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Demographics, Clinical Characteristics, Management, and Outcomes of Acute Heart Failure Patients: Observations from the Oman Acute Heart Failure Registry

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ABSTRACT

Objectives: We sought to describe the demographics, clinical characteristics, management and outcomes of patients in Oman with acute heart failure (AHF) as part of the Gulf aCute heArt failuRe rEgistry (CARE) project. ***Methods***: Data were analyzed from 988 consecutive patients admitted with AHF to 12 hospitals in Oman between 14 February and 14 November 2012. ***Results:*** The mean age of our patients was 63±12 years. Over half (57%) were male and 95% were Omani citizens. Fifty-seven percent of patients presented with acute decompensated chronic heart failure (ADCHF) while 43% had new-onset AHF. The primary comorbid conditions were hypertension (72%), coronary artery disease (55%), and diabetes mellitus (53%). Ischemic heart disease (IHD), hypertensive heart disease, and idiopathic cardiomyopathy were the most common etiologies of AHF in Oman. The median left ventricular ejection fraction of the cohort was 36% (27–45%) with 56% of the patients having heart failure with reduced ejection fraction (< 40%). Atrial fibrillation was seen in 15% of patients. Acute coronary syndrome (ACS) and non-compliance with medications were the most common precipitating factors. At discharge, angiotensin converting enzyme inhibitors and beta-blockers were prescribed adequately, but aldosterone antagonists were under prescribed. Within 12-months follow-up, one in two patients were rehospitalized for AHF. In-hospital mortality was 7.1%, which doubled to 15.7% at three months and reached 26.4% at one-year post discharge. ***Conclusions:*** Oman CARE was the first prospective multicenter registry of AHF in Oman and showed that heart failure (HF) patients present at a younger age with recurrent ADCHF and HF with reduced ejection fraction. IHD was the most common etiology of HF with a low prevalence of AHF, but a high prevalence of acute coronary syndrome and non-compliance with medications precipitating HF. A quarter of patients died at one-year follow-up even though at discharge medical therapy was nearly optimal. Our study indicates an urgent need for prevention, early diagnosis, and treatment of AHF in Oman.

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Heart failure (HF) is a global endemic affecting an estimated 26 million people worldwide. It is currently the leading cause of hospitalization with high early post-discharge mortality and readmission rates.[1]

There are multiple hospital-based worldwide registries that are the primary sources of real-world data on HF from America and Europe and even Africa and Asia-Pacific.[2-5] However, there is no prospective large-scale data from the Middle-East with regard to etiology, presentation, management, and outcome of HF patients. From the recent Gulf registry of acute coronary events (Gulf RACE), we know that the average age of acute coronary syndrome (ACS) and diabetic patients from this region is a decade younger than their Western counterparts. It is intriguing to know how HF affects the younger population from this area, how they present, the etiology, and outcomes. Hence, the Gulf Heart Association initiated a large prospective registry called Gulf CARE (aCute heArt failuRe rEgistry). Gulf CARE is a multinational multicenter registry of patients admitted with the diagnosis of acute heart failure (AHF) to 47 hospitals in seven Middle Eastern countries including Oman.[6,7]

There is currently a lack of reliable statistics with regard to HF in Oman. The aim of this paper was to describe the demographics, clinical characteristics, management, and outcomes of AHF patients from the Oman CARE study (part of Gulf CARE).

METHODS

Oman CARE was a prospective, hospital-based, multicenter registry of patients admitted with the diagnosis of AHF to 12 hospitals in Oman. In our previous publication, the main registry design paper, we detailed the methodology and hospital characteristics.[6,7] Briefly, between 14 February and 14 November 2012 we recruited males and females aged > 18 years old with a diagnosis of AHF. We recorded demographic data, co-morbidities, risk factors, clinical presentation and investigations including troponin and B-type natriuretic peptide (BNP), medication history with dosages, interventions, in-hospital outcome, etiology, and precipitating factors for AHF. Follow-up was done by telephone at three months and either by phone or clinic visit at one-year. Data was entered online using a custom designed electronic case record form (CRF) at the Gulf CARE website (www.gulfcare.org). The Ministry of Health Research and Ethics Committee gave approval for the study. The study, as part of the overall Gulf CARE Registry, was registered at clinicaltrials.gov (NCT01467973).

