Characteristics and in-hospital outcomes of patients with acute coronary syndromes and heart failure in the United Arab Emirates

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Abstract

Background: Heart failure (HF) is a serious complication of acute coronary syndromes (ACS), and is associated with high in-hospital mortality and poor long-term survival. The aims of this study were to describe the clinical characteristics, management and in-hospital outcomes of coronary syndrome (ACS) patients with HF in the United Arab Emirates.

Findings: The study was selected from the Gulf Registry of Acute Coronary Events (Gulf RACE), a prospective multi-national, multicenter registry of patients hospitalized with ACS in six Middle East countries. The present analysis was focused on participants admitted to various hospitals in the UAE with a diagnosis of ACS in 2007 and were analyzed in terms of HF (Killip class II/III and IV) on admission. Of 1691 patients (mean age: 52.6 ± 11.7 years; 210 Females, 1481 Males) with ACS, 356 (21%) had an admission diagnosis of HF (Killip class II/III and IV). HF patients were less frequently males (19.2% vs. 34.3%; P < 0.001). HF was more frequently associated with hypertension (64.3% vs. 43.9%; P < 0.001), hyperlipidemia (49.4% vs. 31.8%; P < 0.001) and diabetes mellitus (DM) (51.1% vs. 36.2%; P < 0.001). HF was significantly associated with in-hospital mortality (OR = 11.821; 95% CI: 5.385-25.948; P < 0.001). In multivariate logistic regression, age, hyperlipidemia, heart rate and DM were associated with higher in-hospital HF.

Conclusions: HF is observed in about 1 in 5 patients with ACS in the UAE and is associated with a significant increase in in-hospital mortality and other adverse outcomes.

Keywords: Heart failure, Acute coronary syndrome, United Arab Emirates

Background

Heart failure (HF) is a growing problem that puts a tremendous burden on health care facilities worldwide. Up to 70% of all patients with HF die within 5 years after their first hospital admission [1]. The most common cause of HF is coronary artery disease (CAD), including the acute coronary syndromes (ACS) of ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina (UA) [2]. The development of HF following ACS significantly worsens short- and long-term prognosis [3]. In developed countries, CAD is a major cause of HF, morbidity and mortality.

Significant advances have been made over the last decade in therapeutic approaches to ACS, particularly the development of new antiplatelet therapies and recognition of the benefits of neurohumoral blockade. Nonetheless, ACS remains among the main causes of death in developing countries [3]. One factor contributing to the poor prognosis is development of HF and left ventricular dysfunction following myocardial infarction (MI) [4]. It is of utmost importance to identify patients at risk of developing HF at admission since it may influence immediate therapeutic choices and subsequent risk stratification strategies which consequently help improve prognosis, personalize patient care, optimize the use of healthcare resources and prevent HF and death.

The aim of this work was to describe the clinical characteristics, and in-hospital management/outcomes of...
ACS patients with HF in the United Arab Emirates, enrolled in the Gulf Registry of Acute Coronary Events (Gulf RACE) [5,6]. We also evaluated HF impact on inhospital mortality.

Methods
Patients and data collection
Patients were selected from the Gulf Registry of Acute Coronary Events (Gulf RACE), a prospective multinational, multicentre registry of patients above 18 years of age hospitalized with the final diagnosis of ACS from various hospitals in 6 Middle Eastern countries, namely: Oman, United Arab Emirates (UAE), Qatar, Bahrain, Kuwait and Yemen [5]. Details of the Gulf RACE design and methods have been previously described [5]. There were no exclusion criteria. The recruitment in the pilot phase started from May 8, 2006, to June 6, 2006. Enrollment in the next phase of the registry started in January 29, 2007, and continued for 5 months till June 29, 2007. The present study included 1691 of 1697 patients hospitalized with an ACS across 18 hospitals in the UAE with complete data on HF (with HF: 356, 21.1%). These hospitals care for more than 85% of patients with ACS in the country. Demographic, historical, and clinical data as well as in-hospital outcomes were recorded by study physicians for all patients admitted with a diagnosis of ACS.

