

# Does prior coronary artery bypass surgery alter the gender gap in patients presenting with acute coronary syndrome? A 20-year retrospective cohort study

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## ABSTRACT

**Objectives:** Previous studies demonstrated women presenting with acute coronary syndrome (ACS) have poor outcomes when compared with men 'the gender gap phenomenon'. The impact of prior coronary artery bypass graft (CABG) on women presenting with ACS is unknown. We hypothesised that the gender gap is altered in ACS patients with prior CABG. The aim of this study was to evaluate patients presenting with ACS according to their gender and history of prior CABG.

**Design:** Retrospective, observational (cohort) study.

**Setting:** Data were collected from hospital-based registry of patients hospitalised with ACS in Doha, Qatar, from 1991 through 2010. The data were analysed according to their gender and history of prior CABG.

**Participants:** A total of 16 750 consecutive patients with ACS were studied. In total, 693 (4.3%) patients had prior CABG; among them 125 (18%) patients were women.

**Primary and secondary outcome measures:** Comparisons of clinical characteristics, in-hospital treatment, and outcomes, including in-hospital mortality and stroke were made.

**Results:** Women with or without prior CABG were older, less likely to be smokers, but more likely to have diabetes mellitus (DM), hypertension and renal impairment than men ( $p=0.001$ ). Women were less likely to receive reperfusion and early invasive therapies. When compared with men, women without prior CABG carried higher in-hospital mortality (11% vs 4.9%;  $p=0.001$ ) and stroke rates (0.9% vs 0.3%;  $p=0.001$ ). Female gender was independent predictor of poor outcome. Among prior CABG patients, despite the fact that women had worse baseline characteristics and were less likely to receive evidence-based therapy, there were no significant differences in mortality or stroke rates between the two groups.

**Conclusions:** Consistent with the world literature, women presenting with ACS and without prior CABG had higher death rates compared with men. Patients with prior CABG had comparable death rates regardless of the gender status.

## ARTICLE SUMMARY

### Article focus

- Robust association between women presenting with acute coronary syndrome (ACS) and worse outcome when compared with men.
- We explored whether prior history of coronary artery bypass graft (CABG) alter the 'gender gap' among patients presenting with ACS.

### Key messages

- Women presenting with ACS were older and had worse clinical profile when compared with men. Women were less likely treated with evidence-based therapies and less likely to undergo invasive procedures when compared with men. Female gender was independent predictor of poor outcome.
- Women without prior CABG had significantly higher death rates when compared with men, while among patients with prior CABG there were no significant differences in death rates according to gender and hence the 'gender gap' is altered among prior CABG patients.

### Strengths and limitations of this study

- This is the first study that evaluates the outcome of patients presenting with ACS according to gender and prior CABG history and involves a large cohort of patients over a 20-year period.
- The relatively smaller number of prior CABG patients is a limitation of this study. This study was constrained by the limitations that inherent to all historical studies of observational design. However, well-designed retrospective observational studies may provide valid results without systematic overestimation, bias or predilection. Finally, we focused on the in-hospital outcomes and detailed surgical and long-term data are not available.

## INTRODUCTION

At present, the awareness of cardiovascular diseases as the leading cause of death in women has increased.<sup>1</sup> We and others have previously shown that women developing

acute coronary syndrome (ACS) are usually 10 years older and more likely to have cardiovascular risk factors such as diabetes mellitus (DM), hypertension and hyperlipidaemia when compared with men.<sup>2-4</sup> In general, women were less likely to be appropriately treated with evidence-based therapy and had poor outcome. The available data are conflicting with regard to whether female gender is independent predictor of poor outcome or not. Despite the benefit of coronary artery bypass grafting (CABG) in reducing morbidity and mortality, women had higher death rates when compared with men. Data on the prognostic impact of prior CABG in patients presenting with ACS are conflicting, while some investigators suggested prior CABG as an independent risk factor for mortality in patients with ACS,<sup>5 6</sup> while others reported an equal or even more favourable prognosis when compared with non-CABG ACS patients.<sup>7 8</sup> This issue is further complicated by the fact that, patients with prior CABG were often underrepresented in ACS clinical trials and data on the impact of prior CABG in patients presenting with ACS according to gender is lacking. We sought to evaluate the impact prior CABG on the outcome of ACS patients according to gender using data from a 20-year registry in a Middle-eastern country. We hypothesised that the gender gap is altered in ACS patients with prior CABG.

## METHODS

This study is based at Hamad General Hospital in Doha, which provides medical and surgical care for all population of Qatar. The Cardiology and Cardiovascular Surgery Database were analysed after approval by the Medical Review Board and Ethics Committee. A case report form with a specific registration identification number for each admitted patient with cardiac illnesses was filled out by the assigned physician who followed the patient throughout hospital stay and completed before discharge. The collected clinical records have been coded and registered at the cardiology department since January 1991.<sup>9</sup> With the described database, all patients presenting with ACS whom hospitalised in the 20-year period between January 1991 and end of 2010 were retrospectively identified. We categorised our study cohort (n=16 750) on the basis of prior bypass surgery into two groups and then each group was subdivided according to gender. Accordingly data were analysed and compared for clinical characteristics, treatment and in-hospital outcomes.