HF was defined by the European Society of Cardiology (ESC) criteria.[8] AHF was further sub-classified as either acute decompensated chronic heart failure (ADCHF) or new-onset acute heart failure (*de novo* AHF) based on ESC guidelines.[8] ADCHF was defined as worsening of HF in patients with a previous diagnosis or hospitalization for HF. New-onset AHF was defined as AHF in patients with no prior history of HF.

Definitions of data variables in the CRF were based on the ESC 2008 guidelines and 2005 American College of Cardiology (ACC) clinical data standards.[8,9] Idiopathic dilated cardiomyopathy was defined as a myocardial disorder in which the heart muscle is structurally and functionally abnormal (in the absence of coronary artery disease, hypertension, valvular disease, or congenital heart disease) sufficient to cause the observed myocardial abnormality.[8] Khat chewing was defined as chewing khat plant/leaves (*Catha edulis*), which contain an amphetamine-like stimulant (which can cause euphoria, hypertension, myocardial infarction, and dilated cardiomyopathy) within one-month of the index admission. HF with preserved ejection fraction (HFpEF) was defined as presence of symptoms and/or signs of HF and a left ventricular ejection fraction (LVEF; ≥ 40%).[8]

Descriptive statistics were used to summarize the data. For categorical variables, frequencies and percentages were reported. For continuous variables, mean and standard deviation (SD) were used to summarize the data while for those variables that were not normally distributed, median and interquartile range (IQR; 25th and 75th percentiles) were used to present the data. Descriptive statistics were conducted using STATA version 13.1 (STATA Corporation, College Station, Texas, US).

RESULTS

Twelve hospitals in Oman participated in the Gulf CARE project, with a total of 988 patients enrolled [Table 1]. The mean age of the cohort was 63±12 years, 57% (n = 563) were males, and 95% (n = 942) were Omani citizens. More than half of the patients

Table 1: Patient characteristics (n = 988).

Characteristics	n (%)
Age, mean ±SD, years	63±12
Males	563 (57.0)
Omani citizen	942 (95.3)
Main care provider	
Cardiologist	477 (48.3)
Internist	511 (51.7)
BMI, median (IQR)	27 (24,31)
Medical history	
Hypertension	711 (72.0)
CAD	547 (55.4)
Diabetes mellitus	528 (53.4)
Hyperlipidemia	454 (46.0)
AF	122 (12.3)
Valvular heart disease	105 (10.6)
CKD/dialysis	109 (11.0)
Stroke/TIA	84 (8.5)
Smoking[1]	85 (8.6)
Khat	6 (0.6)
Alcohol[2]	38 (3.8)
PVD	26 (2.6)
Clinical presentation	
Dyspnea	958 (97.0)
Orthopnoea	723 (73.1)
Paroxysmal nocturnal dyspnoea	539 (54.6)
Chest pain	433 (43.8)
Easy fatiguability	427 (43.2)
Palpitation	310 (31.4)
Weight gain	204 (20.6)
Basal lung crepitations	938 (94.9)
Peripheral edema	465 (47.1)
Raised JVP	360 (36.4)
Gallop	369 (37.3)
Enlarged tender liver	203 (20.5)
Ascites	129 (13.1)
Signs of pleural effusion	90 (9.1)
HR, mean ±SD, BMP	97±23
SBP, mean ±SD, mmHg	145±37
DBP, mean ±SD, mmHg	85±20
NYHA I	35 (3.5)
NYHA II	204 (20.6)
NYHA III	427 (43.2)
NYHA IV	292 (29.6)
NYHA not known	30 (3.0)
ADCHF	566 (57.3)

IQR: interquartile range; CAD: coronary artery disease; AF: atrial fibrillation; CKD: chronic kidney disease; TIA: transient ischemic attack; PVD: peripheral vascular disease; JVP: jugular venous pressure; HR: heart rate; BPM: beats per minute; SBP: systolic blood pressure; DBP: diastolic blood pressure; NYHA: New York Heart Association status; ADCHF: acute decompensated chronic heart failure. Smoking[1] includes chewing tobacco and smoking a water-pipe. Alcohol[2] consumption daily.

