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Risk Factors Associated With the Extent of Coronary Vessel Involvement Across the Spectrum of Coronary Artery Disease

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Abstract

Background: Cardiovascular Disease (CVD) is one of the most important causes of mortality and morbidity in developed and developing countries.
Objectives: This study aimed to evaluate the risk factors associated with the extent of coronary vessel involvement across the spectrum of Coronary Artery Disease (CAD) in patients referring to the Cardiac Ward of Vali-Asr Hospital of Birjand, Iran.
Methods: A cross-sectional study was conducted on 3,394 patients undergoing coronary angiography at the Cardiac Ward of Vali-Asr Hospital of Birjand, Iran, in 2011-2015. Subjects were assigned to four groups in terms of the extent of coronary vessel involvement: Normal CAD, non-significant CAD, CAD, and non-obstructive CAD. Adjusted odds ratios and 95% confident intervals were calculated by including all variables with P values < 0.05 into the multivariate model to control for confounding factors. Data were analyzed using SPSS version 22.
Results: Among male and female patients, those aged 45-65 years needed angiography more than other groups. Multiple logistic regression analysis showed that diabetes, male gender, FBS, and history of hypertension significantly increased the likelihood of coronary vessel involvement ($P \leq 0.05$).
Conclusions: The findings of the present study imply that age, male gender, FBS, and history of hypertension are the independent risk factors for the extent of coronary vessel involvement in CAD and non-significant CAD groups. To reduce the rates and consequences of CAD, it is paramount to control cardiovascular risk factors, screen susceptible populations at risk, and improve coronary interventional services.

Keywords: Risk Factors, Coronary Artery Diseases, Coronary Artery Stenosis

1. Background

Cardiovascular diseases (CVD) is one of the most important causes of mortality and morbidity in developed and developing countries (1), and one of the commonest life-threatening, progressive, and chronic diseases worldwide (2). The pattern of Coronary Artery Disease (CAD) is fundamentally different between men and women. More than 60% of women and 30% of men with angina have either normal arteries or non-obstructive lesions (3). The relationships of CAD and its adverse clinical outcomes with risk factors such as age, gender, family history of CAD, hypertension, dyslipidemia, diabetes, smoking, obesity, and CAD have been examined in various studies. Nevertheless, there are controversial results on the relationship between these factors and the extent of coronary vessel involvement (4-7). Different scores such as gender, SYNTAX, and vessel scores are used to determine the extent of coronary vessel involvement in atherosclerosis (8). The prevalence of CAD in diabetic patients has been reported as 9.5-55%, while it is reported to vary between 1.6 and 4.1% in the general population (9).

2. Objectives

Since CAD is the first leading cause of death in Iran (10) and the extent of coronary vessel involvement has a significant role in treatment planning and prognosis of many important diseases (11), this study was carried out to investigate the risk factors associated with the extent of coronary

vessel involvement across the spectrum of CAD in patients referring to the Cardiac Ward of Valiasr Hospital of Birjand.

3. Methods

A cross-sectional study was conducted on 3,394 patients undergoing coronary angiography at the Cardiac Ward of Valiasr Hospital of Birjand, Iran, in 2011-2015. All patients who required angiography in the Cardiac Ward of Valiasr Hospital were entered into this study by the census. Participants aged less than 18, loss of consciousness, or inability to communicate verbally were excluded from this study. The present study was approved by the Ethics Committee of Birjand University of Medical Sciences (ir.bums.rec.1395.257). All patients expressed their written informed consent, and we considered ethical issues on the confidentiality of information of the patients.

Demographic and clinical characteristics were age, gender, history of CAD (yes/no), smoking (yes/no), opium use (yes/no), dyslipidemia (yes/no), history of hypertension (yes/no), blood glucose level ((< 100 & without medication;100-126 or medication use; > 126 mg/dl), Body Mass Index (BMI), High-density Lipoprotein (HDL), Low-density Lipoprotein (LDL), triglyceride, and cholesterol levels. The required data were extracted from interviews with the patients and/or patients' records before angiography. The results of angiographies carried out by a cardiologist were documented from the angiographic report papers.