Definitions of the sets of variables collected from the patients, outcome parameters as well as the diagnosis of ACS types were done following the American College of Cardiology (ACC) clinical data standards [7], for example:

1. DM: history of diabetes, regardless of duration of disease, need for antidiabetic agents, or a fasting blood sugar greater than 7 mmol/l or 126 mg/dl.
2. Hypertension: documented by: 1. History of hypertension diagnosed and treated with medication, diet, and/or exercise. 2. Blood pressure greater than 140 mmHg systolic or 90 mmHg diastolic on at least 2 occasions and 3. Current use of antihypertensive pharmacological therapy.
3. Hyperlipidemia: diagnosed and/or treated by a physician. National Cholesterol Education Program criteria include documentation of the following: 1. Total cholesterol greater than 200 mg/dl (5.18 mmol/l); or 2. Low-density lipoprotein (LDL) greater than or equal to 130 mg/dl (3.37 mmol/l); or 3. High-density lipoprotein (HDL) less than 40 mg/dl (1.04 mmol/l). Treatment is also initiated if LDL is greater than 100 mg/dl (2.59 mmol/l) in patients with known coronary artery disease, and this would qualify as hypercholesterolemia.
4. Past revascularization: including CABG or PCI of any type (balloon angioplasty, atherectomy, stent, or other) done before the current admission with the dates noted.
5. Prior CAD: includes history of angina before the current admission and if it existed more than 2 weeks before admission and/or within 2 weeks before admission. “Angina” refers to evidence or knowledge of symptoms before this acute event described as chest pain or pressure, jaw pain, arm pain, or other equivalent discomfort suggestive of cardiac ischemia. MI: the patient at least had 1 documented previous MI before admission with the date noted.

All the patients were assigned to one of the following categories: ST-elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), left bundle branch block myocardial infarction (LBB MI) and UA. These definitions take into account clinical presentation, ECG findings, and the results of serum biochemical markers of myocardial necrosis (troponin and CPK-MB). Following ACS incidents after admissions, serial of cardiac enzymes were recorded and the highest (peak) values were used in our paper. Particularly, UA was defined as ACS with normal biochemical markers of necrosis. Patients were categorized at the time of hospital admission according to the classification of Killip and Kimball [8] for signs of HF. Killip class (scale 1–IV) is a risk stratification tool for patients after acute myocardial infarction (AMI); a low Killip class indicates a lower likelihood of death within the first 30 days than a high Killip class. Smokers were defined as smoking cigarettes or sheesha (water pipe) within 1 month prior to index admission. A positive family history of coronary heart disease was defined as evidence of this disease in a parent, sibling, or children before the age of 55 years. The protocols of this study were approved by the Al Ain Medical District Human Research Ethics Committee, Abu Dhabi and Dubai Health Authorities and the Ministry of Health. All patients gave informed written consent to participate and care was taken to ensure data anonymity.

Statistical analysis
All data were analyzed with SPSS statistical software version 19.0 (Chicago, Illinois, USA). The comparison of continuous variables between patients with and without HF was performed using the Student t-test. Categorical variables were compared using the Pearson’s chi-square test (or Fisher exact test for expected cells less than 5). Continuous variables with (approximately) normal distribution were expressed as mean ± SD. Multivariable backward stepwise logistic binary regression analysis was performed to estimate adjusted odds ratios (OR) of the potentially independent predictors (note: such predictors
are not necessarily causes of outcome) of in-hospital HF adjusted for the following baseline covariates: age, gender, heart rate, smoking, DM, hypertension, hyperlipidemia, past revascularization including coronary artery bypasses graft surgery (CABG) or percutaneous coronary intervention (PCI) and prior coronary artery disease (CAD) including angina or myocardial infarction (MI).

Similarly, the association between HF and in-hospital mortality was examined using step-wise logistic regression models adjusting for the following covariates: age, gender, heart rate, smoking, DM, hypertension, hyperlipidemia, past revascularization including CABG or PCI and prior CAD including angina or MI. In all cases a P-value below 0.05 was considered statistically significant.

