In-hospital complications and 1-year outcome of acute coronary syndrome in patients with hypertension: findings from the 2nd Gulf Registry of Acute Cardiac Events

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مضاعفات المتلازمة التاجية الحادة في المستشفى والحصائل بعد مضي عامٍ واحد لدى مرضى ارتفاع ضغط الدم: نتائج من السجل الخليجي الثاني للأحداث القلبية الحادة

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الخلاصة: وقد استفاد الباحثون من المعطيات في السجل الخليجي الثاني للأحداث القلبية الحادة للعامين 2008–2009 لاستقصاء المضاعفات في المستشفى والحصائل بعد مضي عام واحد من ارتفاع ضغط الدم الجهازي لدى مرضى بالمتلازمة التاجية الحادة ينتمون إلى ستة بلدان خليجية. وشملت الدراسة 7847 مريضاً تم قبولهم في المستشفيات لإصابتهم بالمتلازمة التاجية الحادة، وكان من بينهم 3746 مريضاً (47.7٪) مصاباً بارتفاع ضغط الدم. واتضح للباحثين أن ارتفاع ضغط الدم أكثر انتشاراً بين النساء منه بين الرجال، وبين العرب منه بين غير العرب في المجموعات المتقدمة بالعمر. وكان يغلب على المرضى المصابين بارتفاع ضغط الدم أن يظهر عليهم ضيق النفس مع صنف متقدم وفق تصنيف كيليب Killip، وبمعدل يزيد عما لدى غير المصابين بارتفاع ضغط الدم. ومن بين المصابين بارتفاع ضغط الدم، كان معدل الوفيات أعلى فقط عند من تم قبولهم وكان لديهم احتشاء في عضلة القلب ترافق مع ارتفاع في الوصلة ST. وبعد أن صحح الباحثون المعطيات بأخذهم المتغيرات في خط الأساس، وجدوا أن ارتفاع ضغط الدم عامل منبئ مستقل للفشل القلبي (معدل الأرجحية OR = 1.31) وللسكتة الدماغية (OR = 2.47). ولم يكن هناك فرق كبير بين معدل الوفيات لدى المصابين بالمتلازمة التاجية الحادة وارتفاع ضغط الدم عند تقسيمهم إلى شرائح بحسب الجنس والعمر والإثنية.

ABSTRACT Using data from the 2nd Gulf Registry of Acute Coronary Events (Gulf RACE-2) in 2008–09 we investigated the in-hospital complications and 1-year outcome of acute coronary syndrome (ACS) in patients with systemic hypertension from 6 Gulf countries. Of 7847 consecutive patients admitted with ACS, 3746 (47.7%) had hypertension. Hypertension was more prevalent in women, in Arabs than non-Arabs and in older age groups. Patients with hypertension were more likely than those without hypertension to present with dyspnoea and advanced Killip class. Among hypertensive patients, the mortality rate was higher only among those admitted with ST-elevation myocardial infarction. After adjustment for baseline variables, hypertension was an independent predictive factor for heart failure (OR = 1.31) and stroke (OR = 2.47). There were no significant differences in mortality in hypertensive ACS patients when stratified by sex, age or ethnicity.

Complications hospitalières et issue à un an d'un syndrome coronarien aigu chez des malades hypertendus : résultats obtenus à partir du deuxième Registre des événements coronariens aigus du Golfe