The subjects were assigned into four groups according to the extent of coronary vessel involvement: Normal CAD group containing patients without coronary involvement in angiography, non-significant CAD group containing patients with coronary involvement less than 50%, CAD group involving patients with coronary involvement more than 50%, and finally non-obstructive CAD group containing patients with Coronary Artery Ectasia (CAE). Those with M-bridge or slow flow without coronary vessel involvement were excluded from the study.The independent variables were age, gender, history of CAD, smoking, opium use, dyslipidemia, history of hypertension, blood glucose level (mg/dl), BMI, HDL, LDL, triglyceride, and cholesterol levels.

The continuous variables with normal distributions were expressed as mean $\pm$ standard deviation. The counting data were expressed as percentages (%). Bivariate analysis was performed to identify the association between dependent and independent variables. Adjusted odds ratios and 95% confident intervals were calculated by including all variables with P values < 0.05 into the multivariate model to control for confounding factors. Data were analyzed using SPSS version 22, with two-tailed tests. The confidence interval in this study was set at 95%, and the significance level was considered less than 0.05.

4. Results

The results of this study showed that among males and females, patients aged 45-65 years needed angiography more than other groups. Also, 50.6% of women in the CAD group, 45.5% of women in the non-obstructive CAD group, 42.1% of women in the non-significant CAD group, and 35.1% of women in the normal CAD group had a history of hypertension. The baseline characteristics of the participants are shown in Table 1. The multivariate regression analysis revealed that in the non-significant CAD group, the patients older than 65 years and those aged 45-65 years were respectively 7.48 (range: 3.95-14.13, $P < 0.001$) and 3.10 (range: 1.70-5.64, $P < 0.001$) times more likely to have coronary vessel involvement. The male patients were 1.56 times more likely to have coronary vessel involvement (range: 1.14-2.14, $P = 0.005$). The patients with a blood glucose level of 126 mg/dl or higher were 1.87 times more likely to have coronary vessel involvement (range: 1.24-2.84, $P = 0.003$) (Table 2).

The results of multivariate regression analysis revealed that in the CAD group, the patients older than 65 years and those aged 45-65 years were respectively 9.48 (range: 6.51-13.82, $P < 0.001$) and 2.67 (range: 1.92-3.70) times more likely to have coronary vessel involvement. The male patients were 4.52 (range: 3.63-5.63, $P < 0.001$) times more likely to have coronary vessel involvement.

The results of multivariate regression analysis showed that an increase in the HDL level significantly reduced the likelihood of coronary vessel involvement in the CAD group [OR: 0.98, 95% CI: 0.97-0.99, $P < 0.001$]. The patients with a glucose level of 126 mg/dl or higher and those with a glucose level of 100-126 mg/dl were respectively 3.58 (range: 2.67-4.80, $P < 0.001$) and 1.65 (range: 1.31-2.09, $P < 0.001$) times more likely to have coronary vessel involvement. The patients with a history of hypertension were 1.43 times more likely to have coronary vessel involvement (range: 1.15- 1.79, $P < 0.001$) (Table 3).

According to the results of multivariate regression analysis, in the CAD group, the male patients were 2.55 (range: 1.92-3.27, $P < 0.001$) times more likely to have coronary vessel involvement. The patients with a glucose level of 126 mg/dl or higher and those with a glucose level of 100-126 mg/dl were respectively 1.94 (range: 1.39-2.71, $P < 0.001$) and 1.88 (range: 1.36-2.58, $P < 0.001$) times more likely to have coronary vessel involvement (Table 4).