Standard definitions were used to diagnose ACS. Formerly acute myocardial infarction (AMI) was defined according to the WHO criteria for Q-wave and non-Q-wave MI. Then, ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI) were defined by a positive serial troponin-T blood test result ( $\geq 0.1$  ng/ml) in the setting of symptoms and electrocardiographic changes consistent with MI. Unstable angina was diagnosed if

the patient had a negative cardiac biomarker and any one of the following characteristics: new-onset angina (<2 months) of at least class III according to the Canadian Cardiovascular Society, prolonged (>20 min) angina at rest, recent (<2 months) worsening of angina pectoris or angina that occurred within 2 weeks of an AMI.

## Statistical analysis

Patients' characteristics are presented in percentages for categorical variables and in mean $\pm$ SD for continuous variables. The frequencies of categorical variables in the two populations (prior CABG and no prior CABG) were compared using the  $\chi^2$  test and continuous variables were compared using the two-tailed Student's t test. Variables influencing in-hospital mortality were assessed with multiple logistic regressions enter method. OR, 95% CI and p values were reported for significant predictors. A p value of less than 0.05 was considered statistical significant. All p values were the results of two-tailed tests. All data analyses were carried out using the Statistical Package for Social Sciences V.18.0 (SPSS Inc).

## RESULTS

A total of 16 750 consecutive patients were admitted with ACS between January 1991 and the end of year 2010. In total, 693 patients (4.31%) had prior CABG; 568 (82%) were men and 125 (18%) were women. Among patients without prior CABG (16 057 patients); 13 648(85%) were men and 2409 (15%) were women.

### Baseline clinical characteristics

Women were older than men (with CABG, mean age 65 $\pm$ 9.9 vs 59.4 $\pm$ 10.6 years; without CABG, mean age 61.6 $\pm$ 12 vs 52.4 $\pm$ 11 years; both p=0.001; [table 1](#)). The body mass index (BMI) mean values showed no significant variation between men and women with prior CABG (27 $\pm$ 4.6 vs 28.4 $\pm$ 5; p=0.17) whereas, women without prior CABG had higher BMI mean when compared with men (30 $\pm$ 10 vs 27.6 $\pm$ 15; p=0.001).

Study of different population ethnicity showed Middle Eastern women were more represented in our cohort with prior bypass surgery than South Asian or other ethnicities (80.4% vs 9.8% vs 9.8%, respectively; p=0.001) and women without prior CABG (76.3% vs 13.1% vs 10.6%, respectively; p=0.001). Subanalysis of age revealed women with or without prior CABG were significantly older than their male counterpart in all ethnicities (p=0.001), except for Middle Eastern with prior CABG, where no significant differences were observed (64.5 $\pm$ 9 vs 63.4 $\pm$ 11 years; p=0.38).

When compared with men, women were less likely to be current smokers (with CABG, 1.6% vs 25.1%; without CABG, 3.7% vs 39.1%; both p=0.001) and had more adverse baseline characteristics. Women were more likely to have hypertension (with CABG, 82.9% vs 55.8%; without CABG, 67.3% vs 35.7%; both p=0.001), DM (with CABG, 87% vs 54%; without CABG, 64.6% vs

**Table 1** Gender variations in baseline demographics, clinical characteristics and outcomes of 16057 patients with ACS

Variable	Prior CABG (n=693)			No prior CABG (n=16057)		
	Men	Women	p Value	Men	Women	p Value
Number of patients (%)	568 (82)	125 (18)		13648 (85)	2409 (15)	
Patient characteristics at admission (%)						
Age in year (mean±SD)	59.4±10.6	65±9.9	0.001	52.4±11	61.6±12	0.001
Body mass index (kg/m <sup>2</sup> ) (mean±SD)	27±4.6	28.4±5	0.17	27.6±15	30±10	0.001
Ethnicity (%)						
Middle Eastern	50	80.4	0.001	36	76.3	0.001
South Asians	40.9	9.8		50.6	13.1	
Others	9.1	9.8		13.4	10.6	
Age in different ethnicities (mean±SD)						
Middle Eastern	63.4±11	64.5±9	0.38	57.3±13	62.9±11.6	0.001
South Asians	54.3±8	59.4±7	0.04	48.9±8	55.8±10	0.001
Others	60±10	78±9	0.001	52.5±11	60±14	0.001
Cardiovascular risk factors (%)						
Current smoker	25.1	1.6	0.001	39.1	3.7	0.001
Hypertension*	55.8	82.9	0.001	35.7	67.3	0.001
Diabetes mellitus†	54	87	0.001	36.7	64.6	0.001
Chronic renal impairment	7	13	0.03	2.6	6.3	0.001
Hyperlipidaemia‡	26.8	26	0.85	19.9	27.2	0.001
Prior cardiovascular disease (%)						
Prior myocardial infarction	17.5	17.9	0.93	6.9	6.8	0.77
Prior heart failure	13.9	17.9	0.25	6.5	14	0.001
Prior or current atrial fibrillation	1.9	3.3	0.36	1.3	4	0.001
In-hospital therapy (%)						
Rate of thrombolysis§	10	3.3	0.02	32.2	12	0.001
Percutaneous coronary intervention	5.4	3.3	0.31	11.1	7.9	0.001
Peak CK-MB (mean±SD)	101±430	85±251	0.65	160±649	242±772	0.001
Left ventricular ejection fraction (%)						
Normal: LVEF of ≥55%	14.4	18.4	0.60	18.2	29.9	0.001
Mild: LVEF of 40%–54%	40.5	44.7		47.4	45.4	
Moderate: LVEF of 30%–39%	25.5	26.3		21.7	15.2	
Severe: LVEF of <30%	19.6	10.5		12.7	9.5	
Hospital days (mean±SD)						
CCU stay	3.4±2	3.7±3	0.59	2.9±2	3.2±2.2	0.001
Total hospital stay	5.5±4.5	7.5±7	0.004	4.8±3	5.5±4	0.001
In hospital outcome (%)						
Death	5.6	3.3	0.28	4.9	11	0.001
Stroke	0.4	0	0.51	0.3	0.9	0.001