(57%, n = 566) presented with ADCHF while the rest (43%; n = 422) had *de novo* AHF. Comorbid conditions were common, particularly hypertension (72%; n = 711), coronary artery disease (CAD) (55%; n = 547), diabetes mellitus (53%; n = 528), and hyperlipidemia (46%; n = 454). The three most common presenting signs and symptoms were dyspnea (97%; n = 958), basal lung crepitations (95%; n = 938), and orthopnoea (73%; n = 723).

Table 2: Laboratory, electrocardiogram (ECG), and echocardiography investigations.

Test	Results
Serum creatinine, mean±SD, µmol/L	128±112
First serum urea, mean±SD, mmol/L	10±7
BNP, median (IQR), pg/ml	5,769 (1556,13384)
NT-pro BNP, median (IQR), pg/ml	3,199 (1486,6934)
e-GFR, median (IQR), ml/min	63 (44,86)
Serum potassium, median (IQR), mmol/L	4.2 (3.8,4.6)
Hemoglobin, median (IQR), g/dL	12.5 (11,14)
Total cholesterol, median (IQR), mmol/L	4.7 (3.8,5.6)
$HbA1_c$, %	7.1 (6.0,8.9)
ECG, n (%)	
Sinus rhythm	808 (81.8)
AF/flutter	153 (15.5)
CHB	1 (0.1)
Paced	4 (0.4)
SVT	6 (0.6)
Others	16 (1.6)
LV hypertrophy	254 (25.7)
ST-Depres./T-inversion	396 (40.1)
STEMI	58 (5.9)
Pathological Q waves	193 (19.5)
QRS duration ≥ 0.12 ms, n (%)	
No	791 (80.1)
LBBB	129 (13.1)
RBBB	51 (5.2)
IVCD	17 (1.7)
Echocardiography	
LVEF, median (IQR), %	36 (27,45)
LVEF < 40%, n (%)	497 (50.3)

Data presented as median (IQR) unless otherwise indicated. BNP: B-type natriuretic peptide; NT-pro BNP: N-Terminal B-type natriuretic peptide; GFR: glomerular filtration rate; AF: atrial fibrillation; CHB: complete heart block; SVT: supraventricular tachycardia; LV: left ventricular; Depres: depression; STEMI: ST-segment elevation myocardial infarction; LBBB: left bundle branch block; RBBB: right bundle branch block; IVCD: intra ventricular conduction delay; LVEF: left ventricular ejection fraction.

The other characteristics are shown in Table 1. On admission, patient's mean heart rate was 97±23 beats per minute and the predominant New York Heart Association (NYHA) class was III/IV (75%; n = 719). Table 2 shows the laboratory, electrocardiogram (ECG), and echocardiography findings. The median hemoglobin (Hb) of the cohort was 12.5 (11–14) g/dL. Eighty-two percent (n = 808) of patients were in sinus rhythm with 15% (n = 153) demonstrating atrial fibrillation or flutter. Overall, 80% (n = 791) of patients had QRS duration < 0.12 ms and 13.1% (n = 129) had left bundle branch block morphology on ECG. The overall median left ventricular ejection fraction (LVEF) of the cohort was 36% (range 27–45). Heart failure with reduced ejection fraction (HFrEF; < 40%) was seen in 50.3% (n = 497) of patients.

Table 3: Etiology, precipitating causes, and in-hospital course of the patient cohort.

Characteristics	n (%)
Etiology of heart failure	
IHD	589 (59.6)
HHD	204 (20.6)
Cardiomyopathy	133 (13.5)
Valvular heart disease	47 (4.8)
Pulmonary hypertension	9 (0.9)
Congenital HD	3 (0.3)
Myocarditis	2 (0.2)
Precipitating causes of heart failure	
Acute coronary syndrome	267 (27.0)
Non-compliance with meds	234 (23.7)
Uncontrolled hypertension	103 (10.4)
Infection	96 (9.7)
Uncontrolled arrhythmias	58 (5.9)
Non-compliance with diet	44 (4.5)
Worsening renal failure	36 (3.6)
Anemia	21 (2.1)
Pulmonary embolism	1 (0.1)
Salt retaining drugs	3 (0.3)
Unknown	124 (12.6)
In-hospital course	
Infection requiring therapy	156 (15.8)
Inotropes	126 (12.8)
NIV	86 (8.7)
Cardiogenic shock	79 (8.0)
Intubation/ventilation	75 (7.6)
AF requiring therapy	57 (5.8)
VT/VF requiring therapy	29 (2.9)
Blood transfusion	26 (2.6)
Acute dialysis/ultrafiltration	22 (2.2)
Stroke	14 (1.4)
Valve repair/replacement	13 (1.3)
IABP	2 (0.2)