5. Discussion

The findings showed that age, gender, history of hypertension, HDL, LDL, and FBS levels were significantly associated with the extent of coronary vessel involvement. The

Table 1. Baseline Characteristics of Participants

Characteristic	Normal CAD		Non-Significant CAD		CAD		Non-Obstructive CAD	
	Female, No. (%)	Male, No. (%)	Female, No. (%)	Male, No. (%)	Female, No. (%)	Male, No. (%)	Female, No. (%)	Male, No. (%)
Age (years)								
≤ 45	67 (13.7)	53 (22.8)	7 (4.2)	12 (9.4)	25 (3.2)	97 (7.4)	5 (5)	17 (15.9)
45-65	347 (71)	137 (59.1)	101 (60.8)	77 (60.6)	415 (52.7)	714 (54.1)	62 (62)	62 (57.9)
>65	75 (15.3)	42 (18.1)	58 (34.9)	38 (29.9)	347 (44.1)	508 (38.5)	33 (33)	28 (26.2)
Family History of CVD								
No	457 (90.7)	214 (89.2)	158 (92.4)	115 (90.6)	730 (91.5)	1232 (91.7)	92 (91.1)	103 (94.5)
Yes	47 (9.3)	26 (10.8)	13 (7.6)	12 (9.4)	68 (8.5)	112 (8.3)	9 (8.9)	6 (5.5)
HTN								
No	327 (64.9)	193 (80.4)	99 (57.9)	96 (75.6)	394 (49.4)	964 (71.7)	55 (54.5)	86 (78.9)
Yes	177 (35.1)	47 (19.6)	72 (42.1)	31 (24.4)	404 (50.6)	380 (28.3)	46 (45.5)	23 (21.1)
DLP								
No	338 (67.1)	194 (80.8)	114 (66.7)	95 (74.8)	452 (56.6)	957 (71.2)	67 (66.3)	78 (71.6)
Yes	166 (32.9)	46 (19.2)	57 (33.3)	32 (25.2)	346 (43.4)	387 (28.2)	34 (33.7)	31 (28.4)
FBS (mg/dL)								
< 100 & without medication	247 (53.8)	139 (63.8)	83 (51.2)	67 (59.3)	264 (35.2)	521 (42.6)	54 (56.3)	54 (57.4)
100-126 or medication use	147 (32.0)	57 (23.8)	44 (25.7)	23 (20.4)	244 (32.4)	414 (33.9)	29 (30.2)	29 (30.9)
>126	65 (14.2)	22 (9.2)	35 (21.6)	23 (20.4)	244 (32.4)	287 (23.5)	13 (13.5)	11 (11.7)
BMI								
< 18.5 (Underweight)	23 (5.3)	18 (8.3)	7 (4.7)	6 (5.3)	36 (5.6)	64 (6)	9 (9.5)	4 (4.4)
18.5 - 24.99 (Normal)	157 (35.8)	106 (49.1)	61 (40.9)	55 (48.2)	234 (36.6)	498 (46.4)	27 (28.4)	39 (42.9)
>25 (Overweight or obese)	258 (58.9)	92 (42.6)	81 (54.4)	53 (46.5)	369 (57.7)	511 (47.6)	59 (62.1)	48 (52.7)
Smoking								
No	485 (96.2)	211 (87.9)	163 (95.3)	109 (85.8)	763 (95.6)	1178 (87.6)	95 (94.1)	96 (88.1)
Yes	19 (3.8)	29 (12.1)	8 (4.7)	18 (14.2)	35 (4.4)	166 (12.4)	6 (5.9)	13 (11.9)
Opium use								
No	466 (92.5)	196 (81.7)	149 (87.1)	102 (80.3)	734 (92)	1136 (84.5)	95 (94.1)	96 (88.1)
Yes	38 (7.5)	44 (18.3)	22 (12.9)	25 (19.7)	64 (8)	208 (15.5)	6 (5.9)	13 (11.9)
Length of stay (days)								
< 4	430 (85.3)	213 (88.8)	142 (83)	103 (81.1)	563 (70.6)	956 (71.1)	88 (87.1)	97 (89)
>4	74 (14.7)	27 (11.3)	29 (17)	24 (18.9)	235 (29.4)	388 (28.9)	13 (12.9)	12 (11)
LDL (mg/dL)	104.96 ± 35.3	94.76 ± 32.69	108.07 ± 34.58	99.18 ± 36.99	112.90 ± 40.1	105.84 ± 37.27	103.89 ± 38.36	101.27 ± 36.73
HDL (mg/dL)	43.77 ± 11.87	39.27 ± 14.96	43.87 ± 11.73	12.77 ± 1.20	41.93 ± 14.02	38.34 ± 11.03	43.98 ± 13.14	39.44 ± 11.09
TG (mg/dL)	147.54 ± 100.5	150.88 ± 90.33	146.63 ± 71.68	136.95 ± 74.49	167.42 ± 99.23	142.03 ± 85.06	145.61 ± 74.73	150.36 ± 106.19
Cholesterol (mg/dL)	183.99 ± 45.39	166.02 ± 47.79	186.92 ± 47.52	174.72 ± 48.13	191.73 ± 54.63	178.58 ± 48.46	180.63 ± 47.19	175.44 ± 46.76

