Mortality and Morbidity in HF*r*EF, HF*mr*EF, and HF*p*EF Patients with Diabetes in the Middle East

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ARTICLE INFO

Article history:
Received: 14 October 2019
Accepted: 27 October 2019

Online:
DOI 10.5001/omj.2020.17

Keywords:
Heart Failure; Diabetes Mellitus; Mortality; Middle East; Patient Readmission.

ABSTRACT

Objectives: We sought to estimate the mortality and morbidity in diabetic acute heart failure (AHF) patients stratified by left ventricular ejection fraction. ***Methods***: We analyzed the data of patients with AHF from seven Middle Eastern countries (Bahrain, Oman, Yemen, Kuwait, UAE, Qatar, and Saudi Arabia) from February to November 2012, who were enrolled in a multinational registry of patients with heart failure (HF). ***Results:*** A total of 2258 AHF patients had diabetes mellitus. The mean age was 63.0±11.0 years (ranging from 18 to 99 years), and 60.3% (n = 1362) of the patients were males. The mean ejection fraction (EF) was 37.0±13.0%. HF with reduced EF (< 40%) (HF*r*EF) was observed in 1268 patients (56.2%), whereas 515 patients (22.8%) had mid-range (40–49%) (HF*mr*EF) and 475 patients (21.0%) had preserved EF (≥ 50%) (HF*p*EF). The overall cumulative all-cause mortalities at three- and 12-months follow-up were 11.8% (n = 266) and 20.7% (n = 467), respectively. Those with HF*p*EF were associated with lower three-months cumulative all-cause mortality compared to those with HF*r*EF (7.6% vs. 5.9%; adjusted odds ratio (aOR) = 0.54, 95% confidence interval (CI): 0.31–0.95; $p = 0.031$), but not significantly different when compared to those with HF*mr*EF (aOR = 0.86, 95% CI: 0.53–1.40; $p = 0.554$). There were largely no significant differences among the groups with regards to the 12-months all-cause cumulative mortality (11% vs. 11% vs. 10%; $p = 0.984$). There were also no significant differences in re-hospitalization rates between the three HF groups not only at three months (23% vs. 20% vs. 22%; $p = 0.520$), but at one-year follow-up (28% vs. 30% vs. 32%; $p = 0.335$). ***Conclusions:*** Three-month cumulative all-cause mortality was high in diabetic HF*r*EF patients when compared to those with HF*p*EF. However, there were no significant differences in mortality at one-year follow-up between the HF groups. There were also no significant differences in re-hospitalization rates between the HF groups not only at three months but also at one-year follow-up in the Middle East.

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The rising prevalence of diabetes mellitus (DM) in heart failure (HF) patients is becoming a global burden. It is a more frequently coexisting risk factor for incident HF, given its increasing role in morbidity and mortality.[1] Reports of its coexistence in HF range from 10% to 47%.[2–4] The optimal therapeutic approach to DM (especially type 2) has gained much importance in the recent past. Early introduction of sodium-glucose transport protein 2 (SGLT2) inhibitors in the treatment strategy seems beneficial to reduce frequent HF-related hospitalizations. The coexistence of both DM and HF warrants a multidisciplinary approach in such patients. The importance of lifestyle modifications along with glucose-lowering agents plays a major role in achieving better outcomes in HF patients with DM.[5] The risk of HF in patients with DM is more evident in women and young adults.[6] The risk of developing HF in DM is multifactorial and is mainly related to poor glycemic control, older age, obesity, hypertension, and coronary artery disease (CAD).[7]

There is scant data on the morbidity and mortality of HF patients with DM stratified by left ventricular ejection fraction (LVEF) in the Arabian Gulf. Hence, we sought to evaluate the morbidity and mortality of diabetic HF patients in the Arabian Gulf stratified by LVEF.

