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, inhospital treatment, and outcomes, including inhospital 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 inhospital 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 inhospital 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.1 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. 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, while others reported an equal or even more favourable prognosis when compared with non-CABG ACS patients. 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 of 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. 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 inhospital 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 (≥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 means±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 inhospital 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±9.9 vs 59.4±10.6 years; without CABG, mean age 61.6±12 vs 52.4±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±4.6 vs 28.4±5; p=0.17) whereas, women without prior CABG had higher BMI mean when compared with men (30±10 vs 27.6±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±9 vs 63.4±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
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).

### In hospital 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

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**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) | 0.001 | 13648 (85) | 2409 (15) | 0.001 |
| 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/m²) (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 | 0.001 | 50.6 | 13.1 | 0.001 |
| Others | 9.1 | 9.8 | 0.001 | 13.4 | 10.6 | 0.001 |
| 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 | 3 | 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 | 0.47 | 47.4 | 45.4 | 0.001 |
| Moderate: LVEF of 30%–39% | 25.5 | 26.3 | 0.21 | 21.7 | 15.2 | 0.001 |
| Severe: LVEF of <30% | 19.6 | 10.5 | 0.12 | 12.7 | 9.5 | 0.001 |
| Hospital days (mean±SD) | | | | | | |
| CCU stay | 3.4±2 | 3.7±3 | 0.59 | 2.9±2 | 3.2±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 | 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, creatinine kinase-MB; LVEF, Left ventricular ejection fraction.
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 3.4±2 vs 3.7±3 days; p=0.59). Women without prior CABG had higher mean values of peak creatine kinase-MB ±2 vs 3.7±3 days; p=0.59). Women without prior CABG had significantly higher frequency of depressed LVEF (<55%) than women (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, 0.47–0.95; p=0.025) and in inhospital death rates (OR 0.69, 0.47–0.95; p=0.025). However, 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).

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 | –   | –    | –      | –   | –    | –     | –   | –    | –      |
| GPIIb/IIIa inhibitors | 4   | 4.9  | 0.67   | –   | –    | –     | 57.4| 66.7 | 0.06   |
| 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, angiotension 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.
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 inhospital 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 of 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 inhospital death. (3) To the best of our knowledge we report for the first time that women with prior CABG had comparable inhospital 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). Women were also consistently shown to be less treated with evidence-based therapies than men including reperfusion therapy. 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. 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. 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. 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. 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.

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
strategy have been debated and data are conflicting for preforming PCI in ACS patients. While, it is clear, that the gender gap in mortality is narrowed in patients undergoing PCI with high-risk ACS,19 STEMI20 and cardiogenic shock complicating AMI,21 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)19 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.11

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.22 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.23 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.24

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 overestimation, 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...
| Author          | Country | Name of study                  | Type of ACS | Year | Women N (%) | Age | Men N (%) | Age | Intervention used       | Mortality (women vs men) | Comment                                                                 |
|-----------------|---------|--------------------------------|-------------|------|--------------|-----|-----------|-----|-------------------------|--------------------------|-------------------------------------------------------------------------|
| Kudenchuk et al | USA     | MITI Registry                  | AMI         | 1996 | 246 (22%)    | 65±11| 851 (78%) | 59±11| Fibrinolysis             | In-hospital mortality     | AMI in women was almost twice that for men (OR 1.95, 95% CI 1.01 to 3.8) |
| Sawaya et al    | Lebanon | The Lebanese MI Study         | AMI         | 1999 | 99 (22.8%)   | –   | 334 (77.2%) | –   | NA                      | Mortality 16.2% vs 8.1%  | Women with AMI had significant higher mortality than men               |
| Gottlieb et al  | Israel  | The Prospective Nationwide Surveys | AMI | 2000 | 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) |
| Barakat et al   | UK      | Hospital-based Prospective study | AMI | 2000 | 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 |
| Zubaid et al    | Kuwait  | –                              | AMI         | 2001 | 89 (25%)     | 61±9.8 | 267 (78%) | 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 et al| Sweden  | FRISC II Trial                 | ACS         | 2001 | 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=0.008) Mortality benefit with early intervention in men but not in women |
| Trappolini et al| Italy   | –                              | AMI         | 2002 | 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
| Author          | Country                  | Name of study            | Year | Type of ACS | Women N (%) | Age (Mean ± SD) | Men N (%) | Age (Mean ± SD) | Intervention used | Mortality (women vs men) | Comment |
|-----------------|--------------------------|--------------------------|------|-------------|--------------|----------------|------------|----------------|----------------------|--------------------------|----------|
| Glaser et al    | North America and Europe | TACTICS-TIMI 18 Trial    | 2002 | ACS         | 757 (34%)    | 64.3 (11.5)    | 1463 (66%)  | 60.5 (11.5)    | Early invasive vs 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 et al     | Canada                   | Population-based Study   | 2003 | AMI and UA  | 10569 (34%)  | AMI: 73 (66%)   | 20839 (66%) | AMI: 64 (66%) | –                    | 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 et al| 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 et al   | 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 vs 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 et al | 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 et al      | Germany                  | The ACS Registry         | 2006 | NSTEMI      | 2168 (34.1%) | –              | 4190 (65.9%) | –              | Fibrinolysis vs PCI | In-hospital mortality: 21% vs 12% (p<0.06) | No difference in age-adjusted mortality |