Table 2. Logistic Regression in Normal and Non-significant CAD Group

Risk Factor	Crude OR (95% CI)	P Value	Adjusted OR (95% CI)	P Value
Age (years)				
45 >	-	-	-	-
45-65	2.32 (1.39 - 3.88)	0.001	3.10 (1.70 - 5.64)	0.001
> 65	5.18 (2.97 - 9.01)	0.001	7.48 (3.95 - 14.13)	0.001
Gender				
Female	-	0.002	-	-
Male	1.56 (1.18 - 2.05)		1.56 (1.14 - 2.14)	0.005
Family History of CVD				
No	-	0.478	-	-
Yes	0.84 (0.52 - 1.35)			
Smoking				
No	-	0.198	-	-
Yes	1.38 (0.84 - 2.27)			
Opium use			-	-
No	-	0.036		
Yes	1.51 (1.02 - 2.22)			
LDL (mg/dL)	1 (0.99 - 1.00)	0.273	-	-
HDL (mg/dL)	1 (0.98 - 1.01)	0.957	-	-
TG (mg/dL)	0.99 (0.99 - 1.00)	0.364	-	-
Cholesterol (mg/dL)	1 (0.99 - 1.00)	0.261	-	-
Creatinine (mg/dL)	1.35 (0.94 - 1.92)	0.096	-	-
Hb (mg/dL)	1 (0.99 - 1.01)	0.35	-	-
Dyslipidemia			-	-
Normal	-	-		
Abnormal	0.93 (0.63 - 1.38)	0.742		
FBS (mg/dL)				
<100 & without medication	-	-	-	-
100- 126 or medication use	0.84 (0.60 - 1.18)	0.324	0.87 (0.61 - 1.25)	0.478
> 126	1.71 (1.17 - 2.51)	0.006	1.87 (1.24 - 2.84)	0.003
History of hypertension			-	-
No	-	0.162		
Yes	1.22 (0.92 - 1.63)			
BMI			-	-
<18.5 (Underweight)	-	-		
18.5 - 24.99 (Normal)	1.39 (0.71 - 2.69)	0.328		
> 25 (Overweight or obese)	1.20 (0.62 - 2.32)	0.573		

Table 3. Logistic Regression in Normal and CAD Groups

Risk Factor	Crude OR (95% CI)	P Value	Adjusted OR (95% CI)	P Value
Age (years)				
45 >	-	-	-	-
45 - 65	2.29 (1.74 - 3.01)	0.001	2.67 (1.92 - 3.70)	< 0.001
> 65	7.18 (5.23 - 9.87)	0.001	9.48 (6.51 - 13.82)	< 0.001
Gender				
Female	-	-	-	-
Male	3.53 (2.96 - 4.22)	0.001	4.52 (3.63 - 5.63)	< 0.001
Family History of CVD			-	-
No	-	-		
Yes	0.84 (0.63 - 1.12)	0.242		
Smoking			-	-
No	-	-		
Yes	1.50 (1.08 - 2.08)	0.015		
Opium use			-	-
No	-	-		
Yes	1.17 (0.90 - 1.52)	0.23		
LDL (mg/dL)	1 (1.00- 1.04)	0.001	1 (1.00 - 1.01)	< 0.001
HDL (mg/dL)	0.98 (0.97 - 0.99)	0.001	0.98 (0.97 - 0.99)	< 0.001
TG (mg/dL)	1 (0.99 - 1.00)	0.482	-	-
Cholesterol (mg/dL)	1 (1.00- 1.02)	0.017	-	-
Creatinine (mg/dL)	3.49 (2.35 - 5.17)	0.001	-	-
Hb (mg/dL)	1 (0.89 - 1.01)	0.943	-	-
Dyslipidemia			-	-
Normal	-	-		
Abnormal	1.04 (0.81 -1.34)	0.731		
FBS (mg/dL)				
< 100 & without medication	-	-	-	-
100- 126 or medication use	1.58 (1.30 - 1.93)	0.001	1.65 (1.31 - 2.09)	< 0.001
> 126	3 (2.32 - 3.88)	0.001	3.58 (2.67 - 4.80)	< 0.001
History of hypertension				
No	-	-	-	-
Yes	1.34 (1.12 - 1.60)	0.001	1.43 (1.15 - 1.79)	< 0.001
BMI			-	-
< 18.5 (Underweight)	-	-		
18.5 - 24.99 (Normal)	1.14 (0.77 - 1.68)	0.507		
> 25 (Overweight or obese)	1.03 (0.70 - 1.51)	0.877		