Data are expressed in percentage of patients unless otherwise indicated.

\*Systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg or current antihypertensive treatment.

†Patient had been informed of the diagnosis by a physician before admission and for type 1 or 2 diabetes.

‡Total cholesterol >5.2 mmol/l or current use of lipid-lowering agent.

§Of patients eligible for thrombolysis (ST-elevation myocardial infarction (previously known Q-wave MI) or new or presumed left bundle branch block).

ACS, acute coronary syndrome; CABG, coronary artery bypass graft; CCU, coronary care unit; CK-MB, creatine kinase-MB; LVEF, Left ventricular ejection fraction.

36.7%; both p=0.001) and chronic renal impairment (with CABG, 13% vs 7%, p=0.03; without CABG, 6.3% vs 2.6%, p=0.001). Dyslipidemia was significantly more evident in women than men without prior CABG (27.2% vs 19.9%; p=0.001), but there were no significant differences between men and women with prior CABG (26.8% vs 26%; p=0.85). In addition, there were no differences between the various groups with regard to history of MI regardless of their history of prior CABG (with CABG, 17.9% vs 17.5%, p=0.93; without CABG, 6.8 vs 6.9, p=0.77). Prior CHF tended to be more prevalent among women without CABG when compared with men

(14% vs 6.5%; p=0.001); likewise, prior or current history of atrial fibrillation were more prevalent among women without history of previous bypass surgery when compared with men (4% vs 6.3%; p=0.001).

### Inhospital management

Fibrinolytic therapy was the primary reperfusion strategy used in STEMI patients in our registry. Women were less likely to receive thrombolysis than men (with CABG, 3.3% vs 10%, p=0.02; without CABG, 12% vs 32.2%; p=0.001). While percutaneous coronary intervention (PCI) as early invasive therapeutic mode for ACS was

significantly less frequently offered to women than men without prior CABG (7.9% vs 11.1%; p=0.001), there were no significant gender differences in early PCI therapy use among patients with prior CABG (5.4% vs 3.3%; p=0.31).

In women without prior CABG, the predischARGE left ventricular ejection fraction (LVEF) was more frequently normal (29.9% vs 18.2%; p=0.001). On the other hand, men without prior CABG had significantly higher frequency of depressed LVEF (<55%) than women (mild LV dysfunction: LVEF of 40–54%, 47.4% vs 45.4%; moderate LV dysfunction: LVEF of 30–39%, 21.7% vs 15.2%; severe LV dysfunction: LVEF<30%, 12.7% vs 9.5%; respectively, for all p=0.001). However, there was no significant gender variation in LV function, in terms of different LVEF% values among patients with a history of prior CABG (p=0.60).

During hospitalisation, the comparison of total days of stay (including coronary care unit (CCU) and step-down ward days) showed a significantly longer stay in women than in men (with CABG, mean 7.5±7 vs 5.5±4.5 days; without CABG, mean 5.5±4 vs 4.8±3 days; both p=0.001). Likewise, CCU days of stay was longer in women without a history of prior CABG (mean 3.2±2.2 vs 2.9±2 days; p=0.001), while there was no significant gender difference in patients with a history of prior CABG (mean 3.4±2 vs 3.7±3 days; p=0.59). Women without prior CABG had higher mean values of peak creatine kinase-MB (242±772 vs 160±649; p=0.001). But, there was no significant gender variation among patients with CABG (CK-MB; 101±430 vs 85±251; p=0.65).

**Medications prescribed**

Among ACS patients with prior CABG (table 2), medications used before admission showed women were more likely to be on aspirin ((84% vs 73%; p=0.007) and calcium channel blockers (CCB), (17.1% vs 8.8%; p=0.006); however, there were no significant variations