METHODS

We used the data from a prospective, multicenter, multinational registry of acute heart failure (AHF) patients admitted to 47 hospitals in seven Middle Eastern countries (Bahrain, Oman, Qatar, UAE, Kuwait, Saudi Arabia, and Yemen). The methods of Gulf Acute Heart Failure Registry (CARE) have been published previously.[8] In summary, demographic and clinical characteristics, as well as outcomes, were captured. Follow-up for all-cause mortality and re-hospitalization history were collected via telephone at three-months and either via telephone or through outpatient clinic visits at one-year. The registry is listed on clinicaltrials.gov (number NCT01467973).

Data entry was carried out online using a custom-designed electronic case-record form (CRF) at the Gulf CARE website (www.gulfcare.org). Institutional ethical committee approvals were obtained. Trained abstractors collected the data from medical records at each participating site, and this information was recorded using an electronic CRF.

AHF was defined, according to the European Society of Cardiology,[9,10] as the rapid onset of symptoms and signs secondary to abnormal cardiac function.

HF with reduced ejection fraction (HF*r*EF) was diagnosed when patients with symptoms and signs of HF had a measured EF < 40%. HF with mid-range EF (HF*mr*EF) was diagnosed when patients with symptoms and signs of HF had a measured EF between 40–49%. HF with preserved EF (HF*p*EF) was diagnosed when patients with symptoms and signs of HF had a measured EF between ≥ 50%.[11–13] Patients with HF that did not require admission were excluded from the registry. Furthermore, those that did not have a record of EF were also excluded from the analysis.

CAD was diagnosed if any of the following conditions were present: at least one major epicardial coronary artery determined by coronary angiography to have > 70% obstruction, history of myocardial infarction associated with wall motion abnormality seen on echocardiography or gated blood pool imaging, and/or stress testing (with or without imaging) results that are diagnostic of CAD. Hypertension was defined when any of the following conditions were present: untreated systolic blood pressure > 160 mmHg or diastolic blood pressure > 105 mmHg for at least three months and/or hypertension requiring at least two drugs for control for ≥ 5 years.[14] DM was diagnosed based on fasting plasma glucose levels (FPG) ≥ 126 mg/dL (7.0 mmol/L), two-hour plasma glucose levels (2-h PG) ≥ 200 mg/dL (11.1 mmol/L) during oral glucose tolerance test, and glycated hemoglobin A1c (HbA_{1c}) ≥ 6.5% (48 mmol/mol).[15]

Descriptive statistics were used to present the data. Categorical variables were summarized as frequencies and percentages and analyzed using Pearson's chi-squared test. Continuous variables were summarized using means and standard deviations and analysis performed using ordinary least squares regression.

Multivariable logistic regression models, utilizing the simultaneous method, were performed to evaluate the impact of HF (HF*r*EF, HF*mr*EF, and HF*p*EF) on all-cause mortality and re-hospitalization (primary outcomes) at three-months and one-year

Table 1: Demographic and clinical characteristics of heart failure patients with diabetes.