IHD: ischemic heart disease; HHD: hypertensive heart disease; HD: heart disease; Meds: medications; NIV: non-invasive ventilation; AF: atrial fibrillation; VT/VF: ventricular tachycardia/ventricular fibrillation; IABP: intra-aortic balloon pump.

Table 4: Pre-admission, in-hospital intravenous and, discharge medications of the patient cohort.

Medication	n (%)
Pre-admission	
Diuretics	715 (72.4)
Beta-blockers	500 (50.6)
ACEi	485 (49.1)
ARB	177 (17.9)
Aldosterone antagonist	197 (19.9)
Hydralazine	50 (5.1)
Aspirin	724 (73.3)
Clopidogrel	105 (10.6)
Statins	704 (71.3)
Nitrates	422 (42.7)
Digoxin	132 (13.4)
CCB	112 (11.3)
Ivabradine	4 (0.4)
Anticoagulant	93 (9.4)
Anti-arrhythmic	25 (2.5)
IV medications in-hospital	
Frusemide, bolus	898 (90.9)
Frusemide, infusion	190 (19.2)
Nitrates, infusion	204 (20.6)
At discharge*	
Diuretics	839 (94.9)
Beta-blockers	605 (68.4)
ACEi	531 (60.1)
ARB	186 (21.0)
Aldosterone antagonist	274 (31.0)
Hydralazine	49 (5.5)
Aspirin	748 (84.6)
Clopidogrel	214 (24.2)
Statins	742 (83.9)
Nitrates	459 (54.1)
Digoxin	152 (17.9)
CCB	109 (12.9)
Ivabradine	5 (0.6)
Anticoagulant	115 (13.6)
Anti-arrhythmic	38 (4.3)

ACEi: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; CCB: calcium channel blocker; IV: intravenous.
**n = 884. Medications at discharge excluded patients that died (n =70; 7.1%) and who left against medical advice (n =34; 3.4%).*

Table 5: Oman CARE in-hospital, three- and 12-month follow-up outcomes.

Outcomes	n (%)
In-hospital	
Died	70 (7.1)
LOS, median (IQR), days	4 (3,7)
Device therapy	3 (0.3)
PCI	35 (3.5)
CABG	6 (0.6)
Three-months	
Died	155 (15.7)
Hospitalization for HF	250 (30.0)
LOS, median (IQR), days	4 (3,6)
Device therapy	6 (0.6)
PCI/CABG	89 (9.0)
12-months	
Died	261 (26.4)
Hospitalization for HF	521 (52.7)
LOS, median (IQR), days	5 (4,8)
Device therapy	19 (1.9)
PCI/CABG	179 (18.1)

The three- and 12-month outcomes are cumulative.
LOS: length of hospital stay; PPM: permanent pacemaker; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; HF: heart failure. Device therapy included cardiac resynchronization therapy with defibrillation (CRT-D), cardiac resynchronization therapy with a pacemaker (CRT-P), and implantable cardioverter-defibrillator (ICD).

The three most prevalent etiologies of HF were ischemic heart disease (IHD) (59.6%; n = 589), hypertensive heart disease (HHD) (20.6%; n = 204) and idiopathic cardiomyopathy (13.5%; n = 133). Valvular heart disease, as an etiology, accounted for 4.8% (n = 47) of patients. The three most common precipitating causes of HF were ACS (n = 267; 27.0%), non-compliance with medications (n = 234; 23.7%) and uncontrolled hypertension (n = 103; 10.4%). The three most prevalent in-hospital events/courses included infection requiring therapy (n = 156; 15.8%), requirement of inotropes (n=126; 12.8%) and non-invasive ventilation (NIV) (n = 86; 8.7%) [Table 3].