RÉSUMÉ À partir de données du deuxième Registre des événements coronariens aigus du Golfe (Gulf RACE-2), pour la période 2008 - 2009, nous avons enquêté sur les complications à l'hôpital et sur l'issue à un an d'un syndrome coronarien aigu chez des patients atteints d'hypertension artérielle systémique dans six pays du Golfe. Sur 7847 patients admis consécutivement pour un syndrome coronarien aigu, 3746 souffraient d'hypertension (47,7 %). L'hypertension était plus fortement prévalente chez les femmes, chez les patients arabes que chez les personnes d'un autre groupe ethnique et dans les tranches d'âge supérieur. Les patients hypertendus avaient une plus grande probabilité que les patients ayant une tension normale de souffrir de dyspnée et d'atteindre un stade élevé dans la classification de Killip. Chez les patients hypertendus, le taux de mortalité était plus élevé uniquement chez les patients admis pour un infarctus du myocarde avec sus-décalage du segment ST. Après ajustement des résultats en fonction des variables de référence, l'hypertension s'est révélé être un facteur prédictif indépendant de l'insuffisance cardiaque (OR = 1,31) et de l'accident vasculaire cérébral (OR = 2,47). Aucune différence significative n'a été observée dans la mortalité des patients atteints d'un syndrome coronarien aigu après stratification par sexe, par âge, ou par groupe ethnique.

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Introduction

Hypertension is widely acknowledged to increase the risk of premature cardiovascular disease, including stroke, coronary artery disease (CAD), heart failure and peripheral vascular disease [1–3]. In the INTERHEART study of patients from 52 countries, hypertension accounted for 18% of the population-attributable risk of a first myocardial infarction [2]. Furthermore, hypertension is the most common and most important risk factor for stroke and intracerebral haemorrhage and the incidence of these disease can be markedly reduced by effective antihypertension therapy [4,5]. The global prevalence of hypertension is high. It is estimated that 26% of the world adult population (972 million) had hypertension in the year 2000 [6]. In the United States, 58 to 65 million people with hypertension were reported in the National Health and Nutrition Examination Survey (NHANES) data from 1999–2000 [7]. The prevalence of hypertension was 28% and 44% in Canada and 6 European countries respectively [8].

We have recently reported a 49.4% prevalence of hypertension among patients with acute coronary syndrome (ACS) using data from the 1st Gulf Registry of Acute Coronary Events (Gulf RACE) [9]. Hypertension was not independently associated with increased risk of in-hospital mortality except in patients with ST-elevation myocardial infarction (STEMI). In the present study, using data from the 2nd Gulf RACE registry (Gulf RACE-2), we evaluated the in-hospital and 1-year outcomes of patients with ACS in relation to their hypertension status. We also evaluated the prevalence of hypertension and outcomes of these patients according to age, sex and ethnicity.

Methods

Sample

The data were collected from the Gulf RACE-2, which was a 9-month prospective, multicentre study of 7847 consecutive patients with ACS from 6 adjacent Gulf countries (Bahrain, Saudi Arabia, Qatar, Oman, United Arab Emirates and Yemen). Patients diagnosed with ACS, including unstable angina and non-ST- and ST-elevation myocardial infarction (NSTEMI and STEMI respectively), were recruited from 65 hospitals. An on-site cardiac catheterization laboratory was available in 43% of the hospitals and a coronary care unit onsite in 71% of hospitals. There were no exclusion criteria and thus all patients with ACS were enrolled.

Diagnosis of the different types of ACS and definitions of data variables were based on the American College of Cardiology clinical data standards [9]. The history of hypertension was obtained and recorded at the time of presentation. The study received ethical approval from the institutions' ethics committees in all participating countries.

Data collection

Details about the Gulf RACE methods have been published previously [10]. A case report form for each patient with suspected ACS was filled out on hospital admission by assigned physicians and/or research assistants working in each hospital using standard definitions and was completed throughout the patient's hospital stay. All forms were verified by a cardiologist then sent online to the principal coordinating centre, where the forms were further checked for mistakes before submission for final analysis. To avoid double-counting of multiple admissions to the registry, the patients' national identification numbers and an assigned registry number were used. Thus, only the second ACS admission

was included for each patient registered more than once.

Patients were divided into hypertensive and non-hypertensive groups. Systemic hypertension was defined in the current registry as: either history of hypertension diagnosed and treated with medication, diet and/or exercise; or blood pressure > 140 mmHg systolic and/or diastolic pressure > 90 mmHg on at least 2 occasions. Any history of hypertension was obtained and recorded at the time of presentation. For this study, patients were analysed according to the presence or absence of a diagnosis of hypertension.