Results

Patient population

The records of 1691 ACS patients represent the total sample of this study. Among these, 356 patients (21.1%) had HF at hospital admission. The clinical characteristics of the study sample, by HF diagnosis at hospital admission are shown in table 1. The mean age of the cohort was 52.5 ± 11.6 years. Patients with HF were significantly older than patients without HF (57.8 ± 13 vs. 51.2 ± 10.8 years; P < 0.001), were less likely to be male (34.3% among females vs. 19.2% among males; P < 0.001) and less likely to smoke (38.2% vs. 50.3%; P < 0.001). Risk factors for coronary artery disease were more common in patients with HF as they were more often hypertensive (64.3% vs. 43.9%), hyperlipidemic (49.4% vs. 31.8%) and diabetic (51.1% vs. 36.2%) (P < 0.001 for all comparisons). Furthermore, the HF group included a significantly higher number of patients with prior angina/MI and past PCI/CABG (50% vs. 34.2%; P < 0.001, 18.8% vs. 14.1%; P = 0.018, respectively) compared to the non-HF group. Patients with HF were slightly less likely to have STEMI on admission, but the overall distribution of admission diagnoses was not statistically different between HF and other patients. Patients with HF had a higher heart rate on presentation versus those without HF (97 ± 27.2 vs. 81.4 ± 19.8 beats/min; P < 0.001).

Medical management

Table 2 outlines medication use and in-hospital management of the study patients. Compared with patients without HF, the use of aspirin, beta-blockers, calcium channel blockers, diuretics and subcutaneous insulin was significantly lower among patients with HF during their hospital treatment (Table 2). At discharge, the use of beta-blockers, calcium channel blockers, statins, nitrates, diuretics, antiarrhythmic agents, digoxin and warfarin was significantly higher among patients with HF (Table 2). Moreover, Patients with HF were more likely to undergo invasive cardiac procedures than patients without HF.

Predictors of HF

Table 3 shows that the odds of HF increases by 3.4% per year of age (OR = 1.034; 95% CI: 1.021-1.047; P < 0.001). Furthermore, patients with a history of hyperlipidemia were 1.5 times (OR = 1.539; 95% CI: 1.096-2.162; P = 0.013) more likely to present with HF than those without history of dyslipidemia. The risk of HF increased by 2.7% (OR = 1.027; 95% CI: 1.021-1.034; P < 0.001), for every 1-beat-per-minute increase in heart rate. Finally, the model also showed that having diabetes mellitus (DM) increased the risk of HF by 42% (OR = 1.425; 95% CI: 1.047-1.938; P = 0.024).

Heart failure and adverse outcomes including in-hospital mortality

Major bleed (n = 15) and stroke (n = 9) were rare outcomes. Stroke was significantly associated with in-hospital mortality, even after adjustment for HF (P < 0.001). Table 4 indicates that HF was significantly associated with in-hospital mortality (OR = 11.821; 95% CI: 5.385-25.948; P < 0.001). The in-hospital mortality rate for male patients was substantially lower than the mortality rate for female patients (OR = 0.419; 95% CI: 0.195-0.902; P < 0.033; using stepwise (backward selection) logistic regression).

