Clinical presentation and outcomes of acute coronary syndromes in the Gulf Registry of Acute Coronary Events (Gulf RACE)

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ABSTRACT

الهدف: دراسة الأمراض الحادة للشرايين التاجية في منطقة الخليج من ناحية خصائص المرضى و طرق العلاج المتوفرة لهم و نتائج هذا العلاج.

الطريقة: مسح موحد شمل ٦ دول و ٦٥ مستشفى في الخليج العربي في آن واحد لإحصاء جميع مرضى الأمراض الحادة للشرايين التاجية خلال فترة ٦ أشهر. تم متابعة هؤلاء المرضى لتاريخ خروجهم من المستشفى. نعرض هنا نتائج الشهر الأول (مايو من عام ٢٠٠٦) من هذا المسح.

النتائج: في الشهر الأول من المسح تم إدخال ١٤٨٤ حالة. متوسط العمر كان ٥٥ عاماً. نسبة مرضى السكري كانت ٤٥٪ و نسبة المدخنين بلغت ٣٨٪. الإصابة بمتلازمة الأيض. كانت ٣٨٪ حيث أصيب ٦٨٪ من النساء و ٣٠٪ من الرجال بهذه المتلازمة. كان تشخيص المرضى لدى خروجهم من المستشفى٧١٪ إصابة بالنوبة القلبية و ٢٩٪ إصابة بالذبحة الصدرية. ٦٥٪ من المرضى المصابين بالنوبة القلبية حصلوا على أدوية ارتواء الشرايين التاجية. معدل الوقت من دخول المريض للحوادث إلى إعطائه الدواء المذيب للجلطة كان ٤٥ دقيقة. كانت نسبة من حصلوا على هذا الدواء خلال ٣٠ دقيقة من وصولهم قسم الطوارئ ٣٧٪. خلال أول يوم من دخول المستشفى حصل ٩٤٪ من المرضى على دواء الأسبرين بينما حصل ٥١٪ على دواء كلوبيدوكرل. خضع ٢١٪ من المرضى لفحص قسطرة القلب أثناء مكوثهم في المستشفى. نسبة الوفيات أثناء المكوث في المستشفى كانت ٣٪.

خاتمة: تمكنا من إحصاء خصائص مرضى الأمراض الحادة للشرايين التاجية بالإضافة إلى إحصاء نوعية العلاج الذي أعطي لهم. يتضح بأن هناك حاجة لتحسين الأداء من ناحية استخدام الأدوية و تقليص فترة إعطاء دواء مذيب الجلطة و زيادة خدمة قسطرة القلب.

Objective: To identify the characteristics, treatments and hospital outcomes for patients diagnosed with acute coronary syndromes (ACS) in the Gulf area.

Method: Prospective, multinational, multicentre, observational survey of consecutive ACS patients who were admitted to 65 hospitals during May 2006.

Results: A total of 1484 ACS patients were recruited. The mean age was 55 years, and 76% were men. The final discharge diagnosis was ST-segment elevation myocardial infarction (STEMI) in 37%, non-ST-segment elevation myocardial infarction (NSTEMI) in 32%, left bundle branch block myocardial infarction (LBBB MI) in 2%, and unstable angina in 29%. Among patients with STEMI and LBBB MI, the reperfusion rate was 65%, with use of primary percutaneous coronary intervention in 7% and thrombolytic therapy in 93%. When thrombolytic therapy was used, the median door to needle time was 45 minutes, with 37% receiving it within 30 minutes of hospital presentation. During the first day of hospitalization, aspirin was administered to 94%, clopidogrel to 51%, and beta blockers to 65%. Angiotensin converting enzyme inhibitors/Angiotensin receptor blockers and statins were used in 62% and 82%, respectively. Coronary angiography during hospitalization was performed in 21%. In-hospital mortality was 3%.

Conclusions: We were able to determine the characteristics, treatments and in-hospital outcomes of patients hospitalized with ACS in our region. There is room for improvement in using medications, reducing needle to door time and utilizing more cardiac catheterization services.

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The diagnosis and management of acute coronary syndrome (ACS) have been redefined during the past 2 decades based on evidence from multiple large randomized clinical trials.[1-3] However, the implementation of such guidelines into clinical practice often lags behind.[4] Furthermore, although the role of clinical trials in setting clinical practice guidelines is indisputable, there are significant differences in characteristics, hospital treatments and outcomes between trial participants and non-participants.[5,6] In this context, several registry-based studies have been conducted to define the characteristics of ACS patients and assess the implementation of practice guidelines in everyday clinical practice.[7-9] Most of these registries are based on western populations. The Gulf Registry of Acute Coronary Events (Gulf RACE) is a 6 month prospective observational study of consecutive patients hospitalized with ACS in 6 countries in the Arabian Peninsula. It is the first multinational unified ACS registry carried out in the Middle East. It aims at identifying the characteristics, treatments and hospital outcomes of patients diagnosed with ACS. It also examines the adherence to established clinical practice guidelines in the participating countries. We report the findings from the first month of the registry (pilot phase).

