Regional Variability in Hospital Mortality in Patients Hospitalized with ST-Segment Elevation Myocardial Infarction: Findings from the Gulf Registry of Acute Coronary Events

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Key Words

In-hospital mortality • Acute coronary syndromes • Middle East • ST-segment elevation myocardial infarction

Abstract

Objectives: To study the short-term mortality from ST-segment elevation myocardial infarction (STEMI) in the Arabian Gulf region of the Middle East, and to examine whether these geographically and culturally related countries had similar or different outcomes. **Subjects and Methods:** The Gulf Registry of Acute Coronary Events recruited consecutive acute coronary syndrome patients from six Middle Eastern countries over a 5-month period. **Results:** Of 6,706 patients recruited, 2,626 (39%) had STEMI, and a total of 165 patients died in hospital, with a crude mortality rate of 6.3%. However, mortality rates varied geographically between 10% in Yemen, 9.6% in Oman and 3.3% in the other countries. The unadjusted odds ratio of mortality for Yemen was 3.2 (95% CI: 2.2–4.7), and 3.1 (95% CI: 1.9–4.8) for Oman, compared to other Gulf countries. Even after adjusting for age

and gender, the mortality remained significantly higher, almost double, in Oman and Yemen compared to other countries. This could be understood in the light of significant differences in a number of practice pattern variables such as reperfusion therapy, timely presentation and use of evidence-based medications. **Conclusion:** We found significant variability in STEMI mortality among Gulf Arab countries and identified areas requiring further efforts to reduce excess mortality in the region.

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Introduction

A regional analysis of the process of care and outcomes for a well-defined disease condition is important as it enables researchers to identify targets for regional quality improvement efforts and to design interventions to reduce inappropriate variations in care. Prior studies of patients with acute myocardial infarction have demonstrated marked geographical variation in patient treatment

Table 1. Variability in crude and age-adjusted STEMI mortality between different Gulf countries

	Yemen	Oman	Other Gulf countries ¹
Number of patients	779	406	1,441
Number of deaths	78	39	48
Mortality rate	10.0%	9.6%	3.3%
Crude OR	3.2 (2.2–4.7)	3.1 (1.9–4.8)	reference
Age-adjusted OR	2.2 (1.5–3.2)	2.2 (1.4–3.5)	reference
Age- and gender-adjusted OR	2.2 (1.5–3.2)	2.2 (1.4–3.4)	reference

Values in parentheses denote 95% CI.

¹ These include Bahrain, Kuwait, Qatar and the UAE.

and outcomes [1–6]. Variations in the rates of case fatality, primary percutaneous coronary intervention (PCI), diagnostic angiography and the use of evidence-based therapies have been reported both regionally and within countries. Recognition of this disparity led to a number of quality improvement projects related to the process of care [5, 6].

The World Health Organization has predicted that cardiovascular disease (CVD) will be the leading cause of mortality and morbidity in developing countries by the year 2020 [6]. The Gulf region of the Middle East is part of the developing world that has seen significant socio-economic transition over the past 40 years, leading to increase in risk factors like obesity, diabetes, hypertension and smoking [7]. As such, CVD burden in this region is expected to increase. One important aspect of combating disease in any given region is formulating unified policies and treatments that will not only reduce the impact of a disease, but will also result in the improvement or the predictability of mortality across the region. To that end we wanted to determine the mortality from ST-segment elevation myocardial infarction (STEMI) in the Gulf region of the Middle East, and to examine whether these geographically and culturally related countries had similar outcomes from treating the same disease.

Subjects and Methods

The Gulf Registry of Acute Coronary Events (Gulf RACE) is a Gulf Heart Association project. It is a prospective, multinational, multicenter survey of patients hospitalized with the final diagno-

sis of acute coronary syndrome (ACS) in six Middle Eastern Gulf countries. The participating countries were Bahrain, Kuwait, Qatar, Oman, the United Arab Emirates (UAE) and Yemen. The study received ethical approval from the institutional ethical bodies in all participating countries. The study recruited consecutive ACS patients from 64 hospitals in these countries. In Bahrain, Kuwait and Qatar, all hospitals nationwide that admit patients with ACS participated in the survey. In Oman, the UAE and Yemen, most hospitals (covering at least 85% of the population) participated in the survey. It was carried out from January 29, 2007, and continued for 5 months. The registry protocol mandated enrolment of all consecutive ACS patients and left their management and daily care to the discretion of the treating physician. Full details of the methods have been described elsewhere [7]. Briefly, diagnosis of the different types of ACS and definitions of data variables were based on the American College of Cardiology clinical data standards [8]. For this report, all those admitted to the hospitals with definite changes on the electrocardiogram indicative of acute STEMI, or new or presumed new left bundle branch block myocardial infarction were grouped as STEMI. We report here on the final 5-month phase of the registry.