Statistical analysis

Patients' characteristics were presented as proportions, mean and standard deviation (SD) as appropriate. Whenever possible, rates were used to describe patient populations. The frequencies of categorical variables in the 2 groups (hypertensive and non-hypertensive) were compared using the chi-squared test. Continuous variables were compared using the 2-tailed Student t-test. Variables influencing in-hospital mortality, cardiogenic shock and stroke were assessed with multiple logistic regressions after adjustment for confounders (i.e. age, sex, diabetes mellitus, hypertension, dyslipidaemia, smoking, thrombolytic therapy and khat use). Odds ratios (OR), 95% confidence interval (CI) and P-values were reported for significant predictors. A P-value < 0.05 was considered significant. All P-values were the results of 2-tailed tests. All data analyses were carried out using $SPSS$, version 14.

Results

Patients' characteristics

Gulf RACE-2 enrolled 7847 patients with ACS from 6 Gulf countries, 3746 (47.7%) of whom had hypertension. Patients with hypertension were

Table 1 Characteristics of hypertensive and normotensive patients with acute coronary syndrome

Variable	Hypertensive (n = 3746)		Normotensive (n = 4101)		P-value
Demographic data					
Age [mean (SD)] (years)	59.7	(11.7)	54.3	(12.8)	< 0.001
Male (No., %)	2239	59.8	3543	86.4	< 0.001
Arab ethnicity (No., %)	2868	76.6	2739	68.8	<0.001
Clinical history					
History of CAD (No., %)	1997	54.0	1229	30.0	< 0.001
History of heart failure (No., %)	382	10.0	140	3.0	< 0.001
Prior coronary revascularization (No., %)	708	19.0	275	6.7	< 0.001
Dyslipidaemia (No., %)	1847	49.0	742	18.0	< 0.001
Family history of CAD (No., %)	469	12.5	336	8.0	0.9
Diabetes mellitus (No., %)	2024	54.7	1089	26.9	< 0.001
Current smoking (No., %)	961	25.7	1839	44.8	< 0.001
History of renal failure (No., %)	277	7.4	39	1.0	< 0.001
History of stroke (No., %)	269	7.0	69	1.7	< 0.001
Prior aspirin use (No., %)	2133	58.5	1058	25.8	< 0.001
Prior β-blocker use (No., %)	1712	45.7	585	14.3	< 0.001
Prior ACE use (No., %)	1558	41.6	473	11.5	< 0.001
Clinical data at presentation					
Presentation within 12 h of event (No., %)	332	53	619	60.9	< 0.001
Heart rate [mean (SD)] (beats/min)	85	(20)	84	(20)	0.02
Systolic BP [mean (SD)] (mmHg)	144	(31)	128	(25)	< 0.001
Diastolic BP [mean (SD)] (mmHg)	84	(19)	78	(16)	< 0.001
BMI [mean (SD)] (kg/m²)	27.7	(6.0)	26.0	(4.8)	< 0.001
Ischemic chest pain (No., %)	2993	74.2	3489	84.4	< 0.001
Dyspnoea (No., %)	574	14.2	226	5.5	< 0.001
Killip class > I (No., %)	1052	28.0	753	18.4	< 0.001
GRACE score (No., %)					< 0.001
Low	2340	63.0	2963	73.6	
Intermediate	1048	28.0	820	20.4	
High	322	8.7	245	6.0	
LV dysfunction (No., %)					
All cases	2124	73.0	2307	74.0	0.3
Severe cases	318	11.0	237	7.7	< 0.001
Coronary angiography (No., %)	1303	34.8	1254	30.6	< 0.001
Left main stem CAD	87	6.7	58	4.6	0.02
Single-vessel CAD	324	24.8	432	34.0	< 0.001
Two-vessel CAD	297	22.7	322	25.7	0.8
Three-vessel CAD	474	36.0	293	23.0	< 0.001
Laboratory findings [mean (SD)]					
First blood sugar (mg/dL)	11	(5.8)	9.7	(5.0)	< 0.001
Fasting blood sugar (mg/dL)	7.5	(3.0)	7.0	(3.0)	< 0.001
Peak CK-MB (ng/mL)	74	(127)	122	(177)	< 0.001
First creatinine (μmol/L)	111	(91)	94	(59)	< 0.001
Total cholesterol (mg/dL)	4.7	(1.8)	4.9	(1.4)	< 0.001
HDL cholesterol (mg/dL)	1.0	(0.5)	1.0	(0.5)	0.5
LDL cholesterol (mg/dL)	3.0	(1.5)	3.2	(1.1)	< 0.001
Fasting TG (mg/dL)	1.8	(1.1)	1.7	(1.1)	0.054
First haemoglobin (g/L)	13	(2)	14	(2)	< 0.001

