# GulfCARE Trial Characterizes AHF Patients in the Middle East

Written by Phil Vinall

The results of the Gulf Acute Heart Failure Registry [GulfCARE; NCT01467973], reported by Kadhim Jaffer Sulaiman, MD, Royal Hospital, Muscat, Oman, showed that patients in the Middle East who are diagnosed with acute heart failure (AHF) are younger than their Western counterparts, have a higher rate of diabetes mellitus (DM), and lower rate of atrial fibrillation (AF). Mortality rates are close to those reported in Western studies; however, this should be re-evaluated in light of the younger age of Middle Eastern patients.

GulfCARE is a prospective registry of patients with AHF who were admitted to participating hospitals between February 14 and November 13, 2012, and who were followed up with at 3 and 12 months. The primary objective of the study was to describe the characteristics, management, and outcomes of hospitalized patients with AHF in the Middle East. GulfCARE comprises 5005 patients (63% men) recruited from 7 Middle Eastern countries. Incident HF was observed in about 45% of patients; the remaining 55% had acute decompensated heart failure (ADHF). HF with reduced ejection fraction (HFrEF) was diagnosed in 69%, with EF preserved in the remaining 31% of patients.

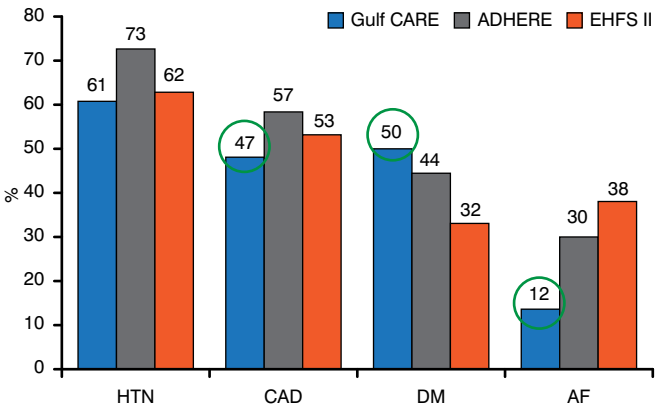
Patients in this study were younger than AHF patients participating in Western studies (mean age, 59 years vs 70 to 73 years, respectively) [Gheorghiade M et al. *JAMA* 2006; Nieminen MS et al. *Eur Heart J* 2006; Adams KF et al. *Am Heart J* 2005]. About half of GulfCARE participants (47%) had coronary artery disease (CAD), and 12% had AF. Hypertension was present in 61% of patients, 50% had DM, and 36% had hyperlipidemia. Compared with the populations in Western AHF studies, patients in the GulfCARE study had lower rates of CAD and AF but higher rates of DM (Figure 1). About 75% of patients in GulfCARE had New York Heart Association Class III or IV at admission.

During hospitalization, 9.5% of GulfCARE patients required noninvasive ventilation, whereas 8.5% required intubation. Almost all patients (94%) were treated with diuretics; 71% received β-blockers, and 78% angiotensin-converting-enzyme inhibitors/angiotensin receptor blockers. Among patients with ADHF, there were increases in discharge medications as compared with that at pre-admission, indicative of a lack of compliance with evidence-based treatment (Figure 2).

The in-hospital mortality rate was 6.3%. The etiology of HF was CAD in 54% of study participants, followed by nonischemic cardiomyopathy in 18% and hypertensive heart disease in 16% of patients. The precipitating cause of HF was acute coronary syndrome in 27% of patients and noncompliance with medications or diet in 21.7%. Most patients (89%) were discharged to home after a median hospital stay of 7 days.

Almost all patients (98.4%) were included in the 3- and 12-month follow-up examinations. Mortality was 13% at 3 months and 20% at 12 months. By 3 months, 21% of patients had been re-admitted. The number of patients receiving device therapy was low over the 12 months, as

Figure 1. Medical History




AF=atrial fibrillation; CAD=coronary artery disease; DM=diabetes mellitus; HTN=hypertension.

ADHERE: Adams KF et al. *Am Heart J* 2005; EHFS II: Nieminen MS et al. *Eur Heart J* 2006.

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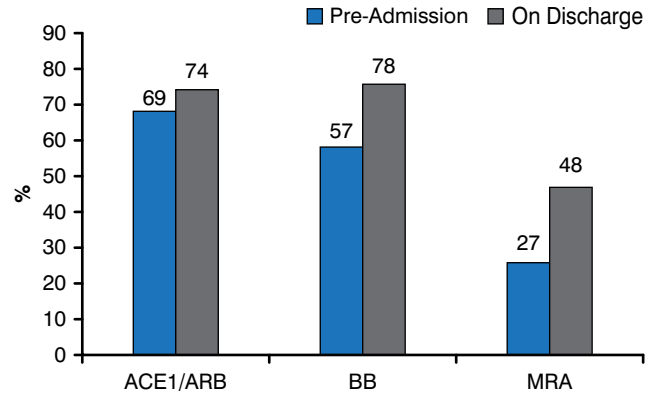
Figure 2. Pre-admission and Discharge Medications among Patients with ADCHF




ACEI/ARB=angiotensin-converting-enzyme inhibitors/angiotensin receptor blockers; ADCHF=acute decompensated congestive heart failure; BB=beta-blockers; MRA=mineralocorticoid receptor antagonists.

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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.