Gender differences in patients presenting with non-ST segment elevation myocardial infarction in the STAR registry

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Abstract

Background: In most acute coronary artery (ACS) related literature, the female gender constitutes a smaller proportion. This study is based on gender-specific data in the Saudi Acute Myocardial Infarction Registry Program (STARS-1 Program). A prospective multicenter study, conducted with patients diagnosed with ACS in 50 participating hospitals.

Results: In total, 762 (34.12%) patients were diagnosed with non-ST segment elevation myocardial infarction. Of this group, only 164 (21.52%) were women. The mean age (64.52 ± 12.56 years) was older and the mean body mass index (BMI) was higher (30.58 ± 6.23). A significantly proportion was diabetic or hypertensive; however, a smaller proportion was smoking. Hyperlipidemia was present in 48%. The history of angina/MI/stroke and revascularization was similar, except for renal impairment. The presentation was atypical as only 70% presented with chest pain, and the rest with shortness of breath or epigastric pain. At presentation, the female group were more tachycardiac, had higher blood pressure, and a higher incidence of being in class 1-111 Killip heart failure. Only 32% had a normal systolic function, and the majority had either mild or moderate systolic dysfunction. In particular, the rate of percutaneous coronary intervention was similar. The in-hospital mortality was similar (5%), with more women diagnosed with atrial fibrillation and heart failure at follow-up.

Conclusions: Women had a higher prevalence of risk factors affecting the presentation and morbidity but not mortality. Improving these risk factors and the lifestyle is a priority to improve the outcome and decrease morbidity.

Keywords: Gender, NSTEMI, STAR registry

Background

Gender differences in scientific publications have always been a concern. Such differences may adversely affect the clinical features, management, and most importantly, the outcome [1]. Exploring gender-related data might positively affect the prognosis. A continuous focus on gender differences is important as it improves our understanding [1]. Saudi Arabia, as a developing country, faced the same challenge and this work presents a detailed analysis of data from 50 centers across the country [2]. The data was extracted from secondary and tertiary hospitals and from different healthcare sectors, including hospitals with and without a catheter laboratory.

Methods

The STAR is a prospective study of all patients presenting with acute coronary syndrome (ACS) to an emergency department at 50 hospitals across Saudi Arabia. The details of the study have been described previously [2].

The design was a prospective, multi-center, recruited all consecutive AMI (STEMI or NSTEMI) admissions. All relevant data were gathered at admission, 1-month and 1-year follow-up.
Table 1 Epidemiological data and presentation characteristics of NSTEMI patients by gender

| Variable                        | Male (N = 598 (78.48%)) | Female (N = 164 (21.52%)) | Total (N = 762) | P value |
|---------------------------------|--------------------------|---------------------------|-----------------|---------|
| Age                             | 56.68 ± 13.30            | 64.52 ± 12.56             | 58.37 ± 13.53   | <.001   |
| Male                            | N = 598                  | Female                    | Total           |         |
| N                               | 78.48%                   | 21.52%                    | 100%            | P value |
| Saudi                           | 322 (53.85%)             | 137 (83.54%)              | 459 (60.24%)    | <.001   |
| Ethnicity                       | 435                      | 513                        | 948             |         |
| Arab                            | 427 (71.40%)             | 155 (94.51%)              | 582 (76.38%)    | <.001   |
| South Asian                     | 152 (25.42%)             | 8 (4.88%)                 | 160 (21.00%)    | 0.008   |
| Others                          | 19 (3.18%)               | 1 (0.61%)                 | 20 (2.62%)      | 0.013   |
| BMI                             | 28.58 ± 5.33             | 30.58 ± 6.23              | 29.01 ± 5.59    | <.001   |
| History of angina               | 202 (33.78%)             | 68 (41.46%)               | 270 (35.43%)    | 0.068   |
| History of MI                   | 139 (23.24%)             | 36 (21.95%)               | 175 (22.97%)    | 0.727   |
| History of MI angina            | 241 (40.30%)             | 74 (45.12%)               | 315 (41.34%)    | 0.267   |
| History of PCI                  | 109 (18.23%)             | 30 (18.29%)               | 139 (18.24%)    | 0.985   |
| History of CABG                 | 32 (5.35%)               | 8 (4.88%)                 | 40 (5.25%)      | 0.810   |
| History of heart failure        | 54 (9.03%)               | 25 (15.24%)               | 79 (10.37%)     | 0.021   |
| History of stroke               | 30 (5.02%)               | 11 (6.71%)                | 41 (5.38%)      | 0.395   |
| History of chronic renal failure| 49 (8.19%)               | 24 (14.63%)               | 73 (9.58%)      | 0.013   |
| DM                              | 334 (55.85%)             | 132 (80.49%)              | 466 (61.15%)    | <.001   |
| HTN                             | 355 (59.36%)             | 140 (85.37%)              | 495 (64.96%)    | <.001   |
| Hypercholesterolemia            | 245 (40.97%)             | 79 (48.17%)               | 324 (42.52%)    | 0.098   |
| Current/ex-smoking              | 343 (57.36%)             | 8 (4.88%)                 | 351 (46.06%)    | <.001   |
| Chief complaint                 | Chest pain               | 507 (84.78%)              | 117 (71.34%)    | 624 (81.89%) |
|                                 | SOB/fatigue              | 58 (9.70%)                | 33 (20.12%)     | 91 (11.94%)  |
|                                 | Epigastric/shoulder/back/neck pain | 21 (3.51%)             | 10 (6.10%)     | 31 (4.07%)  |
|                                 | Cardiac arrest            | 2 (0.33%)                 | 1 (0.61%)       | 3 (0.39%)  |
|                                 | Others                    | 10 (1.67%)                | 3 (1.83%)       | 13 (1.71%) |
|                                 | First medical contact     | 163 (27.26%)              | 27 (16.46%)     | 190 (24.93%) |
|                                 | Visited emergency department | 142 (87.12%)          | 25 (92.59%)    | 167 (87.89%) |
|                                 | Clinic doctor             | 27 (16.56%)               | 4 (14.81%)      | 31 (16.32%) |
|                                 | Visited a pharmacy        | 3 (1.84%)                 | 1 (3.70%)       | 4 (2.11%)  |
|                                 | Transferred by Saudi Red Crescent | 15 (2.51%)            | 7 (4.27%)      | 22 (2.89%)  |
|                                 | HR (bpm) upon arrival     | 84.01 ± 19.36             | 91.64 ± 18.94   | 85.65 ± 19.51 |
|                                 | SBP (mm Hg) upon arrival  | 135.8 ± 25.56             | 144.3 ± 30.82   | 137.6 ± 26.99 |
|                                 | HR > 100 bpm              | 93 (15.55%)               | 42 (25.61%)     | 135 (17.72%) |
|                                 | SBP < 90 mm Hg            | 8 (1.34%)                 | 3 (1.83%)       | 11 (1.44%)  |
|                                 | Cardiac arrest upon arrival | 7 (1.17%)           | 1 (0.61%)       | 8 (1.05%)  |
|                                 | CHF Killip class          | Class I                   | 507 (84.78%)    | 109 (66.46%) |
|                                 |                           | Class II/III              | 84 (14.05%)     | 53 (32.32%) |
|                                 |                           | IV                        | 7 (1.17%)       | 2 (1.22%)  |
|                                 | Echo options              | Normal LV systolic function (EF > 50%) | 237 (43.33%) | 53 (35.33%) |
|                                 |                           |                           | 290 (41.61%)    | 0.025    |
The recruiting hospitals were both the one who had catheterization laboratory or not and included various health sectors in Saudi Arabia.