Characteristics	All (N = 2258)	HF categories			*p*-value
		HF*r*EF EF (< 40%) (n = 1268)	HF*mr*EF EF (40–49%) (n = 515)	HF*p*EF EF (≥ 50%) (n = 475)	
Demographic					
Age, mean ± SD, years	63.0 ± 11.0	61.0 ± 11.0	64.0 ± 11.0	66.0 ± 11.0	< 0.001
Male, gender	1362 (60.3)	896 (70.7)	286 (55.5)	180 (37.9)	< 0.001
Smoking	413 (18.3)	273 (21.5)	95 (18.4)	45 (9.5)	< 0.001
Clinical history					
Coronary artery disease	1658 (73.4)	960 (75.7)	414 (80.4)	284 (59.8)	< 0.001
Atrial fibrillation	274 (12.1)	156 (12.3)	43 (8.4)	75 (15.7)	0.002
Stroke/transient ischemic attack	254 (11.2)	154 (12.1)	49 (9.5)	51 (10.7)	0.260
Chronic kidney disease/dialysis	525 (23.3)	273 (21.5)	116 (22.5)	136 (28.6)	0.007
Hypertension	1843 (81.6)	989 (78.0)	429 (83.3)	425 (89.5)	< 0.001
Dyslipidemia	1228 (54.4)	673 (53.1)	289 (56.1)	266 (56.0)	0.368
Sleep apnea requiring therapy	72 (3.2)	23 (1.8)	17 (3.3)	32 (6.7)	< 0.001
Clinical presentation					
Orthopnoea	1760 (77.5)	998 (78.7)	381 (74.0)	381 (80.2)	0.038
Physical examination					
Body mass index, mean ± SD, kg/m^2	29.7 ± 6.6	28.7 ± 5.9	30.0 ± 6.7	31.9 ± 7.9	< 0.001
Weight circumference, mean ± SD, cm	96.0 ± 18.0	95.0 ± 18.0	97.0 ± 18.0	100.0 ± 17.0	0.012
Gallop	716 (31.7)	457 (36.0)	167 (32.4)	92 (19.4)	< 0.001
Basal lung crepitations	2079 (92.1)	1162 (91.6)	483 (93.8)	434 (91.4)	0.257
Raised (> 6 cm) jugular venous pressure	1095 (48.5)	653 (51.5)	224 (43.5)	208 (43.8)	0.001
Abdominal/lower limb swelling	977 (43.3)	553 (43.6)	185 (35.9)	239 (50.3)	< 0.001
Signs of pleural effusion	354 (15.7)	235 (18.5)	60 (11.7)	59 (12.4)	< 0.001
HbA_{1c}, mean ± SD, mmol/L	8.5 ± 2.0	8.5 ± 2.0	8.7 ± 2.1	8.2 ± 2.0	0.091
Fasting blood glucose, mean ± SD, mmol/L	12.5 ± 6.6	12.7 ± 7.1	12.6 ± 6.3	11.8 ± 5.7	0.019
Total cholesterol, mean ± SD, mmol/L	4.7 ± 2.5	4.8 ± 2.9	4.8 ± 2.1	4.4 ± 1.5	0.023
First hemoglobin, mean ± SD, g/dL	12.3 ± 2.3	12.4 ± 2.1	12.4 ± 2.4	11.7 ± 2.4	< 0.001
NT-Pro BNP, median (IQR), pg/mL	2846 (1112–7160)	3372 (1348–7728)	2962 (995–7627)	1885 (688–4486)	0.008
eGFR, mean ± SD, mL/min/m^2	61.0 ± 32.0	63.0 ± 32.0	60.0 ± 32.0	57.0 ± 33.0	0.001
PAP, mean ± SD, mmHg	53.0 ± 12.0	53.0 ± 11.0	52.0 ± 11.0	55.0 ± 14.0	0.015

HFrEF: Heart failure (HF) with reduced ejection fraction (EF); HFmrEF: HF with mid-range EF; HFpEF: HF with preserved EF; HBA_{1c}: glycated hemoglobin A1c; eGFR: estimated glomerular filtration rate; IQR: interquartile range; NT-Pro BNP: N-terminal pro-B-type natriuretic peptide; PAP: pulmonary artery pressure; SD: standard deviation.

HbA_{1c} in diabetics with non-missing values (n = 963); Waist circumference was populated in only 683 patients, heart rate in 2191 patients, systolic and diastolic blood pressure in 2192 patients, total cholesterol in 1726 patients, NT-Pro BNP in 515 patients, eGFR in 2217 patients, and pulmonary artery pressure in only 632 patients only.

Data were given as n (%) unless specified otherwise.

post-hospital discharge. The multivariate logistic models were adjusted for significant demographic and clinical characteristics as well as medications outlined in Tables 1 and 2. The goodness-of-fit of the multivariable logistic model was examined using the Hosmer and Lemeshow goodness-of-fit statistic, and the discriminatory power of the logistic model was assessed by the area under the receiver operating characteristics curve also known as *C*-index. An a priori two-tailed level of significance was set at $p < 0.050$. Statistical analyses were conducted using STATA version 13.1 (STATA Corporation, College Station, TX, USA).

