

## Original Article

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## Sex Differences in Risk Factors Profile and Angiographic Pattern of the Patients Undergoing Coronary Angiography

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### Abstract

**Introduction:** Coronary artery disease (CAD) is a costly problem and its presentations and risk factors may differ by sex.

**Objective:** This study aimed to evaluate the risk factors profile and angiographic pattern of the patients undergoing coronary angiography, according to their gender.

**Methods:** This cross-sectional study was conducted on 741 patients who were referred for coronary angiography from March to August 2018 at Imam Ali cardiovascular center, western Iran. Using a checklist, we collected the demographic, clinical, biochemical, and lab parameters and angiographic findings in these patients. Also, differences between groups were compared using Chi-square and independent t-tests.

**Results:** Women were different from men in terms of the prevalence of hypertension (71.7% vs. 45.3%), diabetes mellitus (34.9% vs. 17.8%), and hypercholesterolemia (26.4% vs. 17.1%). Whereas, men were more likely to be smoker (28.7% vs. 0%) and obese (42.09±16.68 vs. 29.12±4.72). Total Cholesterol and Triglycerides were higher in women compared to men, which were statistically significant. Glucose plasma was significantly higher in women compared to men (p=0.01). Both atherogenic (low-density lipoprotein (LDL)) and protective (high-density lipoprotein (HDL)) cholesterol were higher in women than men. Women were more likely to take antiplatelet (i.e. Aspirin) and antihypertensive therapies (i.e. beta-Blocker, angiotensin receptor blockers (ARBs), and angiotensin converting enzyme (ACE) inhibitors) than men. Also, it was shown that, Men were more likely to have two-vessel disease (p=0.041) and three-vessel disease (P=0.013) compared to women. Disease in the right coronary artery (RCA) (28.9% vs. 14.4%), circumflex (LCx) (26.0% vs. 15.3%), and left anterior descending (LAD) (37.8% vs. 26.4%) was more plausible to occur in men compared to women (p≤0.05).

**Conclusion:** Access and use of health care programs are needed to control CAD risk factors. The findings of the current study showed the significance of gender in the extent of coronary artery blockages.

**Key words:** Coronary Angiography; Coronary Artery Disease; Iran; Risk Factors; Sex

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### INTRODUCTION

Coronary artery disease (CAD) is a costly condition and is considered as the leading cause of death in both women and men worldwide (1, 2). Directly, CAD is responsible for half of the cardiovascular deaths (3). It is estimated that, between 4% and 10% of the patients with CAD are aged less than 45 years old (4, 5). Furthermore, the patients with CAD are suffering from comorbidity diseases that potentially affect the treatment and risk of mortality (6).

Coronary angiography is the gold standard for assessing the CADs. The extent and severity of coronary artery stenosis, the number of culprit vessels, the presence or the absence of atherosclerosis, and some other factors are useful indexes to determine the CAD patient's prognosis.

This evidence is based on the coronary angiography findings (7, 8). Likewise, the angiographic evaluation of disease is very important for deciding on the treatment strategy. However, previous studies clearly demonstrated the limitations of coronary angiography (9, 10). For example, angiographic evaluation is based on visualizing the vessel lumen; therefore, it is not ideal for the assessment of complex lesions like bifurcation lesions (8).

Risk factors of CAD are classified into modifiable and non-modifiable factors. Accordingly, Non-modifiable are some factors such as age, family history, and gender. Also, Modifiable risk factors are hypertension, dyslipidemia, obesity, smoking, diabetes, and psychosocial stress. Moreover, there

are differences in the prevalence of risk factors between men and women (11); though, the reasons for this sex-based difference have not been clear, yet.

To this end, the current study was conducted on the patients who were referred for coronary angiography at Imam Ali cardiovascular center at Kermanshah University of Medical Science (KUMS) between March and April 2018, to assess the gender differences in risk factor profile and coronary angiography, and also the other likely associated factors.