between men and women with regard to ACE inhibitors/angiotensin receptor blockers (ARB), (20.7% vs 21.1%; p=0.91), β-blockers (28.2% vs 22.8%; p=0.22) and clopidogrel use (20.5% vs 23.6%; p=0.45). Likewise, during hospital admission, there were no significant differences between men and women in the medications provided, including, aspirin (90.5% vs 91.9%; p=0.64), clopidogrel (33% vs 31.7%; p=0.78), β-blockers (43.2% vs 35%; p=0.09), CCBs (16.1% vs 22%; p=0.12), ACE inhibitors/ARBs (37.5% vs 30.9%; p=0.16), glycoprotein IIb/IIIa inhibitors (4% vs 4.9%; p=0.67) and low-molecular-weight heparin (enoxaparin) (21.1% vs 21.1%; p=0.98), yet women with prior CABG were less likely prescribed unfractionated heparin (23.6% vs 33%; p=0.04). While at discharge, there was no significant difference in treatment with aspirin (84.9% vs 91.1%; p=0.08), clopidogrel (35.1% vs 28.5%; p=0.16), β-blockers (28.6% vs 28.5%; p=0.98) and ACE inhibitors/ARBs (42.1% vs 43.1%; p=0.84), yet women with prior CABG were more likely prescribed CCBs than men (36.6% vs 19.5%; p=0.001).

**Outcome**

A significantly higher inhospital death rates were observed in women without history of prior CABG compared to men (11% vs 4.9%; p=0.001) (figure 1); likewise, stroke as a complication showed higher rates in women (0.9% vs 0.3%; p=0.001). However, in patients with history of prior CABG, no significant gender variations were observed in both inhospital mortality (5.6% vs 3.3%; p=0.28) and stroke rates (0.4% vs 0.0%; p=0.51; figure 2).

**Multiple logistic regression analysis**

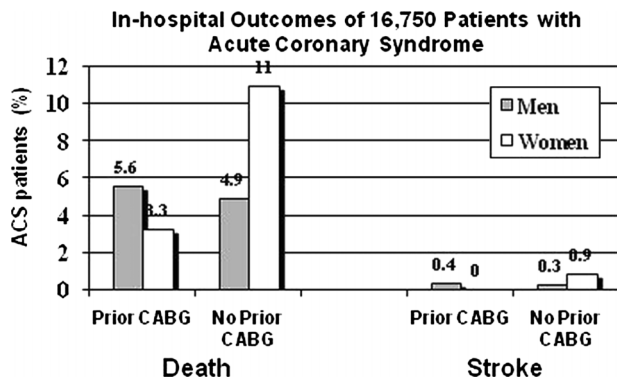
The multivariate analysis for predictors of mortality following adjustment of other variables revealed that female gender was an independent predictor of mortality in patients presenting with ACS. History of CABG was associated with reduction in inhospital mortality (OR 0.69,

**Table 2** Medication received before, during admission and at discharge in men and women with ACS and prior CABG

Medications (%)	Before admission			During admission			At discharge		
	Prior CABG (n=693)			Prior CABG (n=693)			Prior CABG (n=693)		
	Men	Women	p Value	Men	Women	p Value	Men	Women	p Value
Aspirin	73	84	0.007	90.5	91.9	0.64	84.9	91.1	0.08
Clopidogrel	20.5	23.6	0.45	33	31.7	0.78	35.1	28.5	0.16
B blockers	28.2	22.8	0.22	43.2	35	0.09	28.6	28.5	0.98
CCBs	8.8	17.1	0.006	16.1	22	0.12	19.5	36.6	0.001
ACE inhibitors/ARBs	20.7	21.1	0.91	37.5	30.9	0.16	42.1	43.1	0.84
HMG-CoA reductase inhibitor	–	–	–	–	–	–	57.4	66.7	0.06
GPIIb/IIIa inhibitors				4	4.9	0.67			
Unfractionated heparin				33	23.6	0.04			
LMWH (enoxaparin)				21.1	21.1	0.98			

Data are expressed in percentage of patients; ACE, angiotension converting enzyme inhibitor; ACS, acute coronary syndrome; ARB, angiotensin receptor blocker; CABG, coronary artery bypass graft; CCB, calcium channel blockers; HMG-CoA, hydroxy methyl glutaryl-coenzyme A; GPIIb/IIIa, glycoprotein IIb/IIIa; LMWH, low-molecular-weight heparin.





**Figure 1** Inhospital outcomes of death and stroke in men and women with ACS according to their history of prior CABG. CABG, coronary artery bypass graft; ACS, acute coronary syndrome.

95% CI 0.48 to 0.98). Likewise, aspirin use on admissions was associated with reduction in death rates in patients with a history of prior CABG (OR 0.24, 95% CI 0.11 to 0.55) and without history of prior CABG (OR 0.19, 95% CI 0.17 to 0.23). On the other hand, chronic renal impairment was a predictor of higher mortality in ACS without history of prior CABG (OR 0.76, 95% CI 1.32 to 2.34). Moreover, age and the presence of DM were consistently associated with higher in-hospital mortality in patients with history of prior CABG (age, OR 1.06, 95% CI 0.002 to 1.10; DM OR 2.54, 95% CI 1.10 to 5.85) and in patients without history of CABG as well (age, OR 1.04, 95% CI 1.03 to 1.05; DM, OR 1.50, 95% CI 1.30 to 1.74; table 3).

**DISCUSSION**

The major findings from this 20-year ACS registry are: (1) Women presenting with ACS *regardless* history of

prior CABG were older and more likely to have worse baseline clinical characteristics including higher prevalence of DM, hypertension and hyperlipidaemia. (2) Among patients without history of prior CABG, female gender was independent risk factor for in-hospital death. (3) To the best of our knowledge we report for the first time that women with prior CABG had comparable in-hospital outcome to men despite the fact that they were older and had worse baseline clinical characteristics, which suggests a role of prior CABG history in the alteration of the ‘gender gap phenomenon’.

