Indicators for Coronary Artery Disease and Criteria for Patient Selection for Invasive Coronary Angiography: Experience from Gaza Strip-Palestine

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ABSTRACT
Background: Identification of risk factors and defining significant obstruction in coronary artery disease (CAD) using only clinical and noninvasive methods are often difficult tasks for the physician. Currently, coronary angiography (ICA) is the gold standard procedure for diagnosis of CAD. Nevertheless, this test should be carefully requested, as it is an invasive procedure. Here, we assess the predictive risk factors of significant CAD and the criteria for patient selection for ICA.
Methods: A cross-sectional study included 250 consecutive patients with suspected significant CAD referred to ICA to explore the extent of significant vessel disease. Patient characteristics, risk factors for CAD, and ICA test results were compared.
Results: 141 (56.4%) of the study patients were considered to have a significant CAD, and 109 (43.6%) of them were considered to have non-significant CAD. The independent predictors for obstructive CAD were: diabetes (odds ratio [OR], 4.35; confidence interval [CI] 95% (1.13-16.76), family history of heart disease (OR, 3.12; CI 95%, 1.11-8.68), currently smoking (OR, 2.89; CI 95%, 1.51-5.52), hypertension (OR, 2.74; CI 95%, 1.22-6.18), obesity (OR, 2.39; CI 95%, 1.26-4.55), and sedentary lifestyle (OR, 2.14; CI 95%, 1.09-4.22).
Conclusions: Strategies for risk stratification are needed to improve the appropriateness of patient selection for ICA.
Keywords: Coronary Artery Disease, Invasive Coronary Angiography, Gaza-Palestine

1. Introduction

Cardiovascular disease (CVD) is a significant public health issue throughout the world. An estimated 17.9 million people died from CVD in 2016, representing 31% of global deaths. Of these deaths, an estimated 7.4 million were due to coronary artery disease (CAD). In the United States (US), 92.1 million adults experienced at least one type of CVD. By 2030, 43.9% of the US adult population is likely to have CVD [1].

Population-based cardiovascular cohort studies make it possible to explore phenotyping of markers of subclinical CVD and long follow-up periods. Small-scale epidemiological studies are needed with deep phenotyping of subclinical CVD to advance our knowledge of CVD [2]. Over 75% of global CVD deaths take place in low and middle-income countries (LMICs). Out of the 17 million premature deaths due to non-communicable diseases (NCDs) in 2015, 82% are in LMICs, and 37% are caused by CVDs [3]. CVD in Arab countries accounts for 45% of deaths [4].

Despite the commitment to improve CVD outcomes by 2025 [5], most countries have been challenged to meet the targets [6]. The poorest LMICs may not be able to achieve the global target of 25% reduction in CVD mortality by 2025 [7]. The burden of CVD is high in Palestine, where it is the leading cause of death and ranked the top of ten NCD killers, accounting for 31.5% of deaths in 2018 [8]. According to statistics from the Gaza Strip, 58.9% of deaths are from CVD [9]. The recognition of risk factors defining the presence of significant CAD is often a difficult task for the cardiologists. It is well known that invasive coronary angiography (ICA) is the standard procedure for diagnosis. However, ICA should be requested with caution, as it is an invasive procedure and not free of complications [10].

Current guidelines recommend ICA for those considered to have a high probability of significant CAD and clinical follow-up for those with a low likelihood of CAD [11]. The present study aimed to assess the indicators and the predictive risk factors of significant CAD to better inform patient selection for ICA.

2. Materials and Methods

2.1 Study Design and Participants

We conducted an observational cross-sectional study with data collected from consecutive patients referred to the primary diagnostic hospital in the Gaza Strip. Those patients were referred to ICA after initial noninvasive and laboratory tests.

The study enrolled 250 eligible patients with suspected significant CAD and who were electively referred for ICA. All data were collected consecutively and registered in a database. The information on demographic characteristics, patient history, risk factors for CAD, patient complains, clinical findings, and the results of non-invasive tests were collected before ICA was performed.

Data retrieved from the patients' files included socio-demographic parameters such as age, sex, and body mass index (BMI). The medical history included a family history of heart disease, low-density lipoprotein (LDL), a history of hypertension, systolic blood pressure (SBP), diastolic blood pressure (DBP), and history of diabetes mellitus (DM). Smoking and lifestyle information was also obtained. BMI was calculated as weight in kilograms divided by the height in meters squared. We classified patients obese whose BMI was more than 30 kg/m^2, according to guidelines of the World Health Organization (WHO) [12]. LDL level < 100 mg/dL (< 2.6 mmol/L) was classified as normal and ≥100 mg/dL (≥ 2.6 mmol/L) as abnormal [13]. Hypertension was defined as having an SBP ≥140 mmHg or DBP ≥ 90 mmHg [14]. DM was defined as fasting plasma glucose values of ≥ 7.0 mmol/L (126 mg/dl) and HbA1c ≥ 6.5% (48 mmol/mol) [15]. Current smokers were defined as having smoked 100 cigarettes in his or her lifetime and is currently smoking [16].