Among the pre-admission medications, excluding aspirin (73.3%) and statins (71.3%), the three most prescribed medications were diuretics (72.4%, n = 715), angiotensin converting enzyme inhibitors/angiotensin II receptor blockers (ACEi/ARB) (67.0%, n = 662) and beta-blockers (50.6%, n = 500) [Table 4]. In-hospital intravenous furosemide and nitrates were administered in 90.9% and 20.6% of patients, respectively. The most medications prescribed on discharge, excluding aspirin (84.6%) and statins (83.9%), the most prescribed medications were diuretics (94.9%, n = 839), ACEis/ARB (81.1%, n = 717), beta-blockers (68.4%, n = 605), and aldosterone antagonists (31.0%, n = 274).

Follow-up status was complete in 97% of patients at 12-months [Table 5]. The in-hospital mortality rate was 7.1% (n = 70) with a median hospital stay of four days. In-hospital device therapy rate was 0.3% (n = 3) with percutaneous coronary intervention (PCI) in 35 patients (3.5%) and coronary artery bypass graft (CABG) in six (0.6%) patients.

At three-months follow-up, 155 patients (15.7%) had died. Hospitalization for HF was 30.0%. At 12-month follow-up, one in two patients were rehospitalized for AHF. At three months mortality had doubled to 15.7%, and reached 26.4% at one-year post discharge.

DISCUSSION

Oman CARE was the first large, multicenter, prospective study of AHF from Oman providing a large amount of data that could be used to implement strategies to diagnose, treat and prevent AHF early and improve outcomes.

There were a number of key findings from our study. HF presented at a younger age, and its predominant presentation was ADCHF. HFrEF was more common than HFpEF. The main risk factors for HF were hypertension, coronary artery disease, and diabetes mellitus. Comorbid atrial fibrillation was less prevalent when compared to Western registries, and IHD, hypertensive heart disease, and idiopathic cardiomyopathy were the most common etiology of AHF. The most common precipitating factors were ACS and non-compliance with medications. At discharge, ACEi and beta-blockers were prescribed adequately, but aldosterone antagonists were under prescribed. Within 12-month follow-up, one in two patients were re-hospitalized for HF, and in-hospital mortality was 7.1%, which doubled to 15.7% at three months, and reached 26.4% at one-year post discharge.

Table 6 shows important differences between Oman CARE and the main Gulf CARE registry as well as the American, European, and Asia-pacific registries. The overall mean age of the cohort was 63 years, which is a decade less than the Western

Table 6: Comparison of Oman CARE with other registries.

Registry	OPTIMIZE-HF[2]	ESC-HF PILOT[3]	ADHERE-I[4]	THESUS-HF[5]	Gulf CARE[6,7]	Oman Gulf CARE
Number of patients	48,612	1,892	10,171	1,006	5,005	988
Region	USA	Europe	International-Asia Pacific*	Africa	Middle East	Oman
Age, years	73	70	67	52	59	63
Male	48	62	57	49	63	57
Diabetes mellitus	41	35	45	11	50	53
Atrial fibrillation	31	43	24	18	14	15
Median EF	39	38	-	38	35	36
HFpEF	51	35	47	NA	31	44
ADCHF/DenovoAHF	NA	75/25	64/36	NA	55/45	57/43
IHD etiology	46	50	NA	7.7	53	60
ACS precipitating factor	14	NA	NA	NA	27	27
Beta blocker	83	81	41	30	71	68
ACEi/ARB	83	78	63	81	78	81
Aldosterone antagonists	NA	54	31	72	48	31
In-hospital mortality	3.8	3.8	4.8	4.2	6.3	7.1
Coronary intervention	27	NA	NA	NA	7.4	4.1
Device therapy	NA	9.3	NA	NA	5.0	0.3
Hospitalization at three months/12 months	29/NA	NA/25	NA	NA	18/40	30/52
Mortality at three months/12 months	8/NA	NA/17	NA	NA	12/20	15/26

All values are percentages unless specified.
**International-Asia Pacific: Australia, Hong Kong, Indonesia, Malaysia, Philippines, Singapore, Taiwan, and Thailand; EF: ejection fraction; AHF: acute heart failure; ADCHF: acute decompensated chronic heart failure; IHD: ischemic heart disease; ACS: acute coronary syndrome; ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; NA: not available. OPTIMIZE-HF: Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure; ADHERE: Acute Decompensated Heart Faliure National Registry; THESUS-HF: The Sub-Saharan Africa Survey of Heart Failure.*

registries, but more than the overall Gulf CARE cohort (59 years) indicating younger age of HF onset in Oman.[2-7] Patients from the African registry were even younger (52 years).[5]