SD = standard deviation; CAD = coronary artery disease; ACE = angiotensin-converting enzyme; LV = left ventricular; BP = blood pressure; BMI = body mass index; GRACE = global registry of acute coronary events; CK-MB = creatine kinase MB-fraction; HDL = high-density lipoprotein; LDL = low-density lipoprotein; TG = triglycerides.

significantly older and significantly more likely to be male than those without hypertension (Table 1). The clinical history showed that patients with hypertension were significantly more likely to have comorbidities, including higher rates of diabetes, dyslipidaemia, prior history of CAD, prior congestive heart failure, chronic renal insufficiency and stroke. However, they were less likely to be current smokers (Table 1).

On presentation to hospital, hypertensive patients with ACS had higher Killip class, body mass index (BMI), heart rate and systolic and diastolic blood pressure. Patients with hypertension were more likely to present with dyspnoea and to seek medical advice early (within 12 hours of the event)

compared with non-hypertensive patients (Table 1).

Baseline serum creatinine, fasting blood sugar and first blood sugar levels were higher in patients with hypertension, whereas fasting serum triglycerides, low-density lipoprotein cholesterol and peak creatine kinase MB-fraction were higher in non-hypertensive patients.

In hypertensive patients with ACS, NSTEMI was the most frequent diagnosis (36.7%), followed by STEMI (33.0%) and unstable angina (30.0%). Among non-hypertensive patients, 56.6% had STEMI, followed by NSTEMI (24.0%) and unstable angina (19.0%) (Table 2). Overall coronary angiography was performed in 38.4% of hypertension patients and 30.6% of non-hypertensive patients. Hypertensive

patients were more likely to have 3-vessel CAD and left main stem CAD, while non-hypertensive patients more commonly had 2- and single-vessel CAD (Table 1).

In-hospital and discharge treatment

On admission, hypertensive patients were more likely to receive angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, calcium-channel blockers and beta-blockers, but less likely to receive thrombolytics, unfractionated heparin and clopidogrel when compared with non-hypertensive patients. At discharge, hypertensive patients were more likely to be prescribed calcium-channel blockers, angiotensin-receptor blockers and beta-blockers and less likely to receive clopidogrel,

Table 2 Management of hypertensive and normotensive patients with acute coronary syndrome

Variable	Hypertensive		Normotensive		*P*-value
	No.	%	No.	%	
Medication at admission					
Thrombolysis	540	46.9	1107	52.6	0.002
Aspirin	3673	98.0	4046	98.7	< 0.03
Clopidogrel	2802	74.8	3171	77.3	0.009
Heparin	1415	37.9	1824	44.5	< 0.001
Heparin (LMW)	1514	40.6	1434	35.0	< 0.001
Glycoprotein IIb/IIIa inhibitor	315	8.0	293	7.0	0.03
β-blocker	2878	76.8	2959	72.0	< 0.001
ACE inhibitor	2798	72.0	2848	69.4	0.01
Angiotensin receptor blocker	331	8.8	63	1.5	< 0.001
Primary percutaneous coronary intervention	562	22.0	574	20.0	0.1
Calcium-channel blocker	454	12.0	116	2.8	< 0.001
Medication at discharge					
Aspirin	3464	95.4	3819	95.5	0.8
Clopidogrel	2463	66.0	2845	69.5	0.01
Statin	3383	90.7	3764	91.9	0.05
β-blocker	3019	80.9	3188	77.9	0.001
ACE inhibitor	2633	70.6	2948	72.0	0.2
Angiotensin receptor blocker	408	10.9	128	3.0	< 0.001
Calcium-channel blocker	488	13.0	123	3.0	< 0.001
Diagnosis at discharge					
STEMI	1246	33.0	2326	56.6	< 0.001
NSTEMI	1374	36.7	993	24.0	
Unstable angina	1128	30.0	789	19.0	