RESULTS

A total of 2258 patients with diabetes with a diagnosis of AHF were recruited to the study; 60.3% (n =

Table 2: Medications at pre-admission, during the hospital stay, and at discharge.

Characteristics	All (N = 2258)	HF categories			*p*-value
		HF*r*EF EF (< 40%) (n = 1268)	HF*mr*EF EF (40–49%) (n = 515)	HF*p*EF EF (≥ 50%) (n = 475)	
Pre-admission					
Diuretic	1468 (65.0)	856 (67.5)	311 (60.3)	301 (63.4)	0.012
Oral nitrate	783 (34.7)	438 (34.5)	183 (35.5)	162 (34.1)	0.884
Calcium channel blocker	431 (19.1)	149 (11.8)	102 (29.8)	180 (37.9)	< 0.001
Aspirin	1696 (75.1)	968 (76.3)	392 (76.1)	336 (70.7)	0.046
Clopidogrel	602 (26.7)	359 (28.3)	146 (28.3)	97 (20.4)	0.003
Statin	1561 (69.1)	866 (68.3)	359 (79.7)	336 (70.7)	0.586
Beta-blocker	1202 (53.2)	717 (56.5)	264 (51.3)	221 (46.5)	< 0.001
Angiotensin-converting-enzyme inhibitor	1015 (45.0)	624 (49.2)	232 (45.0)	159 (33.5)	< 0.001
Angiotensin-receptor blocker	405 (17.9)	200 (15.8)	89 (17.3)	116 (24.4)	< 0.001
Aldosterone antagonist	378 (16.7)	310 (24.4)	39 (7.6)	29 (6.1)	< 0.001
In-hospital					
IV furosemide-bolus	2081 (92.2)	1171 (92.3)	478 (92.8)	432 (90.9)	0.513
IV furosemide-infusion	422 (18.7)	274 (21.6)	85 (16.5)	63 (13.3)	< 0.001
IV nitrates-infusion	589 (26.1)	320 (25.2)	151 (29.3)	118 (24.8)	0.161
During discharge[a]					
Diuretic	1970 (94.9)	1109 (97.2)	461 (94.1)	400 (90.9)	< 0.001
Oral nitrate	1015 (48.8)	564 (49.5)	245 (50.0)	206 (46.8)	0.529
Calcium channel blocker	451 (21.7)	128 (11.2)	123 (25.1)	200 (45.5)	< 0.001
Aspirin	1826 (87.8)	1022 (89.6)	440 (89.9)	364 (82.7%)	< 0.001
Clopidogrel	951 (45.7)	541 (47.4)	251 (51.2)	159 (36.1%)	< 0.001
Statin	1793 (86.2)	978 (85.8)	434 (88.6)	381 (86.6%)	0.122
Beta-blocker	1481 (71.2)	880 (77.2)	351 (71.6)	250 (56.8%)	< 0.001
Angiotensin-converting-enzyme inhibitor	1188 (57.1)	732 (64.2)	275 (56.1)	181 (41.1%)	< 0.001
Angiotensin-receptor blocker	401 (19.3)	199 (17.5)	94 (19.2)	108 (24.5%)	0.006
Aldosterone antagonist	744 (35.8)	575 (50)	104 (21.2)	65 (14.8)	< 0.001

*HF*r*EF: Heart failure (HF) with reduced ejection fraction (EF); HFmEF: HF with mid-range EF; HF*p*EF: HF with preserved EF; IV: intravenous.*
[a]Only included 2079 patients. Excluded those patients that died in-hospital as well as those that left the hospital against medical advice.
Data were given as n (%).

1362) of the patients were male. The mean age was 63.0±11.0 years, ranging from 18 to 99 years. A total of 1658 (73.4%) had CAD, 1843 (81.6%) patients had hypertension, and 1228 (54.4%) patients had known dyslipidemia. Atrial fibrillation was observed in 274 (12.1%) patients and chronic kidney disease was observed in 525 (23.3%) patients.

