Disparity in ST-segment Elevation Myocardial Infarction Practices and Outcomes in Arabian Gulf Countries (Gulf COAST Registry)

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ABSTRACT

Objectives: The objective of this study is to describe contemporary management and 1-year outcomes of patients hospitalized with ST-segment elevation myocardial infarction (STEMI) in Arabian Gulf countries.

Methods: Data of patients admitted to 29 hospitals in four Gulf countries [Bahrain, Kuwait, Oman, United Arab Emirates (UA)] with the diagnosis of STEMI were analyzed from Gulf locals with acute coronary syndrome (ACS) events (Gulf COAST) registry. This was a longitudinal, observational registry of consecutive citizens, admitted with ACS from January 2012 to January 2013. Patient management and outcomes were analyzed and compared between the four countries.

Results: A total of 1039 STEMI patients were enrolled in Gulf COAST Registry. The mean age was 58 years, and there was a high prevalence of diabetes (47%). With respect to reperfusion, 10% were reperfused with primary percutaneous coronary intervention, 66% with fibrinolytic therapy and 24% were not reperfused. Only one-third of patients who received fibrinolytic therapy had a door-to-needle time of 30 min or less. The in-hospital mortality rate was 7.4%. However, we noted a significant regional variability in mortality rate (3.8%–11.9%). In adjusted analysis, patients from Oman were 4 times more likely to die in hospital as compared to patients from Kuwait.

Conclusions: In the Gulf countries, fibrinolytic therapy is the main reperfusion strategy used in STEMI patients. Most patients do not receive this therapy according to timelines outlined in recent practice guidelines. There is a significant discrepancy in outcomes between the countries. Quality improvement initiatives are needed to achieve better adherence to management guidelines and close the gap in outcomes.

Key words: Arabian Gulf, Middle East, registries, ST-segment elevation myocardial infarction

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INTRODUCTION

Patients with acute coronary syndrome (ACS) in the Arab Middle East are about a decade younger than in developed countries and have a higher prevalence of diabetes and smoking.[1] A 6-month registry, Gulf RACE, conducted in 6 countries of the Arabian Gulf in 2007 showed that the great majority of patients with ST-segment elevation myocardial infarction (STEMI) were treated with fibrinolytic therapy.[2] High in-hospital mortality of 6.2% was reported in these patients that may be related to delayed administration of fibrinolytic therapy and low rate of primary percutaneous coronary intervention (PPCI).[1] From the previous ACS studies in the region, we learned that nearly 1 in 10 eligible patients did not receive any reperfusion therapy, and this reperfusion shortfall was more common in sicker patients and those with prior stroke or no chest pain on presentation.[3]

Cardiac catheterization was used in only 20% of the patients with ACS, which is very low when compared with Western countries, and its use was more related to the availability of onsite cardiac catheterization than to risk scores of patients.[4] Furthermore, guideline adherence to the concurrent use of an antplatelet agent, an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB), a beta-blocker, and a statin in patients with ACS at discharge was suboptimal.[5] However, these studies lacked 1-year outcomes and may reflect relatively old practice.

The Gulf locals with ACS events (Gulf COAST) registry were designed to assess management and outcomes of ACS patients in the Arabian Gulf region of the Middle East. In this manuscript, we report on the management and 1-year outcomes of STEMI patients.

METHODS

Gulf COAST registry was a prospective, multinational, longitudinal, observational, cohort-based registry of consecutive citizens, from the Arabian Gulf, admitted with a diagnosis of ACS from January 2012 to January 2013. Patients were enrolled from hospitals in Bahrain, Kuwait, Oman, and the United Arab Emirates (UAE). Of the 29 participating hospitals, 14 were community hospitals, 18 nonuniversity teaching hospitals, and 1 private sector hospital. On-site cardiac catheterization was available in 9 hospitals, while another 10 had a cardiac catheterization laboratory within 1-h drive.