Methods. The Gulf Registry of Acute Coronary Events is a prospective, multinational, multicentre survey of consecutive patients hospitalized with the final diagnosis of ACS in 6 Arabian Peninsula/Gulf countries over a period of 6 months. An attempt was made to include everyone with the final diagnosis of ACS, and there were no exclusion criteria. The study received ethical approval from the institutional ethical bodies in all participating countries. Recruitment in the pilot phase started on May 8, 2006 for 30 days. Enrollment in the next phase of the registry started on January 29, 2007 and continued for 5 months. This report describes the findings of the first month (pilot phase). Of 74 medical centres invited to participate in the registry, 65 confirmed their participation and enrolled patients according to the survey inclusion criteria. In Bahrain, Kuwait and Qatar, all hospitals that admit patients with ACS participated in the survey, while in Oman, UAE and Yemen, most hospitals (covering at least 85% of the population) participated. Each participating hospital completed a questionnaire giving a description of the medical center. The number of patients enrolled by each country were: Kuwait 390, UAE 372, Oman 306, Yemen 271, Bahrain 80, and Qatar 65. Diagnosis of the different types of ACS and definitions of data variables were based on the American College of Cardiology (ACC) clinical data standards, published in December 2001.[10] These definitions are based on clinical presentations, electrocardiogram (ECG) findings and cardiac biomarkers. The biomarkers were measured locally at each hospital's laboratory using its own assays and reference ranges. Data collected included patients' demographics, past medical history, provisional diagnosis on admission and final discharge diagnosis, clinical features at hospital presentation, ECG findings, laboratory investigations, early in-hospital (administered within 24 hours of admission) and discharge medications, use of cardiac procedures and interventions, in-hospital outcomes and in hospital mortality. All management decisions were at the discretion of the treating physician. A national coordinator was assigned to each country to oversee the implementation of the survey protocol. A chief site officer was assigned to each site to maintain a logbook of all suspected ACS admissions and to oversee the enrollment and completeness of the Case Report Form (CRF) at his/her site. All national coordinators and chief site officers received full training involving a review of the survey protocol and methods for filling the CRF, which contained 231 fields. In addition to the formal training, a powerpoint presentation of the protocol and CRF was created for the purpose of these meetings This presentation was distributed to the national coordinators, chief site officers, and site officers for their future reference. The site officers identified consecutive patients at the time of hospital admission and collected data prospectively on a standardized CRF. Filling of the CRF was initiated once an admission with a provisional diagnosis of ACS was made. If during hospital follow up a patient was found not to be an ACS case, then that patient and CRF were not included in the survey. Once CRFs were filled, they were checked for completeness by the designated chief site officer at each site. Then they were sent to a clinical research organization, where they were edited for missing data, inconsistencies and outliers. Site visits were carried out in all countries. Ten percent of CRFs and source documents were inspected. In Kuwait, Bahrain and Qatar, all sites were audited. In Oman, UAE and Yemen, the number of sites audited varied from 20%-30%. The purpose of the site audits was to verify the data collected in the CRFs against the source documents. They were not intended to validate the accuracy of the discharge diagnosis by the attending physician.

Statistical analysis. Baseline and clinical characteristics of patients were presented as frequencies and means. The characteristics of patients with and without metabolic syndrome were compared, using a 2 sample T-test for continuous independent variables and Chi-square Z-test of proportion for categorical variables. A p-value of < 0.05 was considered statistically

Table 1 - Baseline characteristics (n=1484).