ACE = angiotensin-converting enzyme; LMW = low molecular weight; STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction.

whereas prescription of aspirin, statin and angiotensin-converting enzyme inhibitors were comparable between the 2 groups (Table 2).

Outcomes

Compared with normotensive patients, hypertensive patients had significantly higher rates of in-hospital heart failure, recurrent myocardial ischaemia, atrial fibrillation and stroke (Table 3). Stroke was predominantly ischaemic in nature. Overall in-hospital, 1-month and 1-year mortality rates were not statistically significant different between the 2 groups. However, hypertensive patients presenting with STEMI had higher rate of in-hospital mortality in addition to higher risk of heart failure, recurrent ischaemia, re-infarction and stroke when compared with non-hypertensive patients with STEMI. Among NSTEMI patients, however, hypertensive patients had a higher risk of heart failure only, while in patients with unstable angina, hypertension was associated with increased risk of heart failure and stroke when compared with non-hypertensive patients (Table 3). Bleeding complications were comparable between the 2 groups.

Multivariate analysis

Age, female sex, hypertension, diabetes mellitus, BMI, smoking and being on thrombolytic drugs were adjusted as confounders in a multivariate analysis for predictors of in-hospital heart failure and stroke in patients with ACS. Hypertension, age, smoking, diabetes mellitus and BMI were independent risk factors for in-hospital heart failure (Table 4). Only hypertension was a significant risk factor for stroke, (OR = 2.47, 95% CI: 1.11–5.47, $P = 0.02$) (Table 4).

Hypertension: prevalence and outcome by sex, age and ethnicity

Hypertension was more prevalent among women with ACS (66.6%) than among men (38.7%) ($P < 0.001$). In the

Table 3 Clinical outcomes of hypertensive and normotensive patients

Variable	Hypertensive		Normotensive		P-value
	No.	%	No.	%	
All patients	(*n* = 4036)		(*n* =4129)		
In-hospital death	168	4.5	185	4.5	1.0
1-month death	266	8.0	297	8.2	0.7
1-year death	386	13.3	374	11.8	0.08
Heart failure	601	16.0	425	10.3	< 0.001
Recurrent ischaemia	613	16.4	601	14.7	0.04
Re-infarction	77	2.1	91	2.2	0.6
Cardiogenic shock	192	5.1	256	6.2	0.2
Major bleeding	24	0.6	22	0.5	0.5
Stroke	35	0.9	18	0.4	0.007
Haemorrhagic	(9)		(7)		
Thrombotic	(20)		(9)		
Unknown	(6)		(2)		
On ventilation	191	5.1	171	4.2	0.05
VF/VT	142	3.8	186	4.6	0.06
Atrial fibrillation	66	1.8	38	0.9	0.001
STEMI	(*n* = 1244)		(*n* = 2319)		
In-hospital death	105	8.4	141	6.1	0.008
Heart failure	229	18.4	275	11.8	< 0.001
Recurrent ischemia	278	22.3	376	16.2	< 0.001
Re-infarction	55	4.4	71	3.1	0.03
Cardiogenic shock	118	9.5	196	8.5	0.2
Stroke	21	1.7	16	0.7	0.005
On ventilation	97	7.8	119	5.1	0.001
VF/VT	69	5.7	109	4.8	0.2
NSTEMI	(*n* =1374)		(*n* = 993)		
In-hospital death	56	4.1	39	3.9	0.8
Heart failure	267	19.4	112	11.3	< 0.001
Recurrent ischemia	193	14.0	135	13.6	0.7
Re-infarction	19	1.4	19	1.9	0.3
Cardiogenic shock	68	5.0	50	5.1	0.9
Stroke	8	0.6	2	0.2	0.1
On ventilation	78	5.7	45	4.5	0.2
VF/VT	21	1.5	16	1.6	0.8
Unstable angina	(*n* = 1128)		(*n* =789)		
In-hospital death	7	0.6	5	0.6	0.9
Heart failure	105	9.3	38	4.8	< 0.001
Recurrent ischemia	142	12.6	90	11.4	0.4
Re-infarction	3	0.3	1	0.1	0.5
Cardiogenic shock	6	0.5	10	1.3	0.08
Stroke	6	0.5	0	0.0	0.04
On ventilation	16	1.4	7	0.9	0.2
VF/VT	3	0.3	5	0.6	0.2

