was the number of patients for whom revascularization had increased (Table 1).

Table 1. Follow-up

	In-hospital	3-month	12-month
Re-admission, % of patients	–	21%	42%
Median hospital stay, days	–	6	6
Device therapy, n (%)	84 (1.7%)	114 (2.3%)	162 (3.2%)
Revascularization, n (%)	368 (7.4%)	613 (12%)	1006 (20%)

Adding Clarity to Worsening HF

Written by Phil Vinall

Beth A. Davison, PhD, Momentum Research, Inc., Durham, North Carolina, USA, presented the results of a pooled analysis that addressed several questions concerning worsening heart failure (HF). The authors attempted to better understand which baseline characteristics are associated with the occurrence of worsening HF among those hospitalized for acute heart failure (AHF). Worsening HF was defined as worsening signs and symptoms of HF during an admission for AHF requiring rescue therapy with intravenous (IV) medications or mechanical support. In addition, the researchers sought to describe the relationship between worsening HF and adverse outcomes, the mechanism by which worsening HF results in poor outcomes, and whether worsening HF treated with therapies other than IV loop diuretics confers a different risk from worsening HF treated with IV loop diuretics alone.

The meta-analysis was based on patient-level data (n=3733) from 4 studies: the RELAX-AHF [Relaxin for the Treatment of Acute Heart Failure; Teerlink JR et al. *Lancet* 2013], the Pre-RELAX-AHF [Teerlink JR et al. *Lancet* 2009], the PROTECT pilot study [Pro-BNP Outpatient Tailored Chronic Heart Failure Therapy; Cotter G et al. *J Cardiac Fail* 2008], and PROTECT [Massie BM et al. *N Engl J Med* 2010]. The authors created multivariable models of worsening HF (through 5 days after baseline) and other outcomes developed in the pooled database. Associations of worsening HF with downstream clinical outcomes were estimated, with adjustment for covariates found in the models to be associated with these outcomes. Estimates were stratified by study. Differences in the patient populations were minor and reflected mainly the differences in eligibility criteria. Subjects in the 2 PROTECT studies had lower systolic blood pressure, a slightly higher proportion of patients with a recent history of HF, and somewhat worse renal function compared with those in the 2 RELAX studies. Approximately 12% of patients (range, 9.5% to 14.5%) overall had worsening HF through Day 5; the length of stay was about 10 days; and an average of 18% of patients (range, 9.8% to 24.3%) experienced cardiovascular death or HF or renal failure rehospitalizations through Day 60. Approximately 14% of patients (range, 9.3% to 18.6%) died by Day 180. Clinical outcomes in the 4 studies are summarized in Table 1.

The strongest multivariable predictor of death or worsening HF through Day 5 was increased blood urea nitrogen, followed by an increase in respiratory rate per 1 breath/minute, a decrease in hematocrit rate per 1%, and a decrease in systolic blood pressure. The C-statistic of the model was 0.6739, which indicated a modest ability to discriminate between patients with and without worsening HF.

Worsening HF by Day 5 was associated with a longer length of initial hospital stay (combined adjusted mean difference, 5.20 days; 95% CI, 4.56 to 5.84 days; p<0.0001) and with an increased risk of HF or renal failure readmission or cardiovascular death by Day 60 (combined adjusted HR, 1.64; 95% CI 1.34-2.01; p<0.0001). The risk of death by 180 days was also higher for those with worsening HF by Day 5 (adjusted HR, 1.93; 95% CI, 1.55 to 2.41; p<0.0001).

Table 1. Clinical Outcomes[a]

	PROTECT Pilot	PROTECT	Pre-RELAX-AHF	RELAX-AHF
Worsening HF through Day 5	29 (9.6)	288 (14.3)	34 (14.5)	110 (9.5)
Length of stay[b]	10.3±7.14	11.1±7.75	10.8±6.74	9.4±6.12
CV death or HF/RF rehospitalization by Day 60	73 (24.3)	412 (20.6)	22 (9.8)	151 (13.1)
Deaths by Day 180	43 (18.6)	347 (17.9)	20 (9.6)	107 (9.3)

CV=cardiovascular; HF=heart failure; PROTECT=Pro-BNP Outpatient Tailored Chronic Heart Failure Therapy; RELAX=Relaxin for the Treatment of Acute Heart Failure ; RF=renal failure.

[a]Values in n (Kaplan-Meier %).

[b]Values in mean±standard deviation. Stays >30 days truncated at 30 days, and in-hospital deaths assigned 31 days.

Worsening HF treated with IV loop diuretics alone is associated with increased risk of 180-day mortality (adjusted HR, 1.80; 95% CI, 1.36 to 2.36; p<0.0001). Worsening HF requiring IV inotropes or mechanical therapy was also associated with increased risk of 180-day mortality (adjusted HR, 3.03; 95% CI, 2.11 to 4.36; p<0.0001). Changes in markers of renal or hepatic impairment, lower cholesterol/albumin, or HF signs and symptoms explained little of the association of worsening HF with future clinical outcomes.