2.2 Statistical Analysis

All statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS) software, version 25. Descriptive analysis cross-tabulation was used to describe the main features of the data; the Chi-square test was used to compare categorical variables. Baseline demographic characteristics, risk factors for CAD, and ICA test results of patients with or without significant CAD were compared. Models for logistic regression were adjusted to identify associated factors and independent predictors for significant CAD. Logistic regression is a predictive analysis that is used to explain the relationship between one dependent binary variable and one or more nominal, ordinal, interval or ratio-level independent variables. Simple logistic regression describes the univariable analysis, which was used to select potential independent variables associated with the risk of CAD. Multiple linear regressions were used to examine the association between risk and significant independent variables. These findings were presented as a regression coefficient (B), an odds ratio (OR), a 95% confidence interval (CI) and a P-value < 0.05.

3. Results

3.1 Baseline Characteristics

The population was comprised of 250 participants. Sex distribution in the sample was 161 (64.4%) male and 89 (35.6%) female. The median age of participants was 52 years (range 42–68 years). The descriptive statistics of the independent categorical variables are summarized in Table 1. The chi-square test (χ^2 test) revealed a significant association between the diagnostic result of ICA and all-independent variables at 0.05 level of significance. The final result of ICA for the diagnosis of eligible patients with suspected CAD is summarized into two categories. The first category includes patients with significant obstructive CAD, defined as more than 50% angiographic diameter stenosis in one or more of the epicardial coronary arteries. In the second category are patients with non-significant obstructive CAD, whose angiographic diameter stenosis is less than 50% [17]. Out of 250 patients diagnosed by ICA, there were 141 (56.4%) with significant and 109 (43.6%) with non-significant CAD.

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Table 1. Chi-square test of independent categorical variables associated with CAD

Variable	Categories	Diagnosis result of ICA		χ^2 test	P-value
		Significant (CAD)	Nonsignificant (CAD)		
Gender	Male	106 (42.4%)	55 (22.0%)	16.384	< 0.001*
	Female	35 (14.0%)	54 (21.6%)		
Obesity	Obese	65 (26.0%)	31 (12.4%)	8.104	0.004*
	Non-obese	76 (30.4%)	78 (31.2%)		
Lifestyle	Sedentary lifestyle	114 (45.6%)	57 (22.8%)	23.195	< 0.001*
	Regular exercise	27 (10.8%)	52 (20.8%)		
Smoking	Currently smoking	79 (31.6%)	27 (10.8%)	24.594	< 0.001*
	Non-smoking	62 (24.8%)	82 (32.8%)		
Family history of heart disease	Yes	32 (12.8%)	6 (2.4%)	14.094	< 0.001*
	No	109 (43.6%)	103 (41.2%)		
Low-density lipoprotein (LDL)	Yes	47 (18.8%)	15 (6.0%)	12.627	< 0.001*
	No	94 (37.6%)	94 (37.6%)		
Hypertension	Yes	36 (14.4%)	14 (5.6%)	6.158	0.013*
	No	105 (42.0%)	95 (38.0%)		
Diabetes mellitus (DM)	Yes	18 (7.2%)	3 (1.2%)	8.012	0.005*
	No	123 (49.2%)	106 (42.4%)		

* Significant at 0.05 level of significance.

3.2 Simple Logistic Regression of Risk Factors

Logistic regression is a predictive model for a categorical dependent variable based on a set of independent predictors. This section identifies the associated factors and independent predictors for significant CAD via logistic regression. A set of nine independent variables are considered to build up the logistic regression, specifically sex, age, obesity, lifestyle, smoking status, family history of heart disease, LDL, hypertension and DM.

The results of this analysis enabled us to determine which characteristics were independently associated with the presence of CAD, while the other factors remain constant as illustrated in Table 2. Among these characteristics, male gender has an odds ratio of 2.97, which means that a male patient has an approximately three times higher risk of CAD than a female. Age has an odds ratio of 1.14, which indicates that with an increase of one year in age, the associated risk of CAD is increased by 14%.

The predicted odds for having a significant CAD are 2.15 times higher for patients who are obese. Regarding lifestyle, a sedentary lifestyle is associated with a 3.85 times increased risk of CAD relative to a regular exerciser independent of physical activity. Current smokers were 3.87 times at higher risk of developing CAD than non-smokers.