The detailed methodology was previously published.[6] Patients enrolled in the registry were citizens, 18 years of age or older with ACS, who gave written consent to participate. We chose to enroll citizens only and excluded expatriates. Citizens formed a more homogenous population, they were all health insured, and they constituted a more stable population which should facilitate a more complete 1-year follow-up.

Data were prospectively collected on a standardized case report form (CRF) and was entered online at www.gulfcoastregistry.org. Data variables collected were in accordance with American College of Cardiology (ACC) key data elements and definitions for measuring the clinical management and outcomes of patients with ACS[7] and included patients demographics, clinical presentation, and management and outcomes during hospital stay. Follow-up was carried out by clinic visit or telephone interview at 1, 6, and 12 months from the date of enrollment.

Data were validated by a clinical research associate, who carried out site visits to all participating hospitals with random data source verification of 10% of paper and electronic CRFs at each visit. For this report, data from patients with STEMI were analyzed.

Statistical analysis

The sample size of 4000 for the overall Gulf COAST cohort was determined based on practical as well as statistical considerations. These have been previously described and were based on the desire to ensure adequate precision in estimating all-cause mortality at 1-year assuming a mortality rate of 10% and accepting a margin of error of 1% with 95% confidence intervals (CIs).[6]

We also considered the precision around estimating 1-year mortality in the subgroup of patients with STEMI assuming that at least 20% of patients with ACS will have STEMI. These assumptions allowed us adequate precision around one-year mortality rate among patients with STEMI with at least 90% confidence and at most 2% margin of error.[8]

Continuous variables were summarized as medians and 25th/75th percentiles and compared using Wilcoxon rank-sum test. Categorical variables were summarized using proportions and were compared using Chi-square test. Relative mortality among countries was assessed using multivariate logistic regression adjusting for country, GRACE risk score, reperfusion (PPCI, Thrombolitics, or none), and medications within 24 h, and quantified with adjusted odds ratios and their 95% CIs. For all comparisons, a P < 0.05 was considered statistically significant.

RESULTS

A total of 4061 patients with ACS were enrolled in Gulf COAST registry, of whom 1039 were diagnosed with STEMI. Table 1 shows the unadjusted baseline characteristics of all patients with STEMI and of patients in each of the four participating countries. The median
age was 58 years (youngest 48; oldest 68). Less than a quarter of patients were women.

There was high prevalence of risk factors (hypertension 47%, diabetes 47%, dyslipidemia 42%, and smoking 35%). Kuwait had the highest prevalence of diabetes and smoking (53% and 56%, respectively). Bahrain had the highest prevalence of hypertension and dyslipidemia (54% and 63%, respectively). Omani patients had the lowest prevalence of all risk factors among the four countries (hypertension 47%, diabetes 47%, dyslipidemia 34%, smoking 17%, and premature family history of coronary artery disease 6%).

One-third of the patients with STEMI had obesity, with the lowest prevalence in Oman (27%) and the highest prevalence in Kuwait (41%).

Table 2 demonstrates reperfusion strategies and medications administered to STEMI patients. Nearly, three-quarters of STEMI patients received reperfusion therapy; the great majority whereby fibrinolysis. Use of PP PCI was significantly more common in the UAE and Bahrain (37% and 24%, respectively) compared to Kuwait and Oman (5% and 1%, respectively), \( P < 0.0001 \).

The median door-to-needle time exceeded the recommended 30 min by about 10 min in all four countries. Overall, only one-third of patients had a door-to-needle time of 30 min or less. Median door-to-balloon time was 51 min in Bahrain and 74 min in the UAE, with the majority of patients having a door-to-balloon time of 90 min or less.

The majority of patients received the recommended oral medications after STEMI that included aspirin, clopidogrel, statins, beta-blockers, and either an ACE-I or an ARB. There were no significant differences in the use of in-patient medications between the four countries with the exception of significantly lower use of clopidogrel in Oman compared with the 3 other countries (63% vs. 97%, \( P < 0.0001 \)).

The unadjusted in-hospital mortality rate was 7.4% and the 1-year mortality was 14.1%. Oman had the highest in-hospital (11.9%) and 1-year (21.9%) mortality rates, whereas Kuwait had the lowest rates (3.8% and 7.9%, respectively), \( P < 0.0001 \) [Table 3].