Baseline characteristics	No. of patients (%)	
Male gender	1130	(76.0)
Age years (mean ± SD)	55 ± 12	
< 55	747	(50.4)
55-64	372	(25.0)
65- 74	255	(17.2)
≥ 75	110	(7.4)
Previous medical history		
Angina	532	(36.0)
MI	345	(23.0)
PCI	171	(12.0)
CABG	63	(4.0)
Previous aspirin use	549	(37.0)
Risk factors		
Current Smoker	669	(45.0)
Known diabetes	566	(38.0)
Known hypertension	681	(46.0)
Known hyperlipidemia	459	(31.0)
Electrocardiogram		
ST elevation/LBBB	611	(41.0)
ST depression	516	(35.0)
Other	357	(24.0)
*Killip Class**		
class 1	1162	(79.0)
class 2-3	266	(18.0)
class 4	39	(3.0)
*Discharge diagnosis***		
STEMI	550	(37.0)
NSTEMI	469	(32.0)
LBBB MI	31	(2.0)
Unstable angina	428	(29.0)

*1467 patients, **1478 patients,
MI - myocardial infarction, PCI - percutaneous coronary intervention, CABG - coronary artery bypass graft, STEMI - ST-segment elevation myocardial infarction, NSTEMI - non-ST-segment elevation myocardial infarction, LBBB MI - left bundle branch block myocardial infarction.

Table 2 - Use of medications.

Medications	No. of patients (%)	
First 24 hours after admission (no= 1484)		
Aspirin	1446	(97.0)
Clopidogrel	763	51.0)
Beta blockers	961	65.0)
Unfractionated heparin	717	(48.0)
LMWH	653	(44.0)
GP IIb/IIIa inhibitors	178	(12.0)
ACE inhibitors/ARBs	925	(62.0)
Statins	1223	(82.0)
*At hospital discharge (n = 1439)**		
Aspirin	1347	(94.0)
Clopidogrel	732	51.0)
Beta blockers	1069	(74.0)
ACE inhibitors/ARBs	992	(69.0)
Statins	1159	(81.0)

*For patients discharged alive
LMWH - low molecular weight heparin, GP IIb/IIIa inhibitors - glycoprotein IIb/IIIa inhibitors, ACE inhibitors - angiotensin converting enzyme inhibitors, ARBs - angiotensin receptor blockers.

Table 3 - In-hospital clinical outcomes and coronary angiography

Outcomes	No. of patients (%)	
Recurrent ischemia	175	(12.0)
Re-infarction	47	(3.0)
Congestive heart failure	225	(15.0)
Ventilation	49	(3.0)
Cardiogenic shock	68	(5.0)
Major bleed	7	(0.5)
Stroke	7	(0.5)
Death	45	(3.0)
Coronary angiography	333	(22.0)

significant. We also evaluated the relationship between patients' Global Registry of Acute Coronary Events (GRACE) risk score at presentation and in-hospital death and re-infarction. We divided patients into 4 groups based on their GRACE risk score (<96, 96-112, 113-133, >133) and determined the frequency of in-hospital death and re-infarction for each category and statistically evaluated this association using Chi-square test for trend. All data analyses were carried out using the Statistical Package for Social Sciences version 14 (SPSS Inc. USA).

Results. The CRF was filled out with 2% missing values. This 2% did not include mortality. There was a total of 1484 ACS patients in the pilot phase of Gulf RACE recruited from 65 hospitals in 6 countries. The baseline characteristics are listed in **Table 1**. The mean age of patients was 55 years, and 76% of them were men. Fifty percent of patients were <55 years old, while only 7.5% were 75 years or older. The most prevalent risk factors were diabetes mellitus (45%) and cigarette smoking (38%). The majority (79%) of patients presented with Killip class 1. The final discharge diagnosis was STEMI in 550 patients (37%), NSTEMI in 469 patients (32%), LBBB MI in 31 patients (2%) and unstable angina in 428 patients (29%). Of all 575 patients presenting ST elevation or new LBBB, 373

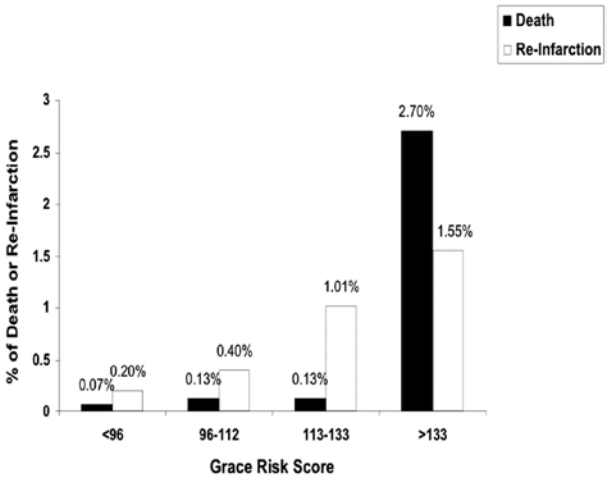

Figure 1 - Incidence of death and re-infarction according to the Global Registry of Acute Coronary Events risk score. Death: Chi square test for independence = 27.118, $p<0.0001$. Chi square test for trend = 19.432, $p<0.0001$. Re - Infarction: Chi square test for independence = 4.279, $p=0.2329$.