The associations and outcomes of worsening HF are more pronounced in the early weeks and months after the event and do not seem to be explained by the baseline characteristics of the patients in the studies analyzed. Worsening HF may be driven by a yet unknown pathophysiologic mechanism that conveys an independent risk for adverse outcomes in AHF.

Nurse-led Care Beneficial for CHF Patients

Written by Brian Hoyle

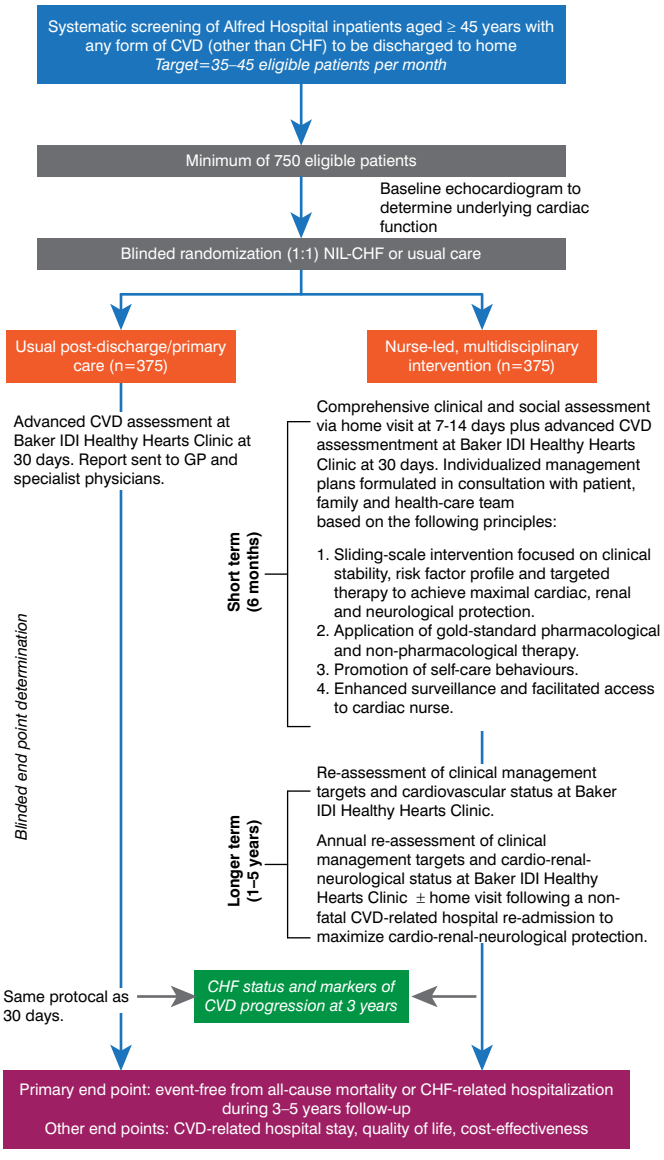
The Nurse-led Intervention for Less Chronic Heart Failure study [NIL-CHF], a randomized controlled trial, has provided evidence that nurse-led care confers greater benefit to heart failure (HF) patients in terms of reduced time in emergency care and improved longer-term cardiac recovery. The results of this study were presented by Simon Stewart, MD, Baker IDI Heart & Diabetes Institute, Melbourne, Australia.

Prevention of chronic HF (CHF) has only recently been studied [Ledwidge M et al. *JAMA* 2013]. Nurse-led care may have potential benefit in reducing hospital admissions due to CHF [Pearson S et al. *Arch Intern Med* 2006]. The NIL-CHF trial explored the influence of nurse-led management of patients with cardiovascular disease or a history of CHF on hospital admissions for CHF and all-cause mortality over a mean follow-up of 4.3 years (range, 41 to 66 months). The study was designed to create and test a program of care that cost-effectively prevents the development of CHF in at-risk patients without CHF.

Patients aged 45 years or older who had been admitted with a diagnosis of any cardiovascular condition except CHF were enrolled in this single-center study. Patients with CHF, as confirmed using echocardiography, or those who were subsequently re-admitted within 35 days for treatment of CHF were excluded. The primary end point was being event free after admission or all-cause mortality. Heart function was assessed (recovered, stable, or worse) 3 years after admission using echocardiography. Hospitalization rate and length of stay, all episodes of HF, emergency care, and any related cardiovascular events were recorded.

Patients were blindly randomized into usual-care or nurse-led clinical management, as described previously (Figure 1) [Carrington MJ & Stewart S. *Eur J Heart Fail* 2010]. The interventions included short- to medium-term support outside of the hospital (6 months) or longer-term support after the index hospital stay (18 months and

Figure 1. Study Design



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