For the PARADIGM-HF trial, 8442 patients were enrolled. These patients had New York Heart Association (NYHA) Class II to IV heart failure with a LVEF of ≤40%, brain natriuretic peptide levels higher than or equal to 100 if hospitalized or less than or equal to 150 if not hospitalized within the past 12 months, a systolic blood pressure greater than or equal to 95 mm Hg, a glomerular filtration rate greater than or equal to 30 ml/min/1.73 m^2, and serum potassium levels less than or equal to 5.4 mEq/L. Patients underwent a single-blind run-in period in which they received enalapril 10 mg BID for 2 weeks, then LCZ 100 mg BID for 1 to 2 weeks, and then LCZ 200 mg BID for 2 to 4 weeks (Figure 1). Patients then entered the double-blind period and were then randomly assigned to receive LCZ 200 mg BID or enalapril 10 mg BID. The primary end point was cardiovascular death or hospitalization for HF up to 4 years from the start of the trial.

At baseline, the mean patient age was 64 years, 22% were women, and 66% were white. In this trial, 70% of patients had NYHA Class II HF, and the cause of LV dysfunction was ischemic heart disease in 60% of the participants.

In conclusion, the PARADIGM-HF trial was designed to establish a new standard of care for patients with CHF with a reduced LVEF. Dr. Packer concluded his presentation by highlighting that the PARADIGM-HF trial was stopped early due to the significant decrease in cardiovascular mortality.

CardShock Score Aids in Risk Stratification for Short-Term Mortality in Patients with CS

Written by Phil Vinall

Cardiogenic shock (CS) is a condition of severe tissue hypoperfusion caused by cardiac dysfunction. Given the high rate of in-hospital and short-term mortality associated with CS, a prediction score could prove useful for risk stratification to guide optimal resource utilization. Johan Lassus, MD, PhD, Helsinki University Central Hospital, Helsinki, Finland, presented a new risk scoring system for patients with CS.

The objective of the CardShock Study and Registry [NCT01374867] was to assess the contemporary clinical picture and outcomes of CS to develop a risk prediction score for short-term mortality. Subjects were enrolled in the study within 6 hours of a diagnosis of CS (defined as systolic blood pressure [SBP] less than 90 mm Hg for 30 minutes or the need for vasopressor therapy to maintain adequate perfusion pressure) and more than or equal to 2 of the following signs of hypoperfusion: altered mental status/confusion, cold periphery, oliguria or blood lactate above 2 mmol/L. The primary outcome measure was all-cause mortality.

The mean age of the subjects (n=220) was 67 years, and 74% were male. Hypertension was present in 61% of participants; 28% had diabetes. Overall, cardiovascular comorbidities were not very prevalent. For many patients, CS was the first presentation of heart disease. About one-third (35%) of subjects had a prior history of coronary artery disease; 25% of subjects had a prior myocardial infarction (MI). The mean SBP at presentation was 78 mm Hg, and the mean ejection fraction was 33%. Clinical signs of hypoperfusion included cold periphery (95%), lactate levels above 2 mmol/L (70%), confusion or altered mental status (68%), and oliguria (55%). Acute coronary syndrome (ACS) was the cause of CS in 81% of subjects. Other etiologies included severe low-output heart failure (11% of subjects), valvular dysfunction (5%), myocarditis (2%), and apical ballooning syndrome (2%).

A coronary angiogram was performed in 81% of subjects (92% of those with ACS). The use of vasopressors (mostly norepinephrine) was common (85% of subjects). Inotropes were used for 65% of subjects. An intra-aortic balloon pump was used in 64% of patients. In-hospital mortality was 37% (n=81).

A stepwise analysis was conducted, and 7 predictors of in-hospital mortality for patients with CS were identified. Each variable was assigned a score of 1 or 2 based on their relative contribution to mortality, with a maximum score of 9 (Table 1). The distribution of patients by risk score is shown in Figure 1.

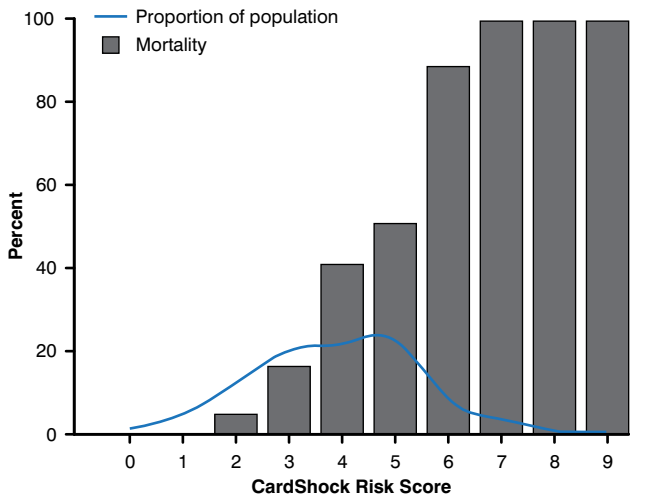
Table 1. Predictors of In-Hospital Mortality. CardShock Score