## Methods

### **Study population and design**

This cross-sectional study was conducted in Imam Ali cardiovascular center at KUMS. Imam Ali hospital, as the main cardiovascular center in western Iran with 280 active beds, is a public hospital, and covers about two millions population who are mostly Kurdish.

With the aim of evaluating only 50% of the patients, six-month data of the patients admitted for coronary angiography were assessed. From March-1 to August-30 2018, we evaluated all the patients (convenience sampling) referred for coronary angiography. Thus, all the patients who met the inclusion criteria were selected to be included in the study. Inclusion criteria were as follows: age  $\geq$  18 years old. The patients were excluded from the study if they were non-residential (living in other countries like Iraq), and/or had incomplete personal or medical information.

### **Instrument and data collection**

A research assistant, extracted the data from the patients' medical records (both paperwork records and electronic medical records) using a checklist. Checklist was developed and then verified by expert opinions comprising a cardiologist, a physician, a statistician, and a PhD in health promotion. For the goals of this study, demographic characteristics (e.g. gender), clinical histories (e.g. previous myocardial infarction), cardiovascular risk factors (e.g. smoking), presentation assessment (e.g. heart rate), biochemical and lab parameters (e.g. total cholesterol), angiographic findings (e.g. topography of significant stenosis), and recommendations were obtained.

### **Statistical methods**

Baseline data including demographic characteristics and cardiovascular risk factors were compared between men and women. Normal distributed variables (e.g., age) were described

using mean  $\pm$  standard deviation ( $\mu \pm SD$ ), and qualitative/categorical variables (e.g., smoking) were expressed as frequencies and percentages. Differences between men and women were assessed using independent t-tests for continuous and normally distributed variables, and chi-square (or Fisher exact tests) for qualitative/categorical variables. The effect size scores were calculated for better comparing the differences between men and women, using Cohen's d for continuous variables and chi-square (or Fisher exact tests) value for qualitative/categorical variables. Cohen's d was calculated by the difference in the means of the two groups divided by the weighted pooled standard deviations of these groups. A test was considered as significant if the probability value (p-value) was less than 0.05. The Statistical Package for Social Science (SPSS) software, version 23 (IBM Corp., Armonk, NY USA) was used for analyzing.

### **Ethical approval**

The research ethics committee at KUMS (IR.KUMS.REC.1398.702) has approved the study protocol and has monitored the research process. Moreover, the individual personal information has been kept confidentially with access limited to researcher.

## RESULTS

During the study period, a total of 741 patients, comprising 415 (56%) men and 326 (44%) women met the inclusion criteria of this study. The demographic and clinical characteristics of patients (N=741), stratified by sex are reported in table 1. The mean age of the women was  $60.77 \pm 9.16$  years old, and for men, it was  $59.30 \pm 11.17$  years old ( $p = 0.284$ ). A significant difference was observed in presenting the risk factors of CAD based on sex. Men had, on average, higher body mass index (BMI) than the women patients as follows:  $42.09 \pm 16.68$  for men and  $29.12 \pm 4.72$  for the women ( $p = 0.001$ ). The prevalence rates of diabetes mellitus, hypertension, and hypercholesterolemia were significantly higher in women compared to men, whereas more men were current smoker ( $p \leq 0.05$ ).

The mean heart rate of the patients was  $79.29 \pm 10.77$  for men vs.  $80.18 \pm 11.07$  for women ( $p = 0.541$ ). The mean systolic blood pressure (SBP) of men was  $145.56 \pm 22.86$  mm hg, whereas for women, it was  $163.27 \pm 20.97$  mm hg ( $p = 0.008$ ). The mean diastolic blood pressure (DBP) of the patients was  $85.0 \pm 10.71$  mm hg for men vs.  $86.29 \pm 12.26$  mm hg for women ( $p = 0.391$ ).

Also, the median ejection fraction (EF) for women was  $48.89 \pm 8.76$  and for men  $46.85 \pm 9.86$  ( $p=0.145$ ).