The median EF was 35% (25–45%). HF*r*EF was observed in 1268 (56.2%) patients, whereas 515 (22.8%) patients had HF*mr*EF and 475 (21.0%) patients had HF*p*EF. At hospital discharge, the etiology of HF was recorded as being acute coronary syndrome in 739 (32.7%) patients, primary cardiomyopathy in 285 (12.6%) patients, hypertensive heart disease in 388 (17.2%) patients, primary valve pathology in 106 (4.7%) patients, and pulmonary hypertension in 41 (1.8%) patients. The median duration of hospitalization was six (4–10) days. The overall in-hospital mortality was 5.3% (n = 120).

Compared with the HF*mr*EF and HF*p*EF groups, patients with HF*r*EF were younger (61.0 vs. 64.0 vs. 66.0 years; $p < 0.001$), more likely to be male (70.7% vs. 55.5% vs. 37.9%; $p < 0.001$) and smokers (21.5% vs. 18.4% vs. 9.5%; $p < 0.001$) and have higher levels of estimated glomerular filtration rate (eGFR) (63.0 vs. 60.0 vs. 57.0 mL/min/m^2; $p = 0.001$) but less likely to have chronic kidney disease requiring dialysis (21.5% vs. 22.5% vs. 28.6%; $p = 0.007$), hypertension (78.0% vs. 83.3% vs. 89.5%; $p < 0.001$), and sleep apnea requiring therapy (1.8% vs. 3.3% vs. 6.7%; $p < 0.001$), respectively. Patients in the HF*p*EF group had an elevated pulmonary artery

Table 3: Mortality and re-hospitalization rates at three-months and one-year follow-up.

Characteristics	All	HF categories				Adjusted odds ratio (95% CI) adjusted *p*-value against reference group		
		HF*r*EF EF (< 40%)	HF*mr*EF EF (40–49%)	HF*p*EF EF (≥ 50%)	*p*-value	HF*r*EF EF (< 40%)	HF*mr*EF EF (40–49%)	HF*p*EF EF (≥ 50%)
Three-months cumulative mortality (n = 2051)	143 (7.0)	86 (7.6)	31 (6.4)	26 (5.9)	0.426	Ref	0.86 (0.53–1.40) *p* = 0.554	0.54 (0.31–0.95) *p* = 0.031
12-months cumulative mortality (n = 1857)	197 (10.6)	108 (11.0)	47 (11.0)	42 (10.0)	0.984	Ref	1.07 (0.71–1.60) *p* = 0.753	0.89 (0.56–1.41) *p* = 0.616
Three-months hospitalization for HF (n = 1906)	421 (22.1)	238 (23.0)	91 (20.0)	92 (22.0)	0.520	Ref	0.80 (0.60–1.09) *p* = 0.159	0.78 (0.56–1.08) *p* =0.135
12-months hospitalization for HF (n = 1633)	490 (30.0)	255 (28.0)	118 (30.0)	117 (32.0)	0.335	Ref	0.99 (0.74–1.33) *p* = 0.948	1.05 (0.76–1.45) *p* =0.764

HFrEF: Heart failure (HF) with reduced ejection fraction (EF); HFmrEF: HF with mid-range EF; HFpEF: HF with preserved EF; NYHA: New York Heart Association.
Multivariable analyses were conducted using logistic regression models utilizing the simultaneous method. The models were adjusted for age, gender, body mass index, smoking, khat chewing, peripheral vascular disease, hypertension, diabetes mellitus, prior stroke/transient ischemic attack, systolic blood pressure, diastolic blood pressure, serum creatinine, in-hospital percutaneous coronary intervention or coronary artery bypass graft, admission diagnosis, NYHA class, in-hospital course (included non-invasive ventilation, intubation/ventilation, cardiogenic shock, inotropes, intra-aortic balloon pump, acute dialysis/ultrafiltration, atrial fibrillation requiring therapy, major bleeding, blood transfusion, stroke, and systemic infection requiring therapy), discharged medications (diuretics, digoxin, oral nitrates, calcium channel blockers, beta-blockers, aldosterone antagonist, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, aspirin, If channel blocker (ivabradine)).
Data were given as n (%).