Variable*	Adjusted Odds Ratio (95% CI)	p Value	CardShock Variable	Score
Age, per year	1.04 (0.99–1.08)	0.09	Age >75 years	1
Confusion	3.3 (1.2–9.0)	0.02	Confusion	1
Prior MI	3.2 (1.3–8.4)	0.02	Prior MI	1
Prior CABG	12.5 (2.0–77.4)	0.007	Prior CABG	2
ACS etiology	7.8 (1.9–32.6)	0.005	ACS etiology	1
LVEF, per % decrease	1.06 (1.02–1.09)	0.001	LVEF <40%	1
Blood lactate, per mmol/L	1.4 (1.2–1.6)	<0.001	Blood lactate	
—	—	—	<2 mmol/L	0
—	—	—	2-4 mmol/L	1
—	—	—	>4 mmol/L	2

ACS=acute coronary syndrome; CABG=coronary artery bypass graft; LVEF=left ventricular ejection fraction; MI=myocardial infarction.

*Model also included a variable adjusting for gender and center.

Figure 1. CardShock Score: Mortality Distribution by Score



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The investigators compared the CardShock scoring system with the Sleeper score, which was developed in the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock Trial Registry [SHOCK] to predict mortality in CS complicating MI [Sleeper LA et al. *Am Heart J* 2010]. Although the predictor variables are similar (eg, age, clinical evidence of hypoperfusion, prior coronary artery bypass graft, and left ventricular function), Dr. Lassus argued that the CardShock score had an advantage of greater simplicity. The area under the receiver operating characteristic score for the CardShock risk score was 0.86 as compared with 0.76 for the Sleeper score when applied to the CardShock cohort.

The in-hospital mortality rate of CS remains very high in the contemporary era, and there is utility in the early identification of those patients at highest risk of death. Using clinical variables readily available on presentation, the CardShock risk score is able to identify those with low- (0 to 2 points), medium- (3 to 5 points), and high-risk (6 to 9 points) of short-term mortality with reasonable discrimination.

Exercise Training Not Offered to Half of Surveyed European Patients With HF

Written by Brian Hoyle

The results of the 41-country Exercise Training in Heart Failure study (ExTra HF), involving more than 76,000 patients, support an argument for the establishment of a therapeutic tool to improve exercise capacity, quality of life, and health outcome in patients with heart failure (HF). The study findings were presented by Massimo F. Piepoli, MD, PhD, Guglielmo da Saliceto Hospital, Piacenza, Italy.

Exercise is recommended for HF patients by organizations such as the European Society of Cardiology [Piepoli MF et al. *Eur J Heart Fail* 2011]. Yet, a 2010 survey in Europe revealed that <20% of HF patients received exercise-based cardiac rehabilitation [Piepoli MF et al. *Eur J Prevent Cardiol* 2010]. To explore this disconnect, the ExTra HF study was conducted at 167 cardiac centers (143 general cardiac centers, 24 rehabilitation centers) in 41 European countries, involving 76,214 patients. A 12-item web questionnaire completed from June 2013 to February 2014 queried whether centers involved in HF rehabilitation included exercise training and, if not, why. ExTra HF researchers also sought to compare the exercise options being provided and to promote a benchmark program.

Of the 167 centers, 99 (59.3%) incorporated exercise training, accounting for 38 304 patients (51% of total). The remaining 68 centers (40.7%), representing 36,910 patients (49%), did not. Reasons for not implementing exercise programs varied and included lack of resources (24.3% of the 68 centers), lack of exercise program in local guidelines/pathways (13.4%), patient referral to other centers (13.0%), provision of exercise program by general practitioner or outpatient department (11.1%), and the absence of exercise therapy for HF patients in the contract between the responding center and the relevant national health service.

Exercise that was delivered soon after hospital discharge (76.8% of cases), in the longer term as a maintenance program (48.5%), and in the hospital before discharge (41.4%) mainly involved increasing aerobic endurance, mostly via stationary bicycles, walking, and treadmills. Other frequently included exercise modalities were dynamic resistance training (71.4%) and balance/coordination training (73.6%).

Exercise programs were most often delivered by rehabilitation specialists (66.7%), physiotherapists (66.7%), cardiac rehabilitation nurses (64.6%), and dieticians (61.6%). Psychologists delivered training in 49.5% of the cases, exceeding the prevalence of cardiac rehabilitation specialists (45.5%). Responsibility for the exercise programs lay predominantly with cardiologists (~33%), cardiac rehabilitation specialists (~30%), and cardiac rehabilitation nurses (~18%).

The data revealed a lack of access to exercise programs for nearly half the HF patients. Exercise for this population is a class 1, level A recommendation by the European Society of Cardiology. When exercise is provided, a number of types are used, in the absence of any guidance standard. Dr. Piepoli and the other investigators opined that a standardized therapeutic tool be adopted, designed to improve aerobic exercise capacity, quality of life, and outcome for HF patients.