This study aimed to see the difference in the management strategy and the outcome of treatment among male and female patients. This snap shot of two groups will assess if temporal changes in AMI care between genders that were noted among different societies in different studies.

**Results**

In total, 762 (34.12%) patients were diagnosed with non-ST segment elevation myocardial infarction. Of this group, only 164 (22.52%) were women. The mean age of the group (64.52 ± 12.56 years) was older than the male group and the mean body mass index (BMI) was higher (30.58 ± 6.23). A significantly higher proportion of the female group was diabetic or hypertensive; however, a smaller proportion was smoking. Hyperlipidemia was not significant between the two groups, although present in almost half (48%) of the female group. The history of angina/MI/stroke and revascularization was similar, except for renal impairment. The presentation was atypical compared to the male group as only 70% presented with chest pain, and the rest with shortness of breath or epigastric pain. At presentation, the female group were more tachycardiac, had higher blood pressure, and a higher incidence of being in class 1-11 Killip heart failure. Only 32% had a normal systolic function, and the majority had either mild or moderate systolic dysfunction (Table 1).

Guideline-directed medical therapy was not different between the two groups, except for the initiation of a beta-blocker on admission. In particular, the rate of percutaneous coronary intervention (PCI) was similar (Tables 2 and 3).

Overall, the in-hospital mortality was similar (5%), and more women were diagnosed with atrial fibrillation and heart failure at follow-up (Table 4). No difference were noted between the groups in recurrent ischemia, recurrent MI, cardiogenic shock, VTVF arrest, stroke, or major bleeding.

### Table 1 Epidemiological data and presentation characteristics of NSTEMI patients by gender (Continued)

| Variable# | Male | Female | Total | P value |
|-----------|------|--------|-------|---------|
| Mild LV systolic dysfunction (EF 40-50%) | 164 (29.98%) | 52 (34.67%) | 216 (30.99%) | .001 |
| Moderate LV systolic dysfunction (EF 30-40%) | 88 (16.09%) | 36 (24.00%) | 124 (17.79%) | .001 |
| Severe LV systolic dysfunction (EF < 30%) | 58 (10.60%) | 9 (6.00%) | 67 (9.61%) | .001 |
| ECG done/transferred | 340 (56.86%) | 68 (41.46%) | 408 (53.54%) | < .001 |
| Arterial access | | | | |
| Femoral | 124 (46.62%) | 28 (59.57%) | 152 (48.56%) | .101 |
| Radial | 142 (53.38%) | 19 (40.43%) | 161 (51.44%) | .101 |