Table 4. Logistic Regression in Non-significant and CAD Groups

Risk Factor	Crude OR (95% CI)	P Value	Adjusted OR (95% CI)	P Value
Age (years)			-	-
45 >	-	-		
45-65	0.98 (0.59 - 1.64)	0.962		
> 65	1.38(0.81 - 2.35)	0.224		
Gender				
Female	-	-	-	-
Male	2.26 (1.77 - 2.89)	0.001	2.51 (1.92 - 3.27)	< 0.001
Family history of CVD			-	-
No	-	-		
Yes	1 (0.64 - 1.55)	0.99		
Smoking			-	-
No	-	-		
Yes	1.08 (0.70 - 1.66)	0.714		
Opium use			-	-
No	-	-		
Yes	0.77 (0.55 - 1.08)	0.141		
LDL (mg/dL)	1 (0.99 - 1.00)	0.099	-	-
HDL (mg/dL)	0.98 (0.97 - 0.99)	0.002	-	-
TG (mg/dL)	1 (1.01 - 1.04)	0.126	-	-
Cholesterol (mg/dL)	1 (0.99 - 1.00)	0.639	-	-
Creatinine (mg/dL)	0.98 (0.95 - 1.01)	0.235	-	-
Hb (mg/dL)	0.99 (0.98 - 1.00)	0.237	-	-
Dyslipidemia			-	-
No	-	-		
Yes	1.11 (0.78 - 1.59)	0.543		
FBS (mg/dL)				
< 100 & without medication	-	-	-	-
100- 126 or medication use	1.87 (1.38 - 2.54)	0.001	1.88 (1.36- 2.58)	< 0.001
> 126	1.74 (1.26 - 2.41)	0.001	1.94 (1.39 - 2.71)	< 0.001
History of hypertension			-	-
No	-	-		
Yes	1.09 (0.84 - 1.41)	0.493		
BMI			-	-
< 18.5 (Underweight)	-	-		
18.5 - 24.99 (Normal)	0.82 (0.44 - 1.51)	0.525		
> 25 (Overweight or obese)	0.85 (0.46 - 1.56)	0.609		

results showed that the likelihood of coronary vessel involvement was higher in men in all study groups (between normal CAD and CAD groups, between normal CAD and non-significant CAD groups, and between CAD and non-significant CAD groups), which complied with previous studies (12).

Cantarelli et al. (2015) reported the odds of coronary vessel involvement as 1.20 times higher in men than in women, which was consistent with the results of our study (13). However, Hochner-Celnikier et al. (2002) found that the number of involved vessels was higher in women than in men, which was inconsistent with the results of the present study (14). In this study, the higher extent of coronary vessel involvement in men may be due to that men have a greater risk of heart attack than women, and men experience heart attacks earlier in life than women.