The mean glucose plasma levels for men was  $117.39 \pm 39.32$  vs.  $123.32 \pm 55.19$  for women ( $p=0.012$ ). Comparing the lipid profiles, we observed that, mean total cholesterol

( $200.41 \pm 59.20$  vs.  $159.37 \pm 48.78$ ) and mean serum triglycerides ( $160.74 \pm 65.97$  vs.  $134.30 \pm 54.52$ ) were significantly higher in women compared to men ( $p \leq 0.05$ ). Likewise, both atherogenic (low-density lipoprotein (LDL)) and protective (high-density lipoprotein (HDL)) cholesterol were significantly higher in women than men ( $p \leq 0.05$ ).

**Table 1:** The demographic and clinical characteristics of patients (N=741), stratified by sex

Variable	Men (n=415)	Women (n=326)	Effect size† (p-value)
Age (y)†	59.30±11.17	60.77±9.16	0.14 (0.284)*
Body mass index (kg/m2)†	42.09±16.68	29.12±4.72	1.07(0.001)*
Current smoker	213 (28.7)	0 (0)	234.22 (<0.001)**
Diabetes mellitus	74 (17.8)	114 (34.9)	28.32 (<0.001)**
Hypercholesterolemia	71 (17.1)	86 (26.4)	9.39 (0.002)**
Hypertension	188 (45.3)	234 (71.7)	52.20(<0.001)**
Prior congestive heart failure	0 (0)	0 (0)	NAN**
Prior myocardial infarction	52 (12.5)	31 (9.5)	1.67 (0.195)**
Prior angina	203 (48.9)	169 (51.8)	0.62 (0.429)**
Prior stroke	6 (1.4)	0 (0)	1.93 (0.261)**
Prior percutaneous coronary intervention	12 (2.9)	3 (0.9)	3.57 (0.058)**
Prior coronary artery bypass grafting	12 (2.9)	3 (0.9)	3.57 (0.058)**
Aspirin user	296 (71.3)	255 (78.2)	4.55 (0.032)**
Clopidogrel user	99 (23.8)	74(22.7)	0.13 (0.711)**
Angiotensin receptor blockers user	105 (25.3)	120 (36.8)	11.43 (<0.001)**
Beta-Blocker user	227 (54.7)	216 (66.2)	10.14 (0.001)**
Angiotensin converting enzyme inhibitors user	48 (11.5)	74 (22.7)	16.45 (<0.001)**
Statin user	249 (60.0)	209 (64.1)	1.30 (0.253)**
Cholesterol†	159.37±48.78	200.41±59.20	1.65 (0.001)*
Low-density lipoprotein †	86.66±26.89	114.65±37.38	1.39 (0.001)*
High-density lipoprotein †	41.13±10.26	49.83±15.29	0.62 (0.021)*
Triglycerides†	134.30±54.52	160.74±65.97	0.45 (0.043)*
Glucose plasma†	117.39±39.32	123.32±55.19	0.53 (0.012)*

† The effect size scores were reported using Cohen's d for continuous variables and chi-square (or Fisher exact tests) value for qualitative/categorical variables.

‡ Continuous variables expressed as mean ± SD, otherwise n (%).