STEMI = ST-elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; VF = ventricular fibrillation, VT = ventricular tachycardia.

Table 4 Multivariate analysis for predictors of in-hospital heart failure and stroke in patients with acute coronary syndrome

Variable	In-hospital heart failure		In-hospital stroke	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age	1.03 (1.02–1.04)	< 0.001	1.02 (0.99–1.05)	0.2
Sex	1.31 (0.97–1.76)	0.08	0.51 (0.14–1.85)	0.3
Hypertension	1.31 (1.05–1.65)	0.02	2.47 (1.11–5.47)	0.02
Dyslipidaemia	0.94 (0.73–1.22)	0.7	0.92 (0.39–1.07)	0.9
Diabetes mellitus	1.54 (1.22–1.94)	< 0.001	1.42 (0.64–3.13)	0.3
Smoking	1.35 (1.05–1.72)	0.01	1.65 (0.68–3.98)	0.3
Thrombolytic therapy	0.58 (0.46–0.73)	< 0.001	0.59 (0.27–1.30)	0.2
BMI	1.03 (1.01–1.05)	0.001	1.00 (0.93–2.17)	1.0

OR = odds ratio; CI = confidence interval; BMI = body mass index.

spectrum of ACS, women with or without hypertension had significantly higher in-hospital mortality (i.e. any death recorded during admission from time of arrival until discharge) and 1-month and 1-year mortality rates compared with men with or without hypertension (Table 5). The differences in mortality between women and men among hypertensive patients were no longer statistically significant after adjustment for age, diabetes mellitus, renal failure, BMI, smoking and hyperlipidaemia.

The prevalence of hypertension increased steadily with age, from 21.6% at age < 40 years to 59.0% at > 70 years. Mortality rates rose consistently with age among hypertensive and non-hypertensive patients with ACS, both in-hospital and during the follow-up period. When adjusted for sex and comorbidities, age was an independent predictor for in-hospital mortality in hypertensive (OR = 1.04, 95% CI: 1.03–1.06, *P* < 0.001) and non-hypertensive patients (OR = 1.06, 95% CI: 1.05–1.07, *P* < 0.001).

Hypertension was more prevalent in Middle-Eastern Arab ethnicity when compared to non-Arabs (51.2% versus 39.2%, *P* < 0.001) and more prevalent in female Arabs (66.8% versus 61.8%, *P* < 0.001). In-hospital, 1-month and 1-year mortality were higher in Arab hypertensive and non-hypertensive patients when compared with non-Arab ethnicity patients. In multivariate analysis, after adjustment for age, sex and comorbidities, Arab ethnicity was an independent predictor of in-hospital mortality (OR = 1.75, 95% CI: 1.20–2.56, *P* = 0.004) but hypertension was not a predictor of in-hospital mortality (OR = 0.84, 95% CI: 0.65–1.10, *P* = 0.21).