Statistical Methods

The differences in patient characteristics, risk factors, in-hospital treatments and hospital outcomes between countries were assessed using the χ^2 test in case of categorical data, and the Kruskal-Wallis test in case of continuous variables. It should be noted that since countries other than Yemen and Oman had statistically similar mortality rates, we combined these countries to form three groups – Yemen, Oman and other Gulf countries – in our analysis. Logistic regression models were used to compare the in-hospital mortality among countries. Further multivariate logistic regression models were used to adjust for age as well as other confounders. We reported crude and adjusted odds ratios (OR) along with 95% confidence intervals (95% CI). Potential confounders such sociodemographic characteristics, clinical presentation at admission, risk factors, in-hospital treatments and process of care variables were compared between these countries to explain differences in mortality.

Results

A total of 2,626 STEMI patients were enrolled from 64 hospitals during the 5-month period between January and June 2007, and 165 patients died in hospital, leading to a crude mortality rate of 6.3%. Yemen (10%) and Oman (9.6%) had significantly higher crude mortality rates than other countries (3.3%). After adjusting for age, STEMI mortality between countries remained significantly different (table 1). Crude OR associated with STEMI mortality were 3.2 for Yemen and 3.1 for Oman, and the corresponding age-adjusted OR were 2.2 for both Yemen and Oman when the other four Gulf countries were taken together as the reference. These differences remained even when adjusted for both age and gender using multivariate models.

Table 2. Variability in the clinical characteristics, risk profile and time to presentation of STEMI patients admitted to hospitals in different Gulf countries

	All	Yemen	Oman	Other Gulf countries ¹	p
Total number	2,626	779	406	1,441	
Age, years	53 (16)	60 (18)	55 (18)	50 (13)	<0.001
Male gender	2,260 (86.1%)	632 (81.1%)	329 (81.2%)	1,299 (90.2%)	<0.001
Citizens ²	1,292 (49.2%)	776 (99.6%)	261 (64.3%)	297 (20.6%)	<0.001
Any past CVD history ³	680 (25.9%)	225 (28.9%)	114 (28.1%)	341 (23.7%)	0.015
Key risk factors					
Diabetes mellitus	848 (32.3%)	200 (25.7%)	124 (30.6%)	524 (30.6%)	<0.001
Hypertension	454 (17.3%)	72 (9.2%)	90 (22.2%)	292 (20.3%)	<0.001
Hyperlipidemia	355 (13.5%)	102 (13.1%)	44 (10.8%)	209 (14.9%)	0.145
Current smoker	1,322 (50.3%)	389 (49.9%)	145 (35.7%)	788 (54.7%)	<0.001
Body mass index	25.9 (5.6)	25.7 (5.5)	25.5 (5.3)	26.2 (5.7)	<0.001
Any comorbidities ⁴	220 (8.4%)	107 (13.7%)	34 (8.4%)	79 (5.5%)	<0.001
Killip class >I	535 (20.4%)	211 (27.1%)	94 (23.2%)	230 (16.0%)	<0.001
Presenting symptoms					
Ischemic chest pain	2,314 (88.2%)	653 (83.8%)	347 (85.5%)	1,314 (91.4%)	<0.001
Atypical chest pain	109 (4.2%)	47 (6.0%)	15 (3.7%)	47 (3.3%)	<0.001
Dyspnea	114 (4.3%)	55 (7.1%)	18 (4.4%)	41 (2.9%)	<0.001
Vital signs at admission					
Heart rate, bpm	83.0 (28.0)	90.0 (20.0)	80.0 (26.0)	80.0 (24.0)	<0.001
Systolic blood pressure, mm Hg	130.0 (35.0)	130.0 (40.0)	130.0 (40.0)	138.0 (36.0)	<0.001
First blood glucose, mM	8.6 (6.6)	8.1 (4.6)	8.2 (6.3)	9.0 (7.1)	<0.001
Fasting blood glucose, mM	14.4 (2.7)	13.1 (2.8)	14.0 (3.0)	14.9 (2.1)	<0.001

Values for age, body mass index and vital signs at admission are medians with interquartile ranges in parentheses.