The results showed that the likelihood of coronary vessel involvement was significantly higher in patients aged older than 45 years. Golmohammadi et al. (2016) proposed that age was positively associated with the number of involved vessels detected by angiography (10). Cantarelli et al. (2015) proposed that patients older than 40 years had doubled odds of developing coronary vessel involvement when compared to patients younger than 40 years of age, which complied with our results (13). Generally, coronary artery disease is more likely to occur with advancing age.

Also, the comparison of the normal CAD group with the CAD and non-significant CAD groups showed a higher likelihood of coronary vessel involvement in diabetic patients. The results of previous studies showed that diabetes mellitus is associated with an increased SYNTAX score and the development of multi-vessel coronary artery disease (12, 15, 16). Yoo et al. (2009) revealed that the odds of coronary vessel involvement were 3.5 times higher in diabetic patients (15). Srinivasan et al. reported a higher SYNTAX score in patients who had diabetes for more than five years compared to non-diabetic patients or those with diabetes for less than five years. They also stated that patients who had diabetes for more than five years were eligible for Coronary Artery Bypass Graft (CABG), and those without diabetes or with diabetes less than five years were eligible for coronary angiography (9). It can be concluded that risk factors associated with increased risk of CAD in diabetic patients include hyperglycemia, dyslipidemia, and insulin resistance, which may lead to endothelial dysfunction, platelet adhesion, and abnormal coagulation (9, 17, 18).

The comparison of the CAD group with normal groups revealed that increased HDL was associated with a reduced likelihood of coronary vessel involvement. Besides, the likelihood of coronary vessel involvement was not different between the two groups. Yang et al. (2011) revealed that the extent of coronary vessel involvement was associated with abnormal lipid metabolism. However, the total LDL/HDL cholesterol and TC/HDL cholesterol ratios were shown to be better indicators than other lipid parameters (16). Momiyama et al. (2012) showed that the LDL/HDL cholesterol ratio was linked with the extent of coronary vessel involvement (18). Jin et al. (2006) examined the relationship between blood lipid level and the extent of coronary vessel involvement in CAD patients. They stated that patients with higher TC, LDL cholesterol and non-HDL-cholesterol rations displayed a higher extent of coronary vessel involvement (19).

Also, the results suggested that patients with a history of hypertension were more likely to develop coronary vessel involvement, which was in line with the results of previous studies (20, 21). The studies conducted in Iran showed a positive relationship between blood pressure and blood glucose levels and the extent of coronary vessel involvement (22). Zandparsa et al. (2012) indicated that the average systolic and diastolic blood pressure was higher in patients with coronary vessel involvement (23).

5.1. Strengths and Weaknesses of the Study

This is the first study on various risk factors for the severity of vascular stenosis in Southern Khorasan province. However, the results of the present study should be interpreted with caution due to bias in the self-report of data. Also, the study design was cross-sectional, necessitating caution in interpreting the causal associations of risk factors with the extent of coronary vessel involvement.

5.2. Conclusion

The findings of the present study imply that age, male gender, FBS, and history of hypertension are independent risk factors for the extent of coronary vessel involvement in CAD and non-significant CAD groups. To reduce the rates and consequences of CAD, it is paramount to control cardiovascular risk factors, screen susceptible populations at risk, and improve coronary interventional services.

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Footnotes

Authors' Contribution: Conception and design were done by Seyyed Ali Moezi Bady, Toba Kazemi, Nazanin

Hanafi Bojd, Neda Partovi, Hamid Reza Mashreghi-moghadam, Mohammad Yousef Ghoddusi, Majid Jafarnejad, and Nahid Azdaki; Collection and assembly of data were done by Maryam Soltani, Saeede Khosravi Bizhaem, and Nasrin Amirabadizadeh; Data analysis and interpretation were done by Maryam Soltani, Saeede Khosravi Bizhaem, and Nasrin Amirabadizadeh; Manuscript writing was done by Maryam Soltani, Saeede Khosravi Bizhaem, and Nasrin Amirabadizadeh; The final approval of the manuscript was done by all authors.

Conflict of Interests: The authors declare that they have no conflicts of interest.

Ethical Approval: This study was approved by the Ethics Committee of the Birjand University of Medical Sciences, Birjand, Iran (IR.bums.Rec.1395.257).

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