pressure than patients with HF*r*EF and HFm*r*EF (57.0 vs. 53.0 vs. 52.0 mmHg; $p = 0.015$). A higher prevalence of atrial fibrillation (15.8% vs. 12.3% vs. 8.4%; $p = 0.002$) but lower levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP) (1885 vs. 2962 vs. 3372 pg/mL; $p = 0.008$) was seen with HF*p*EF patients when compared to those with HF*mr*EF and HF*r*EF [Table 1].

At hospital discharge, compared with the HF*mr*EF and HF*p*EF groups, patients with HF*r*EF were more likely to receive diuretics (97.2%. vs. 94.1% vs. 90.9%; $p < 0.001$), beta-blockers (77.2% vs. 71.7% vs. 56.8%; $p < 0.001$), angiotensin-converting-enzyme inhibitors (64.2% vs. 56.1% vs. 41.1%; $p < 0.001$), and aldosterone antagonists (50.4% vs. 21.2% vs. 14.8%; $p < 0.001$), whereas they were less likely to be administered calcium antagonists (11.2% vs. 25.1% vs. 45.5%; $p < 0.001$) and angiotensin-receptor blockers (17.5% vs. 19.2% vs. 24.5%; $p = 0.006$) [Table 2]. During hospitalization, patients with HF*mr*EF and HF*p*EF were less likely to receive IV furosemide infusion than the HF*r*EF group (16.5% vs. 13.3% vs. 21.6%; $p < 0.001$).

The overall cumulative all-cause mortalities at three-month and 12-month follow-up were 11.8% (n = 266) and 20.7% (n = 467), respectively. Those with HF*p*EF were associated with lower three-month cumulative all-cause mortality compared to those with HF*r*EF (7.6% vs. 5.9%; adjusted odds ratio (aOR) = 0.54, 95% confidence interval (CI): 0.31–0.95; $p = 0.031$) but not significantly different when compared to those with HF*mr*EF (aOR = 0.86, 95% CI: 0.53–1.40; $p = 0.554$). There were no significant differences among the groups with regards to the 12-month all-cause cumulative mortality (11% vs. 11% vs. 10%; overall $p = 0.984$). There were also no significant differences in re-hospitalization rates between the three HF groups not only at three-months (23% vs. 20% vs. 22%; overall $p = 0.520$), but also at one-year follow-up (28% vs. 30% vs. 32%; overall $p = 0.335$) [Table 3].

DISCUSSION

The observations from this multinational registry showed that three-month cumulative all-cause mortality was high in diabetic HF*r*EF patients compared to those with HF*p*EF. However, there were no significant differences in mortality at one-year follow-up between the HF groups. There were also no significant differences in re-hospitalization

rates between the HF groups not only at three-months but also at one-year follow-up in the Middle East.

In the Framingham Heart Study, the risk of incident HF was two-fold higher in diabetic males and four-folds higher in diabetic females.[16] The study has also shown a 34% mortality at one-year for diabetic HF patients.[17] In the Heart and Soul Study in a cohort of CAD patients with DM were associated with a higher risk of incident HF.[18] The risk of incident HF rises from 8% to 36% with each 1% rise in HbA_{1c}.[19] The Atherosclerosis Risk in Communities (ARIC) study has shown rising HF-related hospitalization rates with increases in HbA_{1c}.[20] Various other studies have also documented poor outcomes in patients with HF and with elevated HbA_{1c}.[21] In another study that consists of 18 084 non-diabetic patients with a higher risk of cardiovascular diseases has also shown that a mild increase in blood glucose of 1 mmol/L increases the risk of hospitalization by 1.23-fold.[22]