patients (65%) received reperfusion therapy. Among 444 patients presenting within 12 hours of symptom onset, 32 (7%) underwent primary percutaneous coronary intervention (PCI), 341 (77%) received thrombolytic therapy, and 71 (16%) did not receive any kind of reperfusion therapy. Among patients receiving thrombolytic therapy, 139 (41%) were given reteplase, 104 (30%) tenecteplase, 94 (28%) streptokinase, and 4(1%) were given tissue plasminogen activator. The median door to needle time was 45 minutes. Only 37% of patients who received thrombolytic therapy were treated within 30 minutes of presentation to hospital. The median time from symptom onset to presentation to hospital was 122 minutes. **Table 2** shows the medications patients received early after admission and at discharge. The use of aspirin, clopidogrel, beta-blockers, ACE inhibitors/ ARBs and statins at discharge had about the same frequency as early after admission. Hospital outcomes are shown in **Table 3**. The frequency of in-hospital death increased significantly with the higher GRACE risk score ($p<0.001$), while the frequency of re-infarction was not significantly associated with the variability in the GRACE risk score (**Figure 1**).

Discussion. By covering 85-100% of the population of each country involved, Gulf RACE presents an accurate description of ACS patients' characteristics and outcomes in 6 Arabian Peninsula countries. Furthermore, being conducted in 2006, this registry reports our management practices following the publication of the latest clinical guidelines. One striking characteristic of our patient population is the relatively young age. The mean age of patients diagnosed with ACS in our study was 55 years, and 50% of patients were <55 years old, while only 7.5% were 75 years or older. Compared to patients in Europe and North America our patients are on a decade younger.[7-9] The reason why ACS develops a decade earlier in Arabian Peninsula populations compared to Western populations is not entirely clear. Possible factors include younger population structure in developing compared to developed countries, increased prevalence of risk factors of coronary artery disease, like smoking and diabetes, at a younger age, and possibly a genetic factor in these populations that merits further investigation. A key aim of this registry was to evaluate the management of patients with ACS. Among patients with ST elevations, our reperfusion rate was 64%. This is similar to rates reported by the second Euro Heart Survey on acute coronary syndromes (EHS-ACS-II)(64%) and the GRACE registry (65%).[8] Administration of thrombolytic therapy was the reperfusion strategy of choice in the great majority of patients, with only 7% receiving primary percutaneous coronary intervention (PCI). This is in contrast to practice in Europe and North America where there has been a significant shift from thrombolytic therapy to primary PCI. This is due to the fact that most participating hospitals did not have a catheterization laboratory on site and that PCI was not available on a 24 hours basis. Although our study had a similar reperfusion rate compared to other registries, our median door to needle time was 45 minutes, a figure that is not in keeping with the guideline recommendations. In fact, only 37% received thrombolytic therapy within 30 minutes of presentation. Therefore, there is plenty of room for improvement. Only 21% of patients underwent in-hospital coronary angiography, which is markedly lower than in other registries. In EHS-ACS-II, 70.2% of patients with ST-elevation ACS and 62.9% of patients with Non-ST-elevation ACS underwent coronary angiography.[8] In the National Registry of Myocardial Infarction 4 (NRMI-4) 62.2% of patients with STEMI and 42.3% of patients with NSTEMI underwent early in-hospital cardiac catheterization.[9] Our comparatively lower rate of coronary angiography may be explained by 2 factors. The first factor is the unavailability of onsite catheterization laboratory at the participating hospitals. Studies have shown that hospitals without onsite catheterization laboratories have lower rates of coronary angiography and percutaneous coronary intervention.[11] The second factor is the fact that our registry was based on a true survey of the entire country, in each of the countries involved. This is fundamentally different from many other registries in which a cluster of hospitals or selected hospitals were studied. The 3% hospital mortality noted in this study is lower than the 4-5% reported in other

registries.[7,8] Possible explanations for this low hospital mortality include a patient population that is young with a better risk profile, and a high rate of reperfusion therapy use. Studies have demonstrated that younger patients are often more intensively treated and have lower mortality rates.[12] Therefore, the younger age of our patient population may have affected management and outcomes. The main limitation of this registry is the absence of long term follow up. Due to the lack of needed infrastructure, we felt that longer follow up would have been logistically very difficult at this stage.

In conclusion, this study has enabled us to determine the characteristics, treatments, and in-hospital outcomes of patients hospitalized with ACS in our region. We hope that this knowledge will form the basis for improving management practices and outcomes for patients with ACS in our region.

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