There was a significant difference in the hospital outcomes of cardiogenic shock and heart failure between the participating countries. Oman had the highest cardiogenic shock (13.8%) and heart failure (20.2%) rates. Table 4 shows mortality rates in patients with STEMI adjusted for Grace Score, reperfusion with either lysis or percutaneous coronary intervention (PCI), and medications administered during the first 24-hour. Compared to Kuwait, Oman had 4 times in-hospital
Table 2: Inpatient treatment

| Variable                        | All patients (n=1039) | Oman (n=420) | Kuwait (n=316) | UAE (n=148) | Bahrain (n=155) | P    |
|---------------------------------|-----------------------|--------------|----------------|-------------|----------------|------|
| Medications administered in the first 24 h |                       |              |                |             |                |      |
| Aspirin                         | 1030 (99)             | 418 (100)    | 311 (98)       | 146 (99)    | 155 (100)      | 0.2222|
| Clopidogrel                     | 864 (83)              | 264 (63)     | 307 (97)       | 142 (96)    | 151 (97)       | <0.0001|
| Beta blocker                    | 766 (74)              | 302 (72)     | 227 (72)       | 108 (73)    | 129 (83)       | 0.0356|
| Statin                          | 1008 (97)             | 408 (97)     | 307 (97)       | 145 (98)    | 148 (95)       | 0.6218|
| ACE inhibitor or ARB            | 804 (77)              | 323 (77)     | 229 (72)       | 120 (81)    | 132 (85)       | 0.0121|
| Medications at discharge        |                       |              |                |             |                |      |
| Aspirin                         | 887 (99)              | 339 (99)     | 284 (99)       | 133 (96)    | 131 (97)       | 0.0164|
| Clopidogrel                     | 739 (82)              | 209 (61)     | 276 (96)       | 132 (96)    | 122 (90)       | <0.0001|
| Beta blocker                    | 792 (88)              | 303 (89)     | 234 (82)       | 129 (93)    | 126 (93)       | 0.0002|
| Statin                          | 880 (98)              | 336 (99)     | 275 (96)       | 136 (99)    | 133 (99)       | 0.0306|
| ACE inhibitor or ARB            | 773 (86)              | 308 (91)     | 224 (78)       | 117 (85)    | 124 (92)       | <0.0001|
| Reperfusion therapy for STEMI   |                       |              |                |             |                |      |
| Primary PCI                     | 107 (10)              | 2 (1)        | 15 (5)         | 53 (37)     | 37 (24)        | <0.0001|
| Thrombolytic therapy            | 671 (66)              | 304 (73)     | 227 (73)       | 63 (44)     | 77 (50)        |      |
| No reperfusion                  | 244 (24)              | 109 (26)     | 68 (22)        | 28 (19)     | 39 (26)        |      |
| D2N (min), median (IQR)         | 40 (25-66)            | 41 (27-61)   | 40 (23-68)     | 41 (28-65)  | 39 (20-95)     | 0.6726|
| D2N ≤30 min                    | 255 (38)              | 103 (33)     | 90 (39)        | 29 (45)     | 33 (42)        | 0.1838|
| D2B (min), median (IQR)         | 70 (41-135)           | 110 (24-195) | 96 (68-145)    | 74 (55-125) | 51 (31-89)     | 0.8000|
| D2B ≤90 min                    | 77 (72)               | 1 (50)       | 9 (60)         | 37 (70)     | 30 (81)        | 0.5363|

All values are n (%) unless stated otherwise. ACE: Angiotensin-converting enzyme, ARB: Angiotensin receptor blocker, D2N: Door-to-needle, D2B: Door-to-balloon, IQR: Interquartile range, PCI: Percutaneous coronary intervention, STEMI: ST-segment myocardial infarction