¹ These include Bahrain, Kuwait, Qatar and the UAE. ² Citizens here indicate the locals who are citizens of the countries as Gulf countries have large expatriate populations who are noncitizens. ³ Any previous history of myocardial infarction, angina, PCI or coronary artery bypass surgery. ⁴ Comorbidities included stroke, peripheral vascular disease, chronic obstructive pulmonary disease or dialysis.

In an attempt to explain the observed differences in STEMI mortality between the countries, we evaluated the differences in age and gender, ACS risk factors, presenting symptoms and comorbidities (table 1). Patients' median ages in Yemen and Oman were 5 and 10 years higher, respectively, compared to other countries. Yemen and Oman also had a significantly higher proportion of females. Although the proportion of patients with past CVD history or any other comorbid conditions was slightly higher in Yemen and Oman, the prevalence of CVD risk factors at admission was relatively lower in these two countries. In terms of clinical presentation, almost 27% in Yemen and 23% in Oman presented with Killip class of more than I, compared to only 16% in other Gulf countries. Other clinical characteristics at admission, such as heart rate, blood pressure and glucose levels, were also different among countries.

Important aspects of hospital care like the use of thrombolytic therapy and evidence-based medications are given in table 2. Fewer patients were eligible for reperfusion therapy in Yemen and Oman due to late hospital presentation compared to other countries. In Yemen, 37% of the patients arrived at hospital within 12 h of symptom onset, compared to 78% in Oman and 84% in other Gulf countries. The reperfusion shortfall, defined as the proportion of eligible patients who did not receive reperfusion, was 18.6% in Yemen, 7.8% in Oman and 6.7% in other Gulf countries. Furthermore, for those who received thrombolytic therapy, the median door-to-needle time was 51 min in Oman, compared to 45 and 42 min in Yemen and other countries, respectively. Oman had the lowest utilization of clopidogrel and heparin, while the use of glycoprotein IIb/IIIa inhibitor was negligible in Yemen and Oman, with only 1–2% of patients receiving it compared to 13% in other countries (table 3).

Table 3. Variability in presentation times, hospital treatments and outcomes of STEMI patients stratified by country

	All	Yemen	Oman	Other Gulf countries ¹	p
Total number	2,626	779	406	1,441	
Symptom onset to presentation ≤12 h	1,799 (69.1%)	285 (36.7%)	309 (77.8%)	1,205 (84.4%)	<0.001
Thrombolysis ²	1,493 (83.1%)	222 (77.9%)	280 (90.6%)	991 (82.4%)	<0.001
Primary PCI ²	146 (8.1%)	10 (3.5%)	5 (1.6%)	131 (10.9%)	<0.001
Reperfusion shortfall ²	158 (8.8%)	53 (18.6%)	24 (7.8%)	81 (6.7%)	<0.001
Door-to-needle time ² , min	45 (41)	45 (30)	51 (69)	42 (44)	0.003
Medications					
Aspirin	2,580 (98.3%)	753 (96.8%)	400 (98.8%)	1,427 (99.0%)	<0.001
β-Blockers	1,639 (62.4%)	452 (58.1%)	231 (57.0%)	954 (66.3%)	<0.001
Statin	2,482 (91.9%)	676 (86.8%)	352 (86.7%)	1,384 (96.0%)	<0.001
ACEI/ARB	1,817 (69.3%)	577 (74.1%)	266 (65.8%)	974 (67.6%)	0.002
Clopidogrel	1,565 (59.6%)	457 (58.7%)	126 (31.0%)	982 (68.1%)	<0.001
Heparin	2,409 (91.7%)	766 (98.3%)	242 (59.6%)	1,401 (97.2%)	<0.001
GPI	199 (7.6%)	13 (1.7%)	4 (1.0%)	182 (12.7%)	<0.001
Hospital outcome					
Death	165 (6.3%)	78 (10.0%)	39 (9.6%)	48 (3.3%)	<0.001
Congestive heart failure	442 (16.8%)	137 (17.6%)	106 (26.2%)	199 (13.8%)	<0.001
Cardiogenic shock	238 (9.1%)	100 (12.8%)	52 (12.8%)	86 (6.0%)	<0.001
Reinfarction	59 (2.2%)	7 (0.9%)	12 (3.0%)	40 (2.8%)	0.010
Stroke	31 (1.2%)	13 (1.7%)	9 (2.2%)	9 (0.6%)	0.010
Major bleeding	31 (1.2%)	4 (0.5%)	9 (2.2%)	18 (1.2%)	0.033
Hospital stay, days	5 (3)	7 (4)	5 (3)	5 (3)	<0.001

Values for door-to-needle time and hospital stay are medians with interquartile ranges in parentheses. ACEI = Angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; GPI = glycoprotein IIb/IIIa inhibitor.