Discussion

The overall incidence of HF complicating ACS in our study was 21% (less so in males which represented 87.6% of the study population). This rate of HF is lower than reported in some previous studies of HF after AMI [9,10] but similar to several other ones [11-13]. Since there is no definitive diagnostic test for HF, these differences may well be due to varying definitions of HF among studies, exclusion criteria or as in the present study, inclusion of all patients with ACS, or could be due to different delays in seeking care thereby not receiving timely diagnosis or optimal therapies. It was observed that one in four ACS patients from six Middle Eastern countries in the entire GULF RACE cohort had HF [11]. In this study and using only the UAE data from the GULF RACE, we observed that one in five patients with ACS had HF during admission. This high rate of HF patients with ACS could be due to the high prevalence of DM in the region [14,15]. There is an increasing recognition that diabetic patients suffer from diabetic cardiomyopathy, including AMI and HF, which was originally described in 1972 on the basis of observations in four diabetic patients who presented with HF without evidence of hypertension, CAD, valvular or congenital heart disease [16]. Not surprisingly DM was also
associated with HF in our study although our methodology precludes definitive causal interpretations. Most likely, because of the proinflammatory, and prothrombotic states associated with DM, diabetic patients with ACS are at high risk of subsequent cardiovascular events with poorer outcome and higher mortality rates [17-19]. This study also shows that HF is a common complication associated with all forms of ACS. Patients with ACS complicated by HF were more likely to die in the hospital or experience other in-hospital complications such as cardiogenic shock, infarction or stroke, although it is unclear from our logistic regression analyses whether this is because HF was the direct cause of in-hospital death (and other complications) in our patients or just a sign of substantial cardiac damage. Of note is that in-hospital mortality in our study of HF patients was 7.3%, which is relatively high. In-hospital mortality in large US registries was about 4% [20,21], whereas in the European registries it ranged from 3.8% (ESC-HF Pilot) to 6.7% (EHFS II) and 7.1% (FINN-AKVA) [22-24].

### Table 1 Demographic and baseline characteristics of the studied acute coronary syndrome patients according to the presence of HF (n = 1691)

| Variable                                  | HF (n = 356) | Non-HF (n = 1335) | P-value |
|-------------------------------------------|--------------|-------------------|---------|
| Age, mean ± SD, years                     | 57.8 ± 13.0  | 51.2 ± 10.8       | < 0.001 |
| Male                                      | 284 (79.8)   | 1197 (89.7)       | < 0.001 |
| Hypertension                              | 229 (64.3)   | 586 (43.9)        | < 0.001 |
| Hyperlipidemia                            | 176 (49.4)   | 425 (31.8)        | < 0.001 |
| Diabetes mellitus                         | 182 (51.1)   | 483 (36.2)        | < 0.001 |
| Smoking                                   | 136 (38.2)   | 672 (50.3)        | < 0.001 |
| Family history of CAD                     | 39 (11.0)    | 221 (16.6)        | 0.008   |
| Prior angina or MI                        | 178 (50.0)   | 457 (34.2)        | < 0.001 |
| Past PCI or CABG                          | 67 (18.8)    | 188 (14.1)        | 0.030   |
| ACS diagnosis:                            |              |                   | 0.66    |
| STEMI                                     | 141 (39.6)   | 572 (42.9)        |         |
| NSTEMI                                    | 81 (22.8)    | 302 (22.6)        |         |
| UA                                        | 131 (36.8)   | 453 (33.9)        |         |
| LBBB MI                                   | 3 (0.8)      | 8 (0.6)           |         |
| Admission characteristics:                |              |                   |         |
| Killip class:                             |              |                   |         |
| I                                         | -            | 1335 (100)        |         |
| II                                        | 221 (62.0)   | -                 |         |
| III                                       | 102 (28.7)   | -                 |         |
| IV                                        | 33 (9.3)     | -                 |         |
| ST deviation                              | 287 (80.8)   | 998 (749)         | 0.021   |
| Heart rate, mean ± SD, beats/min          | 97 ± 27.2    | 81.4 ± 19.8       | < 0.001 |
| Systolic blood pressure, mean ± SD, mm Hg | 145.7 ± 40.5 | 141.7 ± 27.9     | 0.028   |
| Diastolic blood pressure, mean ± SD, mm Hg | 87.2 ± 23.7 | 85.6 ± 17.1      | 0.167   |

Laboratory investigations:

- Peak CPK, mean ± SD, (U/l) 1269.9 ± 1930.5 1295.2 ± 1941.3 0.167
- Peak CPK-MB, mean ± SD, (U/l) 99.1 ± 157.9 96.4 ± 135 0.109
- Peak troponin, mean ± SD, (µg/l) 19.2 ± 79.3 15.8 ± 55.9 0.581
- Percent with LVEF ≤ 40% 138/282 (49) 700/959 (73) < 0.001

Values were log10 transformed to approximate normality for the independent sample t-test.