Table 3: Unadjusted hospital outcomes and mortality

| Variable                  | All patients (n=1039) | Oman (n=420) | Kuwait (n=316) | UAE (n=148) | Bahrain (n=155) | P    |
|---------------------------|-----------------------|--------------|----------------|-------------|----------------|------|
| In-hospital outcomes      |                       |              |                |             |                |      |
| Cardiogenic shock         | 100 (9.6)             | 58 (13.8)    | 20 (6.3)       | 9 (6.1)     | 13 (8.4)       | 0.0020|
| Heart failure             | 159 (15.3)            | 85 (20.2)    | 43 (13.6)      | 17 (11.5)   | 14 (9.0)       | 0.0019|
| Stroke                    | 14 (1.3)              | 5 (1.2)      | 2 (0.6)        | 4 (2.7)     | 3 (1.9)        | 0.2910|
| Bleeding                  | 42 (4.0)              | 17 (4.1)     | 12 (3.8)       | 7 (4.7)     | 6 (3.9)        | 0.9707|
| In-hospital mortality     | 75 (7.4)              | 49 (11.9)    | 12 (3.8)       | 6 (4.1)     | 8 (5.5)        | <0.0001|
| 1 month mortality         | 86 (8.6)              | 55 (13.4)    | 15 (5.0)       | 8 (5.5)     | 8 (5.5)        | 0.0001|
| 6 months mortality        | 114 (11.9)            | 72 (19.4)    | 19 (6.3)       | 12 (8.3)    | 11 (7.9)       | <0.0001|
| 12 months mortality       | 139 (14.1)            | 87 (21.5)    | 24 (7.9)       | 13 (9.0)    | 15 (11.2)      | <0.0001|

All values are n (%) unless stated otherwise.

Table 4: Association of country with mortality among patients with ST-segment elevation myocardial infarction*

| Country                  | In-hospital mortality | 1-month mortality | 6 months mortality | 12 months mortality |
|--------------------------|-----------------------|-------------------|-------------------|--------------------|
| Oman versus Kuwait       | 4.18 (1.87-9.35)      | 3.21 (1.55-6.6)   | 3.64 (1.88-7.05)  | 3.42 (1.90-6.18)   |
| Bahrain versus Kuwait    | 1.64 (0.56-4.82)      | 1.13 (0.41-3.10)  | 1.27 (0.52-3.10)  | 1.37 (0.62-3.04)   |
| The UAE versus Kuwait     | 1.35 (0.42-4.34)      | 1.18 (0.42-3.31)  | 1.55 (0.64-3.74)  | 1.27 (0.56-2.92)   |

*The models are adjusted for GRACE risk score, reperfusion (primary PCI, thrombolytics, or none), and medications within 24 h. PCI: Percutaneous coronary intervention

Deaths (95% CI: 1.87–9.35) and about 3.5 times 1-year deaths (95% CI: 1.90–6.18).

**DISCUSSION**

The goal of Gulf COAST registry was to evaluate management, and long-term outcomes of patients with ACS admitted to hospital in the Arabian Gulf countries. Informed by our previously-conducted regional registries, we chose citizens of four Gulf countries as a homogeneous group of patients.\cite{1,8} This meant that these patients lived a relatively similar lifestyle, were comparable financially, and they all received free medical care by their governments.\cite{8}

More importantly, we were able to achieve 97% 1-year follow-up in this large cohort of all comers. The present study revealed 3 major findings as follows: (1) STEMI patients in this region have high prevalence of risk factors, including diabetes and obesity; (2) use of fibrinolytic therapy is the most common means of reperfusing patients with STEMI, but unfortunately, the timeline for its administration is not in keeping...
with guidelines recommendations; (3) there was clear difference in short- and long-term clinical outcomes between the participating countries, with Oman having the highest rates of cardiogenic shock, heart failure, in-hospital and 1-year mortality.