\* t-test; \*\* chi-square; \*\*\* Fisher exact test

**Table 2:** Procedural and angiographic characteristics according to sex

Variable	Men (n=415)	Women (n=326)	Effect size† p-value
<b>Final diagnosis</b>			
Normal coronary	151 (36.4)	188 (57.7)	33.32 (<0.001)**
One-vessel disease	57 (13.7)	41 (12.6)	0.21 (0.644)**
Two-vessel disease	77 (18.5)	31 (9.5)	11.99 (<0.001)**
Three-vessel disease	121 (29.1)	63 (19.3)	9.45 (0.002)**
Left main disease	18 (4.3)	10 (3.0)	0.80 (0.368)**
<b>Culprit vessel</b>			
Left Anterior Descending	157 (37.8)	86 (26.4)	10.86 (<0.001)**
Left Main Stem	18 (4.3)	10 (3.0)	0.80 (0.368)**
Right Coronary Artery	120 (28.9)	47 (14.4)	21.98 (<0.001)**
Circumflex	108 (26.0)	50 (15.3)	12.42 (<0.001)**
Posterior Descending Artery	15 (3.8)	9 (2.7)	0.42 (0.514)**
First Diagonal branch	61 (14.7)	43 (13.2)	0.34 (0.557)**
Second Diagonal branch	31 (7.4)	15 (4.6)	2.58 (0.108)**
Ramus	13 (3.1)	9 (2.7)	0.08 (0.767)**
Saphenous Vein Graft	0 (0)	0 (0)	NAN**
First Obtuse Marginal branch	27 (6.5)	21 (6.4)	0.001(0.971)**
Second Obtuse Marginal branch	9 (2.2)	4 (1.2)	0.93 (0.332)**
<b>Recommendations after angiography</b>			
Percutaneous Coronary Intervention	83 (20.0)	54 (16.5)	1.42 (0.231)**
Coronary Artery Bypass Grafting	130 (31.3)	69 (21.2)	9.59 (0.001)**
Medical Follow Up	183 (44.1)	192 (58.9)	15.99 (<0.001)**

† The effect size scores were reported using Cohen's d for continuous variables and chi-square (or Fisher exact tests) value for qualitative/categorical variables.

\*\* chi-square

Similar treatment patterns existed for medication use, however, women were more likely to take beta-blocker ( $p=0.001$ ), angiotensin converting enzyme (ACE) inhibitors ( $p<0.001$ ), Aspirin ( $p=0.032$ ), and angiotensin receptor blockers (ARBs) ( $p<0.001$ ) compared to men.

Angiographic findings (Table 2) demonstrated that, men were more likely to have two-vessel disease ( $p<0.001$ ) and three-vessel disease ( $p=0.002$ ), whereas women were more likely to have normal coronary ( $p<0.001$ ). No significant sex differences were observed in left main disease. The distribution of stenosis in different coronary arteries was compared in both genders. Stenosis in left anterior descending (LAD) was observed in 51 (37.8%) men compared to 28 (26.4%) women ( $p<0.001$ ). right coronary artery (RCA) stenosis was more frequent in men (120(28.9%) vs. 47(14.4%)) ( $p<0.001$ ). In circumflex (LCx), stenosis was observed in 108(26.0%) men ( $p<0.001$ ). Also after angiography evaluation, men were significantly recommended to seek treatment with coronary artery bypass grafting (CABG) ( $p=0.001$ ), whereas medical follow up was significantly recommended to women ( $p<0.001$ ).

## DISCUSSION

The results of this study illustrated that, women who were referred for coronary angiography, had significantly higher prevalence of diabetes, hypertension, and hypercholesterolemia. This result was in line with the findings reviewed from the West (12-14). However, men were more likely to be current smokers and had higher BMI compared to their women counterparts. Consistent with the results of this study, Deepti et al. reported that, women were more likely to be hypertensive and were less likely to be current smokers (15). Bajaj's study performed in India, reported a higher prevalence of diabetes and hypertension among women in 2013, whereas men were more likely to be smoker and obese.<sup>11</sup> Hemal K et al. have reported that, women who undergoing coronary angiography were more likely to be hypertensive and dyslipidemic. In current study, women were more likely to be dyslipidemic, which this result support the findings of study done by Hemal K et al (16).

On the other hand, many others report found converse results. For instance, Gupta et al. and Anand et al., showed a higher prevalence of diabetes and hypertension among men compared to women (17, 18). Conversely, Butala NM et al. and Jarrah et al., reported a higher BMI in women

compared to men (13, 19). Also in contrast, in previous studies done by Yasar et al., Bajaj et al., and Enas et al., dyslipidaemia was more common among men compared to women patients (11, 14, 20).

Smoking was one of the significant risk factors in men who undergone coronary angiography, whereas it was totally absent in women. In fact, the potential reason why women refuse from smoking may be due to the socio-cultural factors in Iran where smoking is less common among women. Our results are in agreement with the findings of previous studies conducted on different populations in other countries (11, 17, 18, 21).