The majority of patients presented with AHF and old age with co-morbidities such as hypertension, coronary artery disease, diabetes mellitus, hyperlipidemia, atrial fibrillation, valvular heart disease, and prior stroke/transient ischemic stroke, indicating uncontrolled severe comorbid conditions and precipitating factors leading to recurrent hospitalizations with decompensated AHF. All florid symptoms and signs of AHF were more prevalent among HF patients, which along with the lower median LVEF and a higher proportion of patients with HFrEF suggests inadequate control of risk factors and sub-optimal treatment. Younger HF patients were also smokers presenting with ACS or uncontrolled hypertension precipitating acute pulmonary edema. These results from Oman are very similar to the Euro Heart Failure Survey II (EHFS II) and the Italian registry, which showed that younger HF patients frequently presented with acute pulmonary edema, cardiogenic shock, and uncontrolled hypertension, with ACS as a predominant precipitating factor.[10,11]

Compared to all registries, the prevalence of diabetes mellitus in our study was highest at 53.4%. This is due to the very high prevalence of diabetes mellitus in Oman.[12] In a recent study published from Oman, the age-adjusted prevalence of type 2 diabetes mellitus varied from 10.4% to 21.1% (when compared to the global average of 9%). The highest prevalence of impaired fasting glucose was found in males (35.1%).[12] The prevalence of atrial fibrillation was low (15.5%) in the Oman population of AHF patients when compared with Western registries (30–40%).[2–4] This low rate of atrial fibrillation can be attributed to the younger age of the cohort, low prevalence of valvular heart disease and the low

prevalence of alcohol consumption in this region. IHD was the most prevalent etiology with ACS one of the most common precipitating factors while HHD was the second most common etiology as noted in the EHS II and IN-HF registries.[10,11] Non-compliance with medications was one of the most prevalent precipitating causes in patients with HF, indicating the need for patient education and monitoring.

Evidence-based medications like ACEi/ARB (81.1%), beta-blockers (68.4%) were adequately prescribed, but aldosterone antagonists were prescribed in low numbers (31.0%). ACEi/ARBs prescription were comparable to other registries except ADHERE-I where it was low at 63%.[2-5] However, in Oman, at discharge, beta-blockers were prescribed less than recorded in the European and American registries, but higher than the ADHERE-I and African registries.[4,5]

Even though AHF patients from Oman were treated adequately, the overall in-hospital mortality (7.1%) was higher when compared to other registries. This was possibly due to IHD etiology along with ACS as a precipitating factor and underlying comorbid conditions that are known to cause systolic and diastolic dysfunction.[13] It has been observed that diabetic patients with HF may not respond well to standard HF therapy when compared to nondiabetic AHF patients.[13]

The Oman registry had an excellent follow-up status at 12 months (97%). Within 12-month follow-up, one in two patients were rehospitalized for HF, which was highest compared to other registries including the main Gulf CARE registry.[2–6] The cumulative mortality of 15.7% at three months and 26.4% at one-year post-discharge were highest among all AHF registries indicating the very poor outcome of AHF patients from Oman, which may be due to the high prevalence of IHD/ACS and diabetes mellitus.

This high prevalence of diabetes and IHD are also noted as important causes of increasing HF in South Asian countries like India.[14,15] These issues need to be addressed urgently so that preventive steps are initiated as soon as possible by health authorities. Starting HF clinics with early diagnosis, risk factor control, and specific treatment will help to reduce disease burden as well as morbidity and mortality in this region.[15]

CONCLUSIONS

Oman CARE was the first prospective multicenter registry of AHF in Oman and showed that HF patients present at a younger age with recurrent ADCHF and HFrEF. IHD was the most common etiology of HF with a low prevalence of AF, but high prevalence of ACS and non-compliance with medications precipitating HF. A quarter of patients died at one-year follow-up even though medical therapy was nearly optimal. This indicates an urgent need for prevention, early diagnosis, and treatment of AHF in Oman.

Disclosure

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