% and 23%, respectively, $P = 0.53$). These investigators, therefore, concluded that advances in disease management, at least as used in the community, had not impacted on the incidence of survival in patients with CHF in the community during the 10-year study period.

A recent epidemiologic study from Scotland also provided evidence of improved prognosis in patients suffering from CHF for over a decade.¹² In Scotland, all hospitalisations and deaths are captured on a single database. This database is linked, with the use of probability matching, to information held by the General Registrar's Office for Scotland on in-hospital, and out-of-hospital deaths. Using this approach, the case fatality in all patients (66,547 patients) admitted with a principal diagnosis of CHF from 1986 to 1995 was studied. Crude case fatality rates at 30 days and at one, five, and 10 years were 19.9%, 44.5%, 76.5%, and 87.6%, respectively. Median survival was 1.47 years in men and 1.39 years in women (2.47 and 2.36 years,

respectively, in those surviving 30 days). Importantly, after adjustment, 30-day case fatality rates declined between 1986 and 1995, by 26% (95% confidence interval [CI] 15 to 35%, $P < 0.0001$) in men and 17% (95% CI 6 to 26, $P < 0.0001$) in women. Longer-term case fatality rates fell by 18% (95% CI 13 to 24%, $P < 0.0001$) in men and 15% (95% CI 10 to 20%, $P < 0.0001$) in women. The one-year case fatality rates over time with the relatively close 95% CIs are illustrated in Table 2. The declining trend over time is evident.

What do the clinical trials tell us?

Large-scale, multicentre clinical trials in CHF constitute a valuable source of information regarding clinical outcomes of patients with CHF for several reasons. Patients in clinical trials are followed closely and systematically and the clinical outcomes, including cause-specific outcomes, such as CHF hospitalisation, are almost always precisely defined and fully documented. In addition, pre-specified subgroup

Table 2

Trends in Case Fatality Rate Over Time in Scotland

Year of Admission	Sample Size	One-Year Case Fatality Rate (95% Confidence Intervals)
1986	5,650	46.68% (46.79-46.81)
1988	6,100	46.25% (46.25-46.26)
1990	6,550	45.01% (45.00-45.02)
1992	7,270	42.96% (42.95-42.97)
1994	7,553	41.15% (41.14-41.16)

Survival was calculated using the actuarial life table method.

Adapted from: MacIntyre K, Capewell S, Stewart S, et al: Evidence of improving prognosis in heart failure: trends in case fatality in 66,547 patients hospitalized between 1986 and 1995. *Circulation* 2000; 102:1126-31.

Table 3

Control Group Mortality Rate From Large-Scale Intervention Trials

Study	Publication year	Study Drug	NYHA Class	One-year Mortality
CONSENSUS ¹³	1987	Enalapril	IV	52%
PROMISE ²²	1991	Milrinone	III,IV	31%
SOLVD* ¹⁴	1991	Enalapril	I-III	16%
PRAISE ²³	1994	Amlodipine	II-IV	25%
DIG ²⁴	1997	Digoxin	I-III	13%
MERIT-HF ¹⁶	1999	Metoprolol CR/XL	II-IV	11%
COPERNICUS ¹⁷	2001	Carvedilol	IIIb, IV	19%
Val-HeFT ²⁵	2001	Valsartan	II-IV	9%
OVERTURE ²⁶	2002	Omapatrilat	III, IV	12%

*Treatment arm of the SOLVD program, control group received enalapril.

analyses often provide mechanistic information and generate new hypotheses. On the other hand, patients who are enrolled in clinical trials tend to be younger, with less comorbid conditions. Most important, patients who are recruited to clinical trials tend to receive more careful and systematic followup that would exert a favourable impact on clinical outcomes. Until recently, all clinical trials have involved almost exclusively patients with CHF accompanied by systolic left ventricular dysfunction. However, it is increasingly recognised that a large number of patients in the community have CHF with preserved systolic function. In general, patients with CHF and preserved systolic function, sometimes referred to as diastolic CHF, are generally older, with more comorbid conditions. Importantly, in contrast to CHF with systolic function, there are only small amounts of information on the mortality rate of patients with CHF with preserved systolic function and little is

known regarding therapy that could modify clinical outcomes in these patients.

Table 3 shows the placebo/control group mortality rate of several large-scale clinical trials based on the year the results were published. Notwithstanding that the severity of the disease of the patients in each trial varied, there is a definite trend for decreasing one-year mortality. The one-year mortality rate in the CONSENSUS (Cooperative North Scandinavian Enalapril Survival Study, a placebo-controlled trial of the ACE inhibitor enalapril in patients with severe CHF) study, published in 1987, was 50%. It fell to 9% in the Val-HeFT (Valsartan Heart Failure Trial, a placebo-controlled trial of the angiotensin receptor blocker valsartan in patients with moderate to severe CHF) study published in 2001. Finally, the rate fell to 12% in the most recent OVERTURE (Omapatrilat Versus Enalapril Randomized Trial of Utility in Reducing Events, a comparison between omapatrilat, a vasopeptidase inhibitor, with

an ACE inhibitor in patients with severe CHF) study.

How do we explain clinical outcomes?

There are several reasons for improved clinical outcomes over the past decade in patients with CHF. Neurohormonal inhibition, specifically blockade of the renin angiotensin-aldosterone system and the sympathetic nervous system, has had a dramatic impact on mortality and morbidity, the latter reflected by reduced CHF hospitalisations in clinical trials.¹³⁻¹⁷ ACE inhibitor therapy could potentially explain the improved mortality in patients studied beyond the early 1990s. The combination of ACE inhibitors and beta blockers likely contributed to the improved outcomes in patients studied in the last two years. Both ACE inhibitors and beta blockers are recommended therapy in patients with CHF and systolic dysfunction according to the latest treatment guidelines.¹⁸

However, the neutral results on mortality of several recently reported large-scale studies of neurohormone or cytokine inhibition suggest that these pharmacologic approaches may have reached the plateau of their efficacy. It is possible the time has come for a paradigm shift in the treatment of patients with CHF, for example using device approaches, such as biventricular pacing, and conducting clinical trials aimed at more cause-specific clinical outcomes, such as hospitalisation.¹⁹


A second potential explanation is the proliferation of programmed care in patients with CHF, often referred to as heart failure clinics. The principal elements of programmed care

in CHF include a multidisciplinary approach, such as treatment from a physician and nurse practitioner, patient education and systematic followup. Although there are many anecdotal reports on the efficacy of this approach, there are only a few randomised controlled trials that have reported favourable effects on clinical outcomes.^{20,21} However, programmed care makes sense intuitively in patients with CHF, given the variable clinical course of these patients.

What are the implications for GPs/FMs?

There is evidence from both epidemiologic and clinical studies that the clinical outcomes of patients with CHF have improved in the past decade. This improvement is likely the result of the increasing use of evidence-based outcome-modifying pharmacologic therapy and to a lesser

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extent multidisciplinary care. While taking comfort that CHF is no longer a condition associated with high mortality, practitioners should be mindful that there are still many patients in the community who are misdiagnosed, or if diagnosed with CHF, treated sub-optimally. If possible, patients should be referred to a specialised programmed care facility at least once. The frequency of followup by the specialised facility will depend on the resources of the facility, as well as the necessities of the patient. The inevitable paradigm shift in the management of CHF will hopefully keep up the pace of improvement into the next decade. 

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