Comparing the lipid profiles, we found that, total cholesterol, serum triglycerides, LDL, and HDL levels were significantly higher in women compared to their male counterparts. These results support the findings of Deepti's study reporting that, total cholesterol, LDL, and HDL levels were more in women than men (15). However, in contrast, in a study conducted by Bajaj et al, the mean LDL, HDL, and serum triglycerides levels were higher among men than women (11).

Our results demonstrated that, the mean SBP was significantly higher in women compared to men. This might be explained by the possible negative effect of menopause on the blood pressure. In this study, women had the age between 40 and 71 years old (menopause age). Increase in plasma rennin activity and salt sensitivity with sympathetic activity due to physiological and hormonal changes in menopause (the declining estrogen levels), can lead to an increase in the blood pressure in peri-menopausal and post-menopausal women (22).

Given that the mean SBP ( $140\leq$ ), total cholesterol ( $160\leq$ ), glucose plasma ( $100\leq$ ), and BMI ( $25\leq$ ) was higher than normal range in both sex. Tailoring healthcare interventions to control the hypertension, dyslipidemia, diabetes and obesity epidemic, including early detection and management, especially those targeted the women (because women had worse risk profiles), should be a top priority in the coming years. Moreover, educational campaigns and programs to promote lifestyle can be cost-benefit in improving the population level. Moreover, policy interventions might be beneficial in modifying unhealthy habits and improving lifestyle, for example Colchero et al. found that implementing the excise tax on sugar sweetened beverages in Mexico leads to a considerable reduction in purchasing the taxed

beverages and an increase in purchasing the bottled water (23).

In our study, similar treatment patterns recommended for both sex, although, women were more likely than men to be taking antiplatelet (Aspirin) and antihypertensive therapies (beta-blocker, ARBs, and ACE inhibitors). Hemal K et al. have reported that women were more likely than men to take  $\beta$ -blockers, however, by contrast, they were less likely to be taking ACE inhibitors or ARBs (16). These differences may be due to the higher incidence of CAD risk factors i.e. hypertension among women.

We found that men were more likely to have two-vessel disease and three-vessel disease. The results were concurrent with the findings of the study conducted by George et al., which have reported two-vessel disease was more common to men (24). Likewise, Bajaj et al. showed multiple vessel disease was more common in men (11). A study by Jong et al. showed women were more likely than men to have normal coronary arteries (25). Some previous studies, although, showed no such gender differences (19, 26-28). In fact, the findings of current study showed the significance of gender in the extent of coronary artery blockages. Likewise, the results of current study indicated that disease in the RCA, LCx, and LAD was more plausible to occur in men. George and colleagues have reported that stenosis in RCA and LCx were more frequent in men, whereas no sex differences were seen in LAD disease (26). Furthermore, our findings show after angiography assessment men were more recommended to seek treatment with CABG and percutaneous coronary intervention, whereas medical follow up were recommended to women. This may be due to nearly half of the men had multi-disease vessel, whereas majority of women had normal coronary.

#### **Limitations**

The most important limitation of the current study was poor documentation in the past medical

recorded information. To move bias, we tested the data through electronic medical records (hospital information system). Furthermore, our data were derived from a single center; hence, our participants may not be the representative of the whole patients undergoing CAG.

#### **CONCLUSIONS**

The results showed that women had the more adverse clinical risk profiles. In general, women were more likely to be hypertensive, diabetic, and dyslipidemic, whereas, men were more likely to be current smokers and obese. Likewise, women were more likely than men to be taking antiplatelet and antihypertensive therapies. Access and use of health care programs to control the hypertension, dyslipidemia, diabetes and obesity epidemic, in particular for women, are needed. Men were more likely than women to have two-vessel disease and three-vessel disease and, also, disease in the RCA, LCx, and LAD was more plausible to occur in men.

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#### **AUTHORS' CONTRIBUTION**

All the authors met the standards of authorship based on the recommendations of the International Committee of Medical Journal Editors.

#### **CONFLICT OF INTEREST**

None declared.

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None declared.

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