*Peak troponin I or T (depending on recruiting centre).

Figures in parentheses are percentages.

Abbreviations: HF heart failure, SD standard deviation, CAD coronary artery disease, MI myocardial infarction, PCI percutaneous coronary intervention, CABG coronary artery bypass surgery, NSTEMI non-ST-segment elevation myocardial infarction, STEMI ST-elevation myocardial infarction, LBBB left bundle branch block, UA unstable angina, CPK creatinine phosphokinase, CPK-MB creatine kinase-myocardial band isoenzyme.
The lower frequency of PCI and use of beta-blockers in the patients with HF. While the lower use of beta-blockers may be explained by the difficulty of starting such therapy early in patients with HF, the reason for the low rate of cardiac catheterization in these patients is uncertain.

The strengths of this investigation include its national perspective, the complete spectrum of ACSs experienced by the large number of patients studied and the use of standardized criteria for defining ACS and hospital outcomes. However, as with any observational registry-type study, the present findings have limitations. Although this registry includes 18 hospitals throughout the UAE, participating sites may not be representative of the whole country. Furthermore, post-admission variables analyses related to physician discretion (medications, interventions) may be strongly influenced by unmeasured confounders. Our analysis is also limited by the lack of adequate follow-up data on long-term mortality and morbidity and it is possible that some patients were misclassified according to the Killip and Kimball [8] classification for signs of HF. Finally, the standard practice management of ACS in the participating hospitals were initially, predominantly conservative. There were few PCI facility centers and hardly any primary PCI center with an established interventional practice.

### Table 2 In-hospital and discharge management of the studied ACS patients with and without HF (n = 1691)

| Criteria                        | HF (n = 356) | Non-HF (n = 1335) | P-value |
|--------------------------------|--------------|-------------------|---------|
| **In-hospital medical treatment:** |              |                   |         |
| Aspirin                        | 344 (96.6)   | 1328 (99.5)       | < 0.001 |
| Clopidogrel                    | 336 (94.4)   | 1290 (96.6)       | 0.061   |
| IV HEP                         | 48 (13.5)    | 204 (15.3)        | 0.451   |
| LMW HEP                        | 311 (87.4)   | 1154 (86.4)       | 0.726   |
| GP                             | 132 (37.1)   | 534 (40.0)        | 0.329   |
| BB                             | 156 (43.8)   | 905 (74.5)        | < 0.001 |
| ACE                            | 231 (64.9)   | 900 (67.4)        | 0.375   |
| AIIRB                          | 18 (5.1)     | 57 (4.3)          | 0.562   |
| CCB                            | 40 (11.2)    | 98 (7.3)          | 0.022   |
| Statins                        | 329 (92.4)   | 1268 (95)         | 0.068   |
| Nitrates                       | 268 (75.3)   | 934 (70.0)        | 0.056   |
| Diuretics                      | 242 (68.0)   | 158 (11.8)        | < 0.001 |
| SQ INS                         | 160 (44.9)   | 368 (27.6)        | < 0.001 |
| IV INS                         | 15 (4.2)     | 33 (2.5)          | 0.104   |
| **Discharge medical treatment:**|              |                   |         |
| Aspirin                        | 321 (90.2)   | 1293 (97.0)       | < 0.001 |
| Clopidogrel                    | 290 (81.5)   | 1105 (82.8)       | 0.012   |
| BB                             | 258 (72.5)   | 1148 (86.0)       | < 0.001 |
| ACE                            | 252 (70.8)   | 999 (74.8)        | 0.193   |
| AIIRB                          | 30 (8.4)     | 84 (6.3)          | 0.151   |
| CCB                            | 43 (12.1)    | 90 (6.7)          | 0.001   |
| Statins                        | 320 (90.9)   | 1273 (95.4)       | 0.001   |
| Nitrates                       | 181 (51.0)   | 543 (40.7)        | < 0.001 |
| Diuretics                      | 208 (58.4)   | 142 (10.7)        | < 0.001 |
| Antiarrhythmic agents          | 21 (6.0)     | 14 (1.0)          | < 0.001 |
| Digoxin                        | 16 (4.5)     | 6 (0.4)           | < 0.001 |
| Warfarin                       | 15 (4.2)     | 15 (1.1)          | < 0.001 |
| **In-hospital procedures:**    |              |                   |         |
| Echocardiography               | 260 (73.0)   | 846 (63.4)        | 0.001   |
| PCI                            | 9 (2.5)      | 13 (1.0)          | 0.025   |
| IABP                           | 10 (2.8)     | 11 (0.8)          | 0.006   |
| **In-hospital outcomes:**      |              |                   |         |
| Death                          | 26 (7.3)     | 8 (0.6)           | < 0.001 |
| Cardiogenic shock              | 44 (12.4)    | 22 (1.7)          | < 0.001 |
| Infarction                     | 16 (4.5)     | 26 (2.0)          | 0.011   |
| Stroke                         | 5 (1.4)      | 4 (0.3)           | 0.023   |