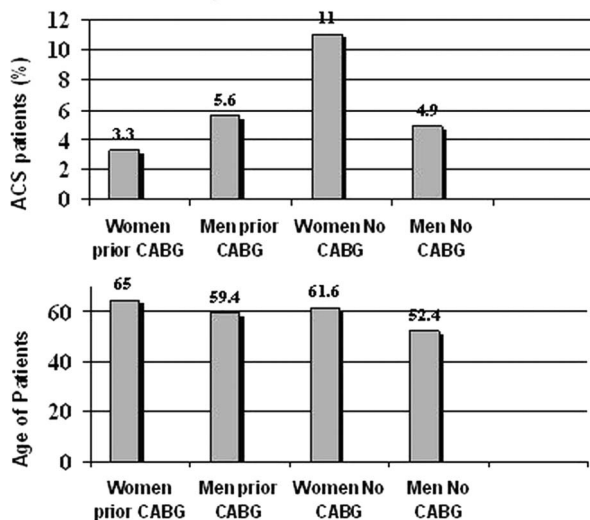
**Outcomes of women versus men with ACS**

We and other investigators have demonstrated that when compared with men, women presenting with ACS were older, less likely smoker and more likely to have worse cardiovascular risk profile including an increased prevalence of DM, hypertension and chronic renal impairment (table 4).<sup>2-4</sup> Women were also consistently shown to be less treated with evidence-based therapies than men<sup>10 11</sup> including reperfusion therapy.<sup>12 13</sup> The current study reports findings consistent with these observations. This discrepancy in treatment may be attributed to several factors including, the tendency to present late and even at presentation, there is a delay in administering treatment when compared to men.<sup>14</sup> Furthermore, women when compared with similarly aged men with ACS were also consistently shown to have worse outcomes including higher risk of heart failure, cardiogenic shock, recurrent myocardial ischaemia and death.<sup>15</sup> Conflicting data were reported for the explanation of this worse outcome; while some investigators reported female gender to be independent predictor of poor outcome, others attributed this worse outcome to older age, variations in cardiovascular risk profile and therapy provided.<sup>16</sup> The current study suggests that female gender to be an independent predictor of worse outcome. Likewise, data from the Global Use of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-1) and International Study of Infarct Survival (ISIS-3) trials found that female gender appeared to be an independent predictor of mortality after AMI.<sup>17 18</sup> It should be noted that women are more likely to have ACS but without obstructive coronary artery disease due to endothelial dysfunction, microvascular disease or coronary artery spasm than men.<sup>2 3</sup>

**Outcomes of women versus men with revascularisation**

In fact, much of what we have learned about the gender gap in patients with coronary artery disease has been gained from studies of patients undergoing coronary revascularisation with PCI and/or CABG, which were done over the past three decades. These reports demonstrated that women were older than men, less aggressively treated and undergoing less invasive procedures, which is consistent with the current study. Women who underwent either PCI or CABG also had worse outcome when compared with men. Gender differences in benefit from an early invasive

**In-hospital Mortality and Ages of 16,750 Patients with ACS According to Gender and CABG Status**



**Figure 2** (A) Inhospital mortality and (B) ages in men and women with ACS according to their history of prior CABG. CABG, coronary artery bypass graft; ACS, acute coronary syndrome.

**Table 3** Multivariate analysis of predictors of in-hospital mortality in ACS patients with or without history of prior CABG

Variables	All patients with ACS			ACS patients with prior CABG			ACS patients without prior CABG		
	OR	95% CI	p Value	OR	95% CI	p Value	OR	95% CI	p Value
Gender male	0.69	0.59 to 0.82	0.001	2.18	0.71 to 6.63	0.17	0.67	0.56 to 0.79	0.001
Age	1.04	1.03 to 1.05	0.001	1.06	0.02 to 1.10	0.003	1.04	1.03 to 1.05	0.001
Current smoking	0.77	0.64 to 0.91	0.003	1.45	0.60 to 3.48	0.40	0.75	0.63 to 0.90	0.002
Diabetes mellitus	1.52	1.32 to 1.76	0.001	2.54	1.10 to 5.85	0.03	1.50	1.30 to 1.74	0.001
Hypertension	0.63	0.55 to 0.74	0.001	0.55	0.26 to 1.15	0.11	0.64	0.54 to 0.74	0.001
Chronic renal impairment	1.65	1.25 to 2.18	0.001	0.54	0.12 to 2.42	0.42	1.76	1.32 to 2.34	0.001
Aspirin	0.19	0.17 to 0.23	0.001	0.24	0.11 to 0.55	0.001	0.19	0.17 to 0.23	0.001
Prior CABG	0.69	0.48 to 0.98	0.04						

ACS, acute coronary syndrome; CABG, coronary artery bypass graft.