### Table 2 Medication at admission

| Medications 24 h | Male | Female | Total | P value |
|------------------|------|--------|-------|---------|
| Aspirin | 592 (99.00%) | 163 (99.39%) | 755 (99.08%) | .640 |
| Clopidogrel | 533 (89.13%) | 154 (93.90%) | 687 (90.16%) | .069 |
| Prasugrel | 3 (0.50%) | 0 (0.00%) | 3 (0.39%) | .363 |
| Ticagrelor | 59 (9.87%) | 5 (3.05%) | 64 (8.40%) | .005 |
| Beta blockers | 531 (88.80%) | 130 (80.49%) | 661 (86.75%) | .001 |
| ACEI/ARB | 462 (77.26%) | 132 (80.49%) | 594 (77.95%) | .377 |
| Statins | 570 (95.32%) | 159 (96.95%) | 729 (95.67%) | .363 |
| Aldosterone inhibitor (spironolactone) | 54 (9.03%) | 18 (10.98%) | 72 (9.45%) | .451 |
| Heparins UH/LMWH | 552 (92.31%) | 148 (90.24%) | 700 (91.86%) | .392 |
| GP_2b3a_inhibitors | 97 (16.22%) | 15 (9.15%) | 112 (14.70%) | .023 |
| Insulin | 284 (47.49%) | 114 (69.51%) | 398 (52.23%) | < .001 |
| Oral hp agents | 74 (12.37%) | 32 (19.51%) | 106 (13.91%) | .019 |
Discussion
Women are still underrepresented in ACS-related literature. Based on the gender distribution in the country, we expected a larger proportion, not only 22% as reported in the current study. Because the data were extracted from the registry, collection bias played no role in the study. Possible explanations could be that the women had ACS but did not reach medical attention or they were incorrectly diagnosed due to their atypical symptoms. Both are major concerns that require further investigation and governmental attention, as previously reported [3, 4].

We also noted the high incidence of diabetes and hypertension in the female group. Both are modifiable risk factors that reflect the need to modify the lifestyle. The medical staff, especially at emergency rooms and paramedics, should be aware of the atypical presentation. The Red Crescent was under-utilized and a mass educational intervention is urgent.

Although the findings are rising alarms, the effort did not match the challenge [5]. The issue is global, extending from east to west [6–8].

Conclusion
Women are underrepresented, frequently had an atypical presentation and presented late. Risk factors are highly prevalent and need immediate attention. It should be stated that when they did present for medical attention, they received appropriate guideline-directed medical therapy and PCI.

Table 3 Medication at discharge

| Medications at discharge | Male | Female | Total | P value |
|--------------------------|------|--------|-------|---------|
| Aspirin                  | 566 (98.26%) | 153 (98.08%) | 719 (98.22%) | 0.875 |
| Clopidogrel              | 483 (83.85%) | 132 (84.62%) | 615 (84.02%) | 0.818 |
| Ticagrelor               | 61 (10.59%) | 12 (7.69%) | 73 (9.97%) | 0.284 |
| Beta blockers            | 529 (91.84%) | 136 (87.18%) | 665 (90.85%) | 0.073 |
| ACEI/ARB                 | 457 (79.34%) | 126 (80.77%) | 583 (79.64%) | 0.694 |
| Statins                  | 562 (97.57%) | 151 (96.79%) | 713 (97.40%) | 0.589 |
| Aldosterone inhibitor (spironolactone) | 65 (11.28%) | 25 (16.03%) | 90 (12.30%) | 0.110 |
| Oral anticoagulant warfarin/dabigatran | 18 (3.13%) | 9 (5.77%) | 27 (3.69%) | 0.120 |
| Insulin                  | 179 (31.08%) | 89 (57.05%) | 268 (36.61%) | < .001 |
| Oral hypoglycemic        | 166 (28.82%) | 54 (34.62%) | 220 (30.05%) | 0.161 |

Table 4 Outcome differences of NSTEMI patients by gender

| In-hospital outcomes          | Male | Female | Total | P value |
|------------------------------|------|--------|-------|---------|
| Recurrent ischemia           | 70 (11.71%) | 28 (17.07%) | 98 (12.86%) | 0.069 |
| Recurrent MI                 | 34 (5.69%) | 14 (8.54%) | 48 (6.30%) | 0.183 |
| Atrial fibrillation/flutter  | 28 (4.68%) | 16 (9.76%) | 44 (5.77%) | 0.014 |
| Heart failure                | 65 (10.87%) | 34 (20.73%) | 99 (12.99%) | < .001 |
| Cardiogenic shock            | 32 (5.35%) | 10 (6.10%) | 42 (5.51%) | 0.711 |
| VTVF arrest                  | 31 (5.18%) | 13 (7.93%) | 44 (5.77%) | 0.182 |
| Stroke                       | 11 (1.84%) | 3 (1.83%) | 14 (1.84%) | 0.993 |
| Major bleeding               | 5 (0.84%) | 1 (0.61%) | 6 (0.79%) | 0.771 |
| In-hospital mortality        | 22 (3.68%) | 8 (4.88%) | 30 (3.94%) | 0.484 |

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