In the Candesartan in Heart failure-Assessment of moRtality and Morbidity (CHARM) trial, the rate of hospitalizations was higher in patients with HF*p*EF than in those with HF*r*EF. Furthermore, the observed all-cause mortality risk in patients with DM was the same in both HF*r*EF and HF*p*EF.[23] In acute HF patients, the presence of DM increases mortality in both ambulatory and hospitalized patients.[23,24] In another community-based study, it was shown that T2DM increases mortality and morbidity in both HF*r*EF and HF*p*EF.[25] In another study, a moderate difference in in-hospital mortality between HF*r*EF and HF*p*EF diabetic patients has been observed.[26] The incidence of DM was high (67%) in AHF patients with cardio-renal anemia syndrome in the Arabian Gulf.[27] A new risk calculator for HF*r*EF (www.hfriskcalc.in) has been suggested.[28,29]

Many HF risk models take DM as an important variable and consider it as an independent risk factor for predicting mortality.[30] In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack (ALLHAT) trial, the presence of diabetes had shown a two-fold rise in mortality and morbidity.[31] In the Irbesartan in Heart Failure With Preserved Systolic Function (I-PRESERVE) trial, cardiovascular mortality and HF-related morbidity was 34% in diabetic HF patients.[32] The Studies of Left Ventricular Dysfunction (SOLVD) trial also demonstrated higher rates of hospitalizations and mortality in asymptomatic ischemic cardiomyopathy patients with diabetes.[33] The same study also showed that African-Americans with HF*r*EF were at higher risk of developing AHF compared to Caucasians.[34] A meta-analysis of eight trials demonstrated that the risk of HF remains same in both strict the glycemic control group and standard treatment group.[35]

Many randomized controlled trials have shown that in diabetic HF patients, strict glycemic control has no benefits in terms of outcome.[36] In the Arabian Gulf, the AHF patients were a decade younger compared to those from the rest of the world.[37] The Dapagliflozin Effect on Cardiovascular Events–Thrombolysis in Myocardial Infarction 58 (DECLARE-TIMI 58) trial has shown mortality and morbidity benefits in diabetic HF patients on dapagliflozin treatment.[38] In a study of black diabetic cardiomyopathic patients, a reduced stroke and end-diastolic volume were associated with an increased left ventricular mass.[39] In the Empagliflozin Cardiovascular Outcome Event (EMPA-REG) trial, HF-related hospitalizations were associated with those treated with SGLT2 inhibitors.[40] In the Saxagliptin Assessment of Vascular Outcomes Recorded (SAVOR)-Thrombolysis in Myocardial Infarction (TIMI) 53 trial, the use of saxagliptin was associated with an increased risk of HF hospitalizations.[41] Middle East data on diabetic and non-diabetic AHF patients showed no significant differences in all-cause mortality and rehospitalizations at three and 12 months.[42] In HF and diabetes, genetics plays an important role and further studies are needed.[43,44]

Various limitations of this registry are noteworthy. In some countries, only a few hospitals took part in the registry; hence, the results might not be entirely generalizable. Since this study was derived from a HF registry in the Arabian Gulf, it is unfortunate that diabetic medications were not captured. Mortality rates at three-months and one-year follow-up were only recorded without the specification of the exact date of death of each patient. Hence, survival analysis, which might have been more appropriate, could not have been performed. Future studies need to overcome these limitations.

CONCLUSION

Three-month cumulative all-cause mortality was high in diabetic HF*r*EF patients compared

to those with HF*p*EF. However, there were no significant differences in mortality at one-year follow-up between the HF groups in the Middle East. There were also no significant differences in re-hospitalization rates between the HF groups not only at three-months but also at one-year follow-up.

Disclosure
The authors declared no conflict of interest. No funding was received for this study.

Acknowledgements
Thanks to Prof. Dr. Eugene Braunwald for introducing the word cardio-diabetology and explaining its importance.

Gulf CARE is an investigator-initiated study conducted under the auspices of the Gulf Heart Association and funded by Servier, Paris, France; and for centers in Saudi Arabia by the Saudi Heart Association.

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