Discussion

The data from the Gulf RACE-2 survey provides an insight into the prevalence and impact of hypertension in a broad Middle East population presenting with ACS. In Gulf RACE-1 we reported a high prevalence of hypertension in a Middle Eastern population presenting with ACS [9]. Hypertensive patients had a higher risk of heart failure than non-hypertensive patients. The mortality rate was also higher but only in hypertensive patients presenting with STEMI. The current study extends these observations using data from Gulf RACE-2, where the prevalence of hypertension was comparable to that reported from the first registry. Furthermore, the in-hospital mortality rate was comparable between the 2 groups. We also report for the first time that this comparable mortality rats extends up to 1 year follow-up with a trend of increased mortality among hypertensive patients. Patients with hypertension had a higher risk of heart failure complications regardless of the ACS subtype. Hypertension patients also had higher risk of recurrent myocardial infarction and the development of atrial fibrillation. We also report for the first time that among hypertensive Middle-Eastern patients presenting with ACS hypertension was the only independent risk factor for stroke, which was primarily ischaemic in nature. Moreover, stroke risk appeared to be most prominent among STEMI patients.

The literature on the effect of hypertension on short- and long-term mortality is conflicting; many studies have claimed a deleterious effect of hypertension in ACS with an increasing risk of death [11–13] while others, including the current study and Gulf RACE-1, failed to show this [6–9,11–19]. Other investigators reported better outcomes in hypertensive patients presenting with ACS [20,21]. These conflicting results might be due to the complex impact of hypertension on ACS and the differences in patients' baseline characteristics such as age, sex and ethnicity as well as therapy among these various studies. Hypertension is well known to be associated with other morbidities, such as diabetes mellitus, dyslipidaemia, obesity and previous CAD, that might collectively contribute to a deterioration in prognosis [13,20,22]. Moreover, left ventricular hypertrophy, heart failure and arrhythmia are known to be induced by hypertension [13,20,22]. However, some characteristics of hypertensive patients might attenuate the

Table 5 Mortality in hospital and at 1-month and 1-year follow-up among hypertensive and normotensive patients with acute coronary syndrome by sex, age and ethnicity

Variable	In-hospital mortality				1-month mortality				1-year mortality			
	Hypertensive		Normotensive		Hypertensive		Normotensive		Hypertensive		Normotensive	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Sex												
Female	63/1107	5.7	48/558	8.6	99/1001	9.9	64/505	12.7	147/881	16.7	79/449	17.6
Male	105/2639	4.0	137/3543	3.9	167/2327	7.2	233/3119	7.5	139/2023	11.8	295/2714	10.9
P-value	0.02		0.008		< 0.01		< 0.001		< 0.001		< 0.001	
Age group (years)												
≤40	4/145	2.8	8/531	1.5	5/129	3.9	21/471	4.5	6/106	5.7	22/411	5.4
41–70	113/2968	3.8	125/3143	4.0	184/2633	6.9	209/2757	7.6	261/2294	11.4	261/2398	10.9
≥71	51/633	8.1	52/427	12.2	77/566	13.6	67/396	16.9	119/504	23.6	91/354	27.7
P-value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	
Ethnicity												
Arab	144	5.0	165	6.0	234	9.1	269	10.8	342	15.1	339	15.3
Non-Arab	24	2.7	20	1.5	32	4.2	28	2.5	44	6.8	35	3.7
P-value	0.004		< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

adverse factors in ACS, including smaller infarction sizes [23], better coronary artery perfusion in the presence of higher diastolic pressure, a well-developed collateral circulation in the setting of greater severity of coronary atherosclerosis and previous treatment with cardioprotective drugs [20]. This hypothesis of a balance between exacerbating and attenuating factors was clearly evident in Gulf RACE-2. Hypertensive patients were older, more often female and were more likely to have diabetes, dyslipidaemia, higher BMI and prior CAD. On the other hand, hypertensive patients were more likely to be on aspirin and beta-blockers prior to admission. Hypertensive patients also were more likely to receive recommended medications at admission including beta-blockers, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers. NSTEMI was the predominant presentation in hypertensive patients and peak creatine kinase MB-fraction was lower, which supports the smaller infarction size, while in non-hypertension, STEMI occurred in almost half of patients.