STEMI patients in Gulf COAST registry were slightly younger and had much higher prevalence of diabetes. Compared with published registries from Europe (Euro Heart Survey ACS III), The United States (NCDR AR-G registry), and Asia (Kerala ACS Registry in India, Korea Acute Myocardial Infarction Registry). Almost half (47%) of the STEMI patients in the Gulf had diabetes, compared to about one-third (34.6%) in Kerala and less than a quarter in Europe, the USA, and Korea (17%–24.6%). The younger age of patients in the Gulf can be mostly tied with a young population in this region, while the high incidence of diabetes in the Arab Gulf countries reflects the high rates of diabetes in the general population that is associated with high prevalence of obesity, inactivity, and inter-family marriages.

Despite the established superiority of PPCI over fibrinolytic therapy in the acute management of STEMI patients, our patients are still largely reperfused using fibrinolytic therapy. Only 10% of STEMI patients underwent PPCI in Gulf Coast compared to 54% in Europe and 83% in the United States. This may relate to fewer PCI-capable hospitals and trained interventional cardiologists in developing countries compared to the United States and Europe. Shah et al. reported that the proportion of hospitals providing PCI for STEMI in the United States increased from 25.1% in 2003 to 33.7% in 2011, with PCI rate increasing four-fold from 53.6% to 80.0% and in-hospital mortality rate decreasing. Health-care systems in our region should therefore aim at making PCI more accessible by increasing the number of PCI-capable hospitals in the region.

Another way to improve reperfusion results is to administer fibrinolysis very early, followed by timely coronary angiography in patients who cannot undergo PPCI. As fibrinolysis is the main reperfusion strategy in the Gulf, it would be expected that logistics was developed so that lytic therapy is administered in a timely fashion, in accordance with the guidelines recommendation of door-to-needle time of 30 min or less. However, this was not the case as only 40% of the patients were lysed within 30 min and the mean door-to-needle time was 38 min. Since a shorter door-to-needle time is associated with lower mortality and better-left ventricular function, the factors responsible for such delays in the Gulf should be further explored and corrected. In addition, paramedics should be trained to administer prehospital fibrinolysis.

Fortunately, there was high adherence to guidelines-recommended medical treatment that included the appropriate use of aspirin, clopidogrel, statins, beta-blockers, angiotensin-converting enzyme inhibitors, and ARBs, both in the first 24 h of hospital stay and at hospital discharge.

Our in-hospital mortality rate of 7.4% is higher than rates reported from Europe and the United States. However, this increase in mortality rate was largely driven by very high mortality rate in Oman. STEMI patients from Oman were four times more likely to die in-hospital compared to STEMI patients from Kuwait, which had the lowest mortality rate among the participating countries in this registry. This higher rate of mortality among Omani patients was also observed at one, 6 and 12 months follow-up. It is not clear why Omani patients have higher rate of mortality and also a higher rate of in-hospital cardiogenic shock and heart failure compared to other Gulf countries. The only significant differences between Omani STEMI patients and STEMI patients from other Gulf countries were that fewer Omani patients were admitted to CCU, and fewer Omani patients received clopidogrel both in-hospital and at discharge compared to patients from other Gulf countries.

CONCLUSION

Gulf COAST registry has provided us valuable insights into the management of STEMI patients in the region. Quality improvement initiatives are needed, focusing on prevention of diabetes mellitus, shifting reperfusion strategy toward PPCI, and decreasing the door-to-needle time of fibrinolytic therapy. In addition, the higher mortality and morbidity rates in Oman need to be explored further.

Limitations

Our study has a number of limitations. Although a registry of consecutive patients allows us to report on real-life STEMI management and outcomes on our population, it does not eliminate unmeasured confounding variables that may affect our comparisons. Our decision to enroll only citizens does not make this report representative of the entire population living in the area, but it has enabled us to achieve a better 1-year follow-up. The hospitals that participated in the registry were not randomly chosen, but they also represented a variety of hospital types, including university, community, private, and ministry of health hospitals. Finally, as informed consent was required, very sick patients dying shortly after presentation might have been excluded from the study.

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Conflicts of interest
The authors Zubaid, Alsheikh-Ali, AlMahmeed receive speaking honoraria from Sanofi and Boehringer Ingleheim and Astra Zeneca.

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