strategy have been debated and data are conflicting for performing PCI in ACS patients. While, it is clear, that the gender gap in mortality is narrowed in patients undergoing PCI with high-risk ACS,<sup>19</sup> STEMI<sup>20</sup> and cardiogenic shock complicating AMI,<sup>21</sup> there are differences in the benefit of early PCI among low-risk NSTEMI patients according to gender. More recently, data from the Treat angina with Aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis In Myocardial Infarction 18 trial (TACTICS-TIMI 18)<sup>19</sup> indicated a beneficial effect of early intervention for death or MI in both men and women. Supporting the results of TACTICS-TIMI 18 a more recent meta-analysis of randomised clinical trials, comparing an early invasive with a conservative treatment strategy in patients with NSTEMI and unstable angina, found that men and high-risk women benefit from an early invasive strategy.<sup>11</sup>

In patients undergoing CABG, women had higher death rates when compared with men and this has been consistently observed over the last three decades, despite improvements in myocardial protection strategies and advances in surgical technique.<sup>22</sup> Studies have suggested that women may be referred for CABG less often than men, and possibly later in the course of disease. The referral bias may have contributed to higher mortality.<sup>23</sup> In addition, female gender was also considered as an independent predictor of early morbidity and mortality in the perioperative period, with increased risk for death.<sup>24</sup>

In general, most of the differences in outcomes following revascularisation had been attributed to the older age in women, comorbidity and to the underlying gender differences in clinical, angiographic and procedural factors. Whether gender per se is inherently a predictor of worse outcome, in both PCI-treated and CABG-treated patients, yet, a matter of ongoing debate and merits further studies. Hence, it might be predicted that women who had prior CABG and presenting with ACS may have worse outcome when compared with men.

**Outcomes of women versus men with prior CABG and presenting with ACS**

To the best of our knowledge the current study is the first that evaluate the association between prior CABG

and presentation with ACS and then to report alteration in the ‘gender gap’. Consistent with current understanding women who presented with ACS were older and had worse cardiovascular risk profile regardless of their history of prior CABG. Despite the worse clinical profile, women had similar outcome when compared with men, and hence the ‘gender gap’ is altered in patients with prior CABG.

It is known that CABG in certain patients’ subsets improves long-term outcome, mainly by reducing death rates. It might be hypothesised that the current study suggests this benefit is augmented among these higher risk patients ‘women’ at the time of ACS. Finally, although our understanding of the gender gap in outcomes following CABG has increased, but a clear concept of how CABG may ameliorate the worse outcomes of female in comparison with male gender as observed in this study, yet need to be further defined.

**Study limitation**

Although the current study is the first study to evaluate the impact of prior CABG on outcome of patients presenting with ACS according to gender, the relatively smaller number of prior CABG patients is a limitation. This study was constrained by the limitations that are inherent to all historical studies of observational design. However, well-designed retrospective observational studies may provide valid results without systematic over-estimation, bias or predilection. An other limitation of the study which is significantly lower number of women when compared with men in the current study; this may be attributed to the fact that the population of Qatar, which has a population of around 1 810 000 according to 2012 Qatar Statistics Authority, more than two-third of the population are male expatriates. Finally, we focused on the in-hospital outcomes and detailed surgical and long-term data are not available.

**CONCLUSION**

Despite the significant improvements in the management of patients presenting with the ACS, death rates among women continued to be high when compared

**Table 4** Comparison studies of death rates in women versus men in patients presenting with acute coronary syndrome

Author	Country	Name of study	Type of ACS	Women		Men		Intervention used	Mortality (women vs men)	Comment
				N (%)	Age	N (%)	Age			
Kudenchuk <i>et al</i> <sup>25</sup>	USA	MITI Registry	1996 AMI	246 (22%)	65±11	851 (78%)	59±11	Fibrinolysis	In-hospital mortality in women was almost twice that for men (OR 1.95, 95% CI 1.01 to 3.8)	AMI in women is not as aggressively treated, and results in less favourable outcome than in men
Sawaya <i>et al</i> <sup>26</sup>	Lebanon	The Lebanese MI Study	1999 AMI	99 (22.8%)	–	334 (77.2%)	–	NA	Mortality 16.2% vs 8.1% (p<0.037)	Women with AMI had significant higher mortality than men
Gottlieb <i>et al</i> <sup>27</sup>	Israel	The Prospective Nationwide Surveys	2000 AMI	742 (26%)	68.7±10.6	2125 (74%)	61±12.4	Fibrinolysis versus PCI	30-day mortality: 17.6% vs 9.6% (p<0.0001) 30-day-to-1-year mortality: 9.1% vs 5.6% (HR 1.18, 95% CI 0.84 to 1.66)	Women significantly do worse than men at 30 days but not thereafter at 1 year
Barakat <i>et al</i> <sup>28</sup>	UK	Hospital-based Prospective study	2000 AMI	463 (26.7%)	69 (61–76)	1274 (73.3%)	61 (53–69)	Fibrinolysis	Survival at 30 days 78.4% (95% CI 74.4% to 81.9%) for women vs 88.0% (86.1% to 89.7%) for men	Failure to treat women as vigorously as men made significant contribution to worse outcome
Zubaid <i>et al</i> <sup>29</sup>	Kuwait	–	2001 AMI	89 (25%)	61±9.8	267 (75%)	56±12.6	Fibrinolysis	In-hospital mortality: 21% vs 11% (p<0.02)	Higher mortality in women<70 while no difference in women and men >70
Lagerqvist <i>et al</i> <sup>30</sup>	Sweden	FRISC II Trial	2001 ACS	749 (30.4%)	68±8	1708 (69.6%)	64±10	Early invasive versus non-invasive strategy	No difference in MI or death at 1 year among women in invasive versus non-invasive (12.4% vs 10.5%), in contrast to favourable effect of invasive strategy in men (9.6% vs 15.8%, p<0.001). Interaction analysis of invasive strategy (p=.008)	Mortality benefit with early intervention in men but not in women
Trappolini <i>et al</i> <sup>31</sup>	Italy	–	2002 AMI	225 (26%)	71.6	653 (74%)	62.3	Fibrinolysis	In-hospital mortality: 24.4% vs 13.2% (p<0.0001)	Mortality higher in women who had not received fibrinolysis