¹ These include Bahrain, Kuwait, Qatar and the UAE. ² Only patients eligible to receive reperfusion therapy were analyzed.

Discussion

We found significant disparity in STEMI mortality across the countries on the Arabian Gulf peninsula. Yemen and Oman had higher STEMI mortality than the other countries in the region. To our knowledge, this is the first study that reports CVD outcomes across Middle Eastern countries. Disparities in cardiovascular and other health outcomes across geographical regions have previously been reported from other parts of the world [1–5]. The higher STEMI mortality in Yemen and Oman, almost 3-fold higher in crude rates, compared to the other Gulf countries might be partly linked to the fact that they had patients who were almost 5–10 years older. It is known that hospital and 1-year mortality rates in older patients with STEMI are higher than in younger patients [9, 10]. Our analysis, nevertheless, showed that age-adjusted differences for STEMI mortality remained significantly higher in Oman and Yemen, suggesting that age differences alone could not explain the disparity in STEMI mortality.

The Gulf RACE was developed by the Gulf Heart Association to provide information about the process of care and outcomes of patients with ACS in this region of the Middle East. Because of the unique requirement of the registry protocol, mandating the coverage of at least 85% of each participating country, we have been able to study each country's STEMI mortality relating to the practice of ACS in a 'real world' setting. We found the unadjusted mortality in hospitalized STEMI patients in the Middle Eastern Gulf region to be 6.3%. This is similar to the mortality rates reported by the Global RACE study (4–7%), which evaluated about 11,543 patients from 94 hospitals in 14 countries [11–13]. However, a slightly lower crude in-hospital mortality rate than ours was reported by a recent Australian audit [14]. Since our patients were almost 10 years younger than those in the Global RACE and the Australian audit, there is a potential for further reduction in our mortality rates. On the other hand, a recent Indian registry (CREATE) that studied over 20,000 ACS patients at similar ages to those of our patient population reported higher mortality rates of 5.5–8.2% [15].

When factors related to patient care and presentation were evaluated as factors that may explain the excess mortality in Yemen and Oman, we noted several significant relationships. There was a delay in presentation to hospitals in Yemen and Oman, and consequently many patients missed the opportunity for reperfusion therapy. Furthermore, Oman and Yemen had the lowest rates of early thrombolysis and primary PCI in the region with higher rates of reperfusion shortfall. Yemen and Oman are geographically much larger than the rest of the countries in the registry, and hospital coverage for the population is much more restricted than in other Gulf countries. This might have been the reason behind the delayed hospital presentation and lower reperfusion rate. Previous studies suggest that when regional differences are detected they can be linked to higher revascularization rates and not to the baseline patient characteristics [16, 17]. Reductions in barriers to timely administration of thrombolytic therapy were previously shown to result in improved survival [18]. This is an area where appropriate health service interventions may lead to reduction in mortality [19–21].

In addition to differences in reperfusion therapy, the difference in use of evidence-based medications, particularly angiotensin-converting enzyme inhibitor/angiotensin receptor blocker and statin, may explain some of the significant excess mortality. This is important because an increased use of thrombolysis and a moderate increase in use of angiotensin-converting enzyme inhibitor has been shown to be associated with parallel reduction in age-adjusted mortality [22]. It should also be noted that the risk factor profiles as well as the clinical features at admission also differed between countries. There were more females in Yemen and Oman. Gender-related differences in early outcomes have been observed to be worse in women following acute myocardial infarction [23]. Researchers have suggested that women present late after first symptoms of myocardial infarction, which is more often unrecognized.

Several limitations of our study should be noted. The main limitation of this registry is the absence of long-term follow up. Another limitation is the lack of detailed data with respect to contraindications to medications needed to properly assess the use of medications in eligible patients. However, given that this study analyzed data from the first and possibly the largest multicountry, multicenter registry of ACS in the Middle East and captured a good proportion of consecutive patients gives utility to our data.

Conclusion

We found significant disparity in STEMI mortality in the Middle East. We also identified variability in a number of practice pattern factors such as reperfusion therapy, timely presentation and use of evidence-based medications. These findings are a cause for concern to local physicians and health care providers. These groups need to work together to establish policies that diminish ACS mortality in general and abolish the mortality disparity in these geographically and socially related countries.

Appendix

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