Figures in parentheses are percentages.

Abbreviations: DM diabetes mellitus, IV HEP intravenous heparin, LMW HEP low molecular weight heparin, GP glycoprotein IIb/IIIa inhibitors, BB beta-blockers, ACE angiotensin-converting enzyme inhibitors, AIIRB angiotensin II receptor blockers, CCB calcium channel blockers, SQ Insulin subcutaneous insulin, IV Insulin intravenous insulin, PCI percutaneous coronary intervention, IABP Intra-aortic balloon pump.

### Table 3 Independent predictors of in-hospital HF using multivariable logistic regression

| Criteria                        | OR  | 95% CI       | P     |
|--------------------------------|-----|--------------|-------|
| Age                            | 1.034 | 1.021-1.047 | < 0.001 |
| hyperlipidemia                 | 1.539 | 1.096-2.162 | 0.013 |
| Heart rate                     | 1.027 | 1.021-1.034 | < 0.001 |
| Prior CAD                      | 1.322 | 0.949-1.841 | 0.100 |
| DM                             | 1.425 | 1.047-1.938 | 0.024 |

Abbreviation: HF heart failure, OR odds ratio, CI confidence interval, CAD coronary artery disease including angina or myocardial infarction (MI), DM diabetes mellitus.

The variables that were dropped out of the multivariable logistic regression using the stepwise-backward elimination method included gender, smoking, hypertension and past revascularization (CABG/PCI).

### Table 4 Relationship between HF and in-hospital mortality using multivariable logistic regression

| Criteria                        | OR  | 95% CI       | P     |
|--------------------------------|-----|--------------|-------|
| HF                             | 11.821 | 5.385-25.948 | < 0.001 |
| Gender                         | 0.419 | 0.195-0.902 | 0.033 |
| Heart rate                     | 1.013 | 1.000-1.026 | 0.068 |

Abbreviation: HF heart failure, OR odds ratio, CI confidence interval. The variables that were dropped out of the multivariable logistic regression using the stepwise-backward elimination method included age, smoking, diabetes mellitus, hypertension, hyperlipidemia, past revascularization (CABG/PCI) and prior coronary artery disease (CAD) include angina or (MI).
cardiology program (24 h/7 days) which has an important impact on the incidence and severity of HF.

Conclusions
In conclusion, in this cohort of patients with ACS in the UAE, HF complicates one-fifth of cases and was associated with age, heart rate, hyperlipidemia and DM. In-hospital mortality rate was associated with HF and gender. Further studies are needed to better risk-stratify patients with HF for more analysis as well as having information about prior history of HF and outcomes of post-hospital discharge in order to optimize the use of medications and cardiovascular interventions for this serious condition.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
AS and BA performed data analysis and interpretation, critically reviewed the data analysis and wrote the paper. BA, NN, and AS performed the statistical analysis. WA and NB were involved in the inception and implementation and AB were involved in the critical revision of the manuscript. All authors have read and approved the final version of the manuscript.

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