Continued

Table 4 Continued

Author	Country	Name of study	Year	Type of ACS		Women		Men		Intervention used	Mortality (women vs men)	Comment
				ACS	ACS	N (%)	Age	N (%)	Age			
Glaser <i>et al</i> <sup>19</sup>	North America and Europe	TACTICS-TIMI 18 Trial	2002	ACS	757 (34%)	64.3 (11.5)	1463 (66%)	60.5 (11.5)	Early invasive versus non-invasive strategy	At 6 months, women had 28% odds reduction in Death /MI/rehospitalisation with an early invasive strategy (adjusted OR, 0.72; 95% CI 0.47 to 1.11), similar benefit in men (adjusted OR, 0.64; 95% CI 0.47 to 0.88; p=0.60 for sex interaction)	Mortality benefit of early intervention in both men and women	
Chang <i>et al</i> <sup>32</sup>	Canada	Population-based Study	2003	AMI and UA	10569 (34%)	AMI:73 UA: 71	20839 (66%)	AMI: 64 UA: 65	–	5-year mortality: AMI: 38.5% vs 26.6% (p<0.001); UA: 21.6% vs 19.5% (p=0.09)	Relative to UA, AMI has a more serious impact on women than men	
Al Suwaidi <i>et al</i> <sup>2</sup>	Qatar	–	2004	AMI	451 (28.2%)	62.1 (11.5)	1147 (71.8%)	59.9 (12.6)	Fibrinolysis	In-hospital mortality: 24% vs 13.9% (p=0.02)	After adjustment, women not independent predictor of higher mortality	
Clayton <i>et al</i> <sup>33</sup>	England and Scotland	RITA 3 Trial	2004	NSTE-ACS	682 (37.6%)	63.3 (9.9)	1128 (62.4%)	61.8 (10.5)	Early invasive versus non-invasive strategy	At 1 year men benefit more from invasive strategy for death or non-fatal MI (adjusted OR 0.63, 95% CI 0.41 to 0.98 for men and 1.79, 95% CI 0.95 to 3.35 for women; interaction p value=0.007)	Mortality benefit with early intervention in men not women	
Blomkalns <i>et al</i> <sup>34</sup>	USA	CRUSADE Trial	2005	NSTE-ACS	14552 (41%)	73.0 (61.0, 82.0)	21323 (59%)	65 (54, 76)	PCI	In-hospital mortality: 5.6% vs 4.3% (unadjusted OR 1.27; adjusted OR 1.01 95% CI 0.90 to 1.13)	Women treated less aggressively, despite their higher risk characteristics	
Heer <i>et al</i> <sup>35</sup>	Germany	The ACS Registry	2006	NSTEMI	2168 (34.1%)	–	4190 (65.9%)	–	Fibrinolysis versus PCI	In-hospital mortality: 21% vs 12% (p<0.06)	No difference in age-adjusted mortality	

Continued



Table 4 Continued

Author	Country	Name of study	Year	Type of ACS		Women		Men		Intervention used	Mortality (women vs men)	Comment
				ACS	STEMI	N (%)	Age	N (%)	Age			
Srichaiveth <i>et al</i> <sup>6</sup>	Thailand	A Multicenter Study	2007	STEMI		1223 (31.9%)	67.5±12	2613 (68.1%)	59.7±12.4	Fibrinolysis versus PCI	In-hospital mortality: Unadjusted: 23.6% vs 13.9% (p<0.001); adjusted OR, 95% CI 1.03 (0.80 to 1.33), p=0.814	Women had a higher risk for in-hospital morbidity and mortality than men
Alfredson <i>et al</i> <sup>12</sup>	Sweden	RIKS-HIA Registry	2007	NSTE-ACS		19761 (37%)	73 (11)	34020 (63%)	69 (12)	Different medical and revascularisation methods	In-hospital mortality: 5% vs 7% (NS; OR 1.03; 95% CI 0.94 to 1.13), 30-day mortality: 7% vs 9% (NS; OR 1.07; 95% CI 0.99 to 1.15, 1-year mortality: significant higher in men 16% vs 19% (OR 1.12; 95% CI 1.06 to 1.19)	Women less intensively treated and had better long-term outcomes after adjustment for background characteristics
O'Donoghue <i>et al</i> <sup>11</sup>	International Clinical Trials	Meta-analysis of randomised trials	2008	NSTE-ACS		3075 (30.2%)	64.1	7075 (69.8%)	61.3	Invasive versus conservative strategy	1 year composite of death, MI, or ACS for invasive versus conservative strategy in women OR 0.81 (95% CI 0.65 to 1.01; 21.1% vs 25.0%) and in men 0.73 (95% CI 0.55 to 0.98; 21.2% vs 26.3%), gender heterogeneity (p for interaction=0.26)	Invasive strategy has comparable reduction in composite of death, MI or ACS re-hospitalisation in men and high-risk women
Berger <i>et al</i> <sup>16</sup>	International Clinical Trials	International, randomised ACS clinical trials	2009	ACS		38048 (28%)	68 (60–75)	98199 (72%)	60 (51-69)	Respect to trial	30-day mortality: 9.6% vs 5.3% (OR, 1.91; 95% CI 1.83 to 2.00). NS adjusted mortality (adjusted OR, 1.06; 95% CI 0.99 to 1.15). Sex by type of ACS interaction (p<0.001)	Sex-based differences existed in 30-day mortality and vary depending on clinical presentation