Family history of heart disease has an odds ratio of five. The odds of significant CAD are more than three times higher for patients who have LDL ≥100 mg/dL (≥ 2.6 mmol/L) than they are for patients who have an LDL level < 100 mg/dL (< 2.6 mmol/L). The odds of significant CAD are 2.33 times higher for patients who have hypertension. Interestingly, diabetes has the highest odds ratio, with the odds of having significant CAD being 5.17 times higher in diabetic versus non-diabetic patients.

Table 2. Risk factors associated with CAD from Simple Logistic Regression analysis

Variable		β Coefficient	Standard error	Unadjusted Odds Ratio (95.0% CI)	Wald statistics	P-value
Sex	Male	1.09	0.27	2.97 (1.74-5.08)	15.90	<0.001*
	Female	-	-	1 [Reference]	-	-
Age		0.13	0.02	1.14 (1.09-1.2)	32.61	<0.001*
Obesity	Obese	0.77	0.27	2.15 (1.26-3.66)	7.98	0.005*
	Non-Obese	-	-	1 [Reference]	-	-
Lifestyle	Sedentary lifestyle	1.35	0.29	3.85 (2.19-6.77)	22.02	<0.001*
	Regular exercise	-	-	1 [Reference]	-	-
Smoking	Currently smoking	1.35	0.28	3.87 (2.24-6.69)	23.47	<0.001*
	Non-smoking	-	-	1 [Reference]	-	-
Family history of heart disease	Yes	1.62	0.47	5.04 (2.02-12.55)	12.07	0.001*
	No	-	-	1 [Reference]	-	-
Low-density lipoprotein (LDL)	Yes	1.14	0.33	3.13 (1.64-5.99)	11.94	0.001*
	No	-	-	1 [Reference]	-	-
Hypertension	Yes	0.84	0.35	2.33 (1.18-4.58)	5.98	0.014*
	No	-	-	1 [Reference]	-	-
Diabetes mellitus (DM)	Yes	1.64	0.64	5.17 (1.48-18.04)	6.64	0.010*
	No	-	-	1 [Reference]	-	-

* Significant at 0.05 level of significance.

3.3 Multiple Logistic Regression of Risk Factors

The final effect model was obtained using forward RL variable selection. Based on the results of the simple logistic regression analysis, all independent variables with a P-value <0.05 were included in the multiple logistic regression analysis. Table 3 presents all of the independent variables appearing in the final model that remained significantly associated with CAD.

The Omnibus Tests of Model Coefficients for the proposed model gives a value of -2 log-likelihood of 248.78 with an associated Chi-square test result of 93.69 at 7 degrees of freedom and P-value <0.001, which reveals the existence of an association between the independent variable and significant CAD status. The Cox and Snell R2 and Nagelkerke R2 statistics show that the independent variables explained 31.3% and 41.9% of significant CAD variance, respectively. The Hosmer and Lemeshow test for the goodness of model fit reveal that significance equals 0.418 (no significant differences between actual and predicted values), which indicates well-fitting of our predicting logistic regression model. A marked improvement showed a correct classification rate in our logistic model for 76.4% of the cases compared to 56.4% in the null model.

Table 3. Risk factors associated with CAD from Multiple Logistic Regression.

Variable		Adjusted β Coefficient	Standard error	Adjusted Odds Ratio (95.0% CI)	Wald statistics	P-value
Age		0.12	0.03	1.12 (1.06-1.18)	18.65	<0.001*
Obesity	Obese	0.87	0.33	2.39 (1.26-4.55)	7.09	0.008*
	Non-Obese	-	-	1 [Reference]	-	-
Lifestyle	Sedentary lifestyle	0.76	0.35	2.14 (1.09-4.22)	4.90	0.027*
	Regular exercise	-	-	1 [Reference]	-	-
Smoking	Currently smoking	1.06	0.33	2.89 (1.51-5.52)	10.53	0.001*
	Non-smoking	-	-	1 [Reference]	-	-
Family history of heart disease	Yes	1.13	0.52	3.12 (1.11-8.68)	4.68	0.030*
	No	-	-	1 [Reference]	-	-
Hypertension	Yes	1.01	0.42	2.74 (1.22-6.18)	5.90	0.015*
	No	-	-	1 [Reference]	-	-
Diabetes mellitus (DM)	Yes	1.47	0.69	4.35 (1.13-16.76)	4.55	0.033*
	No	-	-	1 [Reference]	-	-

* Significant at 0.05 level of significance

4. Discussion

The health economics of care pathways in the Gaza Strip have come under greater scrutiny due to increasing financial pressures on healthcare providers resulting from a scarcity of medical supplies. As a result of the overestimation of CAD using traditional risk tables, noninvasive testing has been utilized to improve risk stratification and initiate appropriate management to reduce the dependence on invasive investigations. Global burden of disease assessment of risk characteristics in the Middle East and North Africa revealed that among the risk factors of CAD, high blood pressure (BP) ranked as the first, followed by obesity, DM, and smoking [18].