The higher mortality rate of hypertensive patients with STEMI in our study is supported by many similar studies including our previous study in Gulf RACE-1 [9,23]. It seems that the deleterious effect of hypertension became more evident when the infarction size was large, resulting in higher recurrent ischaemia, heart failure and stroke, which in turn led in a higher risk of death.

Several factors may explain the higher risk of heart failure among hypertensive patients presenting with ACS. Diastolic dysfunction, due to hypertrophic and interstitial changes in chronic hypertension, ventricular remodelling and greater activation of neurohormonal systems (both in the early post-infarction period and several months later) [24], plus the higher incidence of diabetes mellitus in hypertensive patients, each independently and collectively enhance the risk of heart failure [25]. Nevertheless, heart failure is a major predictor of mortality in ACS [26] and the higher mortality in our study was limited to hypertensive patients with STEMI only. Although severe left ventricular dysfunction (systolic dysfunction) was higher among hypertensive patients compared with non-hypertensive patients in our study group, the overall prevalence of left ventricular dysfunction was comparable between the 2 groups, suggesting that a significant proportion of heart failure in hypertension may be attributed to diastolic dysfunction.

We found a higher incidence of stroke in hypertensive patients with ACS, which is unsurprising given that hypertension and acute myocardial infarction are independently associated with higher risk of stroke

Table 6 Mortality among hypertensive and normotensive patients with acute coronary syndrome, unadjusted and adjusted to age and comorbidities by sex, age and ethnicity

Variable	OR (95% CI)	
	Unadjusted	Adjusted
Sex		
In-hospital mortality	1.78 (1.42–2.23)	1.80 (1.42–2.85)
1-month mortality	1.54 (1.27–1.86)	1.57 (1.30–1.91)
1-year mortality	1.63 (1.38–1.93)	1.59 (1.34–1.89)
Age		
In-hospital mortality	1.05 (1.04–1.06)	1.05 (1.04–1.06)
1-month mortality	1.04 (1.03–1.05)	1.05 (1.03–1.05)
1-year mortality	1.05 (1.04–1.06)	1.05 (1.04–1.06)
Ethnicity		
In-hospital mortality	2.92 (2.13–4.0 0)	2.94 (2.13–4.05)
1-month mortality	3.38 (2.58–4.41)	3.42 (2.61–4.51)
1-year mortality	3.41 (2.69–4.33)	3.40 (2.67–4.32)

OR = odds ratio; CI = confidence interval.

[27]. Ischaemic stroke was the main type in our registry, which means that atherosclerosis or embolic events are the likely causes, not thrombolytic therapy. Additionally we observed a higher prevalence of atrial fibrillation among hypertensive patients, which may be related to left atrial enlargement and the poor left ventricular function due to heart failure, both of which can make the heart the source of embolic stroke in hypertension patients with ACS. These findings emphasize the need for awareness of the risk of stroke by physicians treating hypertension in ACS patients.

Finally, the prevalence of hypertension in women presenting with ACS was higher than in men. The high prevalence of hypertension among Middle Eastern women was also reported in Gulf RACE-1 (70% versus 43%) [28]. Furthermore, the overall mortality rate was higher among women compared with men. This may be attributed to multiple factors including late and atypical presentations, less medication prescribed and a higher incidence of heart failure in women than men, as was reported by other investigators [29].

Some limitations of the study can be noted. Our data were collected from an observational study and the fundamental limitations of observational studies cannot be eliminated because of their non-randomized nature and unmeasured confounding factors. However, well-designed observational studies provide valid results and do not systematically overestimate the results compared with the results of randomized controlled trials. Finally, although long-term follow-up was reported, this was limited to mortality rates only and data about compliance with medical therapy in addition to the risk of other cardiovascular complications including recurrent myocardial ischaemia, infarction and heart failure were lacking.

Conclusions

Hypertension is highly prevalent among Middle-Eastern patients presenting with ACS particularly in women, older age groups and among Middle-Eastern Arab ethnicity. Hypertension was independently associated with increased risk of heart failure and stroke. In cases of STEMI, hypertension was associated with a higher risk of in-hospital mortality and stroke.

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