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Table 4 Continued

Author	Country	Name of study	Type of ACS	Women		Men		Intervention used	Mortality (women vs men)	Comment
				N (%)	Age	N (%)	Age			
El-Menyar <i>et al</i> <sup>8</sup>	Gulf Countries (Middle East)	Gulf RACE Registry	2009 ACS	1983 (24%)	62 (17)	6183 (76%)	53 (16)	Fibrinolysis versus PCI	In-hospital mortality: 14% vs 5% (p<0.001) persist after adjusting for all confounders (OR 1.76, 95% CI 1.1 to 2.8; p<0.01).	Women present with higher risk factors and they independently predict poor STEMI outcomes
Dey <i>et al</i> <sup>87</sup>	USA	GRACE Trial	2009 ACS	7638 (28.5%)	–	19117 (715%)	–	PCI	Mortality of advanced disease (4% vs 3%, p<0.01). Adjusted outcomes of death, MI, stroke and re-hospitalisation at 6-months more in women (OR 1.24, 95% CI 1.14 to 1.34)	Women with advanced disease had a higher risk of death. At 6-months, women more likely to have adverse outcomes compared to men
Hvelplund <i>et al</i> <sup>88</sup>	Denmark	The Danish Heart Registry	2010 ACS	9561 (36.8%)	71.1 (12.7)	16406 (63.2%)	65.1 (12.6)	Coronary angio. and revascularisation	60-day death rate using the Kaplan-Meier estimator, averaging the estimated survival for both genders to a 70-year-old person was NS (p=0.32)	Women approached less aggressively by invasive and interventional therapy even after adjustment of co-morbidity and significant stenoses
Mehta <i>et al</i> <sup>89</sup>	International Clinical Trials	GUSTO I&III; ASSENT 2&3; HERO-2 and GUSTO-lib	2011 STEMI	25385 (25.5%)	With bleeding: 71 (63,77) without bleeding: 68 (59,75)	73994 (74.5%)	With bleeding: 65 (56,73) without bleeding: 59 (50,68)	Fibrinolysis, With or without bleeding	Adjusted 1-year mortality: was similar (without bleeding; HR 1.08, 95% CI 0.97 to 1.19) but lower With bleeding; HR 0.85, 95% CI 0.73 to 0.98, interactive p for gender by bleeding=0.0016)	Fibrinolytic-treated STEMI women had a higher incidence but lower mortality with bleeding than men
Alfredsson <i>et al</i> <sup>40</sup>	Sweden	SWEDE HEART Registry	2011 NSTEMI-ACS	14819 (32%)	Invasive: 66 ±9.7 non-invasive: 70.3±8.4	31636 (68%)	Invasive: 63.5 ±9.7 non-invasive: 68±9.3	Invasive versus non-invasive strategy	1 year mortality of invasive: 3.1 vs 2.8; p=0.61; non-invasive strategy: 13.2 vs 12.9; p=0.61	Men and women are similar and better outcome with invasive strategy

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Table 4 Continued

Author	Country	Name of study	Year	Type of ACS	Women N (%)	Age	Men N (%)	Age	Intervention used	Mortality (women vs men)	Comment
Poon <i>et al</i> <sup>f</sup>	Canada	ACSI, ACSII, GRACE/GRACE2, and CANRACE prospective multicenter registries	2012	NSTE-ACS	4874 (34%)	Varied with registries	9322 (66%)	Varied with registries	Different medical and revascularisation methods	In-hospital mortality higher in female (adjusted odds ratio 1.26, 95% CI 1.02 to 1.56, p=0.036)	Female gender was independently associated with higher in-hospital mortality, irrespective of age

AMI, acute myocardial infarction; ACS, acute coronary syndrome; NS: non significant; PCI, percutaneous coronary intervention; STE-MI, ST segment elevation myocardial infarction; UA, unstable angina.

with men. Women with or without prior CABG were older and had a higher risk profile than men. The gender gap observed after CABG in term of outcomes might be altered in favour of women. Yet women with prior CABG need to be more represented in studies for better understanding of these findings.

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