To the best of our knowledge, few studies have explored the prevalence and investigated the risk factors for CAD in the Gaza Strip. Ours is the first study to examine criteria for patient selection for ICA. Patients with CVD risk place a substantial economic burden on the budget of Gaza Strip hospitals. ICA is considered one of the best choices for diagnosis of CAD and remains the cornerstone of diagnosis and treatment of patients with significant or unstable chest pain symptoms.

The low diagnostic yield of elective ICA was prominent in our study, with only 56.4% of patients who underwent ICA determined to have significant CAD. Consequently, baseline characteristics such as gender, age, obesity, lifestyle, smoking status, family history of heart disease, LDL, high BP and DM were collected to inform patient selection for ICA in suspected CAD. Not surprisingly, in multiple logistic regression analysis, we observed that the strongest independent predictors of the presence of significant CAD at the ICA were the traditional risk factors of age, obesity, lifestyle, smoking, the presence of a family history of heart disease, hypertension, and DM.

The strongest association was found for DM; the odds of having a significant CAD are 4.35 times higher in diabetic versus non-diabetic patients. Family history of heart disease remains a significant predictor with an odds ratio of 3.12. Smoking was assessed only qualitatively through patient reports, whereas quantitative characteristics such as exposure time and intensity of consumption were not considered. Current smokers were 2.89 times higher risk of developing CAD than non-smokers. Hypertension and obesity also increase the risk of developing CAD, with odds ratios of 2.74 and 2.39, respectively. With respect to lifestyle, regular exercise is associated with significant reductions in the incidence of CAD, which is reported in an odds ratio 2.15 times lower relative to a sedentary lifestyle.

Consistent with our results, a study by Khwaiter and Abed [19] identified the risk factors associated with CAD in Gaza and reported that overweight, DM, female gender, a sedentary lifestyle, and smoking increased the risk of CAD occurrence. In parallel, a study conducted by Eljedi and Mushtaha [20] to identify the risk factors of CAD in Palestinian patients undergoing ICA revealed that the most common risk factors were physical inactivity (OR 3.96, P=0.002), hypertension (OR 2.73, P<0.001), DM (OR 2.21, P=0.006), smoking (OR 1.96, P=0.031), and positive family history (OR 2.12, P=0.012). Persons with hypertension and DM were more vulnerable and had 2.73 and 2.18 times the odds of developing CAD, respectively. Positive family history of CAD was strongly correlated with developing CAD among the study group.

Applying a structured lifestyle program in clinical practice to change unhealthy habits will enhance the care of patients diagnosed with hypertension, diabetes and cardiovascular risk [21]. Furthermore, a structured lifestyle program in primary care contributes to significant improvements of CVD risk factors and the reduction of 10-year risk for CVD for both men and women at high cardiovascular risk [22].

Costa et al. [23] assessed the efficacy of patient selection for ICA in suspected CAD. Their results indicated that the odds of having a significant CAD were 3.95 times higher for males than for females, 1.15 times higher for each year of patient age, and 2.02 times higher for patients who have high cholesterol.

A study by Shahwan et al. [24] explored the epidemiology of CAD and associated risk factors in the Gaza–Palestine community. Their results revealed that the associated risk factors were obesity (47.8%), hypertension (28.4%), current smoking (23.2%), DM (19.1%), high cholesterol level (8.8%), and low physical activity (48.3%).

Medical staff perceptions and diagnostic interest in ICA in Gaza-Palestine was explored in a recent study conducted by Mansour et al. [25]. Their results revealed that risk factors such as the family history of heart disease, obesity, high cholesterol and DM were more frequent in patients with significant CAD. Remarkably, 96.5% of CAD patients had high cholesterol, 94.3% were obese, 92.2% were diabetics, and 72.3% had a family history of heart disease.

5. Conclusion

The low diagnostic yield of elective ICA was a prominent feature of the current study, with approximately 43.6% of subjects found to have non-significant CAD. Consequently, baseline characteristics such as sex, age, obesity, lifestyle, smoking status, family history of heart disease, LDL, hypertension, and DM should be considered when selecting possible CAD patients for ICA. These traditional risk factors are strong independent predictors for the presence of significant CAD. The study concludes that ICA should be considered for patients whose history and physical examination and whose clinical characteristics and results of noninvasive testing indicate a high likelihood of severe stenosis.

Conflict of Interest Disclosures

The authors declare no conflict of interest concerning the research, authorship, or publication of this article.

Ethical Statement

Ethical approval for this study was obtained from the Helsinki Committee, Gaza strip-Palestine.

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