Continued
| Author            | Country      | Name of study                  | Year ACS | Type of ACS | Women N (%) | Women Age | Men N (%) | Men Age | Intervention used | Mortality (women vs men) | Comment                                                                                                                                 |
|-------------------|--------------|--------------------------------|----------|-------------|--------------|------------|------------|---------|-------------------|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| Srichaiveth et al | 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 et al   | 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 et al  | International Clinical Trials | Meta-analysis of randomised trials | 2008 NSTE-ACS | 3075 (30.2%) | 64.1 (30.2%) | 7075 (69.8%) |           |         | 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 et al      | 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 |

Continued
| Author          | Country            | Name of study          | Year of ACS | Type of ACS | Women N (%) | Age | Men N (%) | Age | Intervention used | Mortality (women vs men) | Comment |
|-----------------|--------------------|------------------------|-------------|-------------|-------------|-----|-----------|-----|-------------------|--------------------------|---------|
| El-Menyar et al | 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 et al       | 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 et al | 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 et al     | 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 et al| Sweden             | SWEDHEART Registry     | 2011 | NSTE-ACS | 14819 (32%) | Invasive: 66 ±8.7 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 |

Continued
Female gender was associated with higher in-hospital mortality, with adjusted odds ratio 1.26 (95% CI 1.02 to 1.56, p=0.036).

Different medical and revascularisation methods varied with registries.

Table 4 continued

| Author | Country | Name of study | Year of study | Type of ACS | Year of ACS | ACS1/ACSII, and/or CANRACE registries | Comment |
|--------|---------|---------------|---------------|-------------|-------------|-------------------------------------|---------|
| Poon et al2 | Canada | 2012 INSTE-ACS, 4874 | 92/22 | Varied with registries | (66%) | Multicenter | Variation with registries |
| Al Suwaidi J, Velianou JL, Berger PB, et al. | 2001 | Primary percutaneous coronary interventions in patients with acute myocardial infarction and prior coronary artery bypass grafting. Am Heart J 2001;142:452–6. |
| Al-Aqeedi R, Asaad N, Al-Qahtani A, et al. | 2004 | Acute coronary syndrome in patients with prior coronary artery bypass surgery: observations from a 20-year registry in a middle-eastern country. PLoS One 2012;7:e40571. |
| Anand SS, Xie CC, Mehta S, et al. | 2005 | Differences in the management and prognosis of women and men who suffer from acute coronary syndromes. J Am Coll Cardiol 2005;46:1845–51. |
| O’Doherty M, Boden WE, Braunwald E, et al. | 2005 | Early invasive vs conservative treatment strategies in women and men with unstable angina and non-ST-segment elevation myocardial infarction. A meta-analysis. JAMA 2006;300:71–80. |
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