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Prevalence and correlated factors for chronic total occlusion in patients with coronary artery disease in Iraqi Kurdistan

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Abstract

Patients with significant coronary artery disease often have at least one vessel with Chronic Total Occlusion (CTO) as demonstrated by coronary angiography. However, the prevalence and determinants of CTO differ according to ethnicity. We aimed to investigate the prevalence and determinants of CTO in the Iraqi Kurdistan population in 2015. Clinical and angiographic data were collected in consecutive patients that underwent coronary angiography at our institution between January and December 2015. Coronary artery disease (CAD) was determined as 50% diameter stenosis in one coronary artery and CTO as total coronary artery occlusion of 3-month duration. Among 260 patients diagnosed with ischemic coronary artery disease and undergone coronary angiography, 28.5% (n=74) were diagnosed to have at least one CTO vessel and 69 (26.5%) patients had a previous history of myocardial infarction. CTOs were located in the left anterior descending coronary artery in 45% of patients while in the right coronary artery in 32%. CTO patients were substantially older (61 vs 56 years; p <0.0001) and more likely to live in non-urban areas. They frequently had more hypertension, dyslipidemia, diabetes mellitus, previous myocardial revascularization, being an exsmoker, and renal dysfunction as compared to patients without CTOs. At univariate analysis, a previous history of coronary artery bypass graft (CABG) surgery was the only predictor of having a diagnosis of CTO. Patients diagnosed with CTO in Iraqi Kurdistan had several comorbidities including cardiovascular risk factors and renal dysfunction. Previous CABG was the only predictor of CTO diagnosis.

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Introduction

Almost half of the patients with a significant coronary artery disease (CAD) have at least one chronic total occlusion (CTO) demonstrated by coronary angiography. Only 10% of all percutaneous interventions (PCIs) are performed for the revascularization of CTO and the majority of patients with CTOs are referred for coronary artery bypass graft surgery (CABG). Different prevalence of CTO in patients undergoing coronary angiography has been reported in the literature, between 16% and 52%.[1-3] Indeed, while Fefer *et al.*[1] reported a prevalence of CTOs of 18.4% in 1,697 patients in Canada, other authors reported higher percentages of CTO, from 33% in Germany[4] to 52% in the USA.[3] In selected populations, the highest prevalence (80%) of CTO has been found in patients with prior CABG. CTO patients have been seen to face a more likelihood of surgery and medical treatment[4] and both cardiac and non-cardiac comorbidities, frequently present with stable angina and have a more extensive stage of CAD compared to the patients without CTOs.[2]

Several factors have been reported to contribute to CTO in patients with CAD, including previous myocardial infarction, gender,[1] previous CABG,[1,5,6] presence of peripheral arterial occlusive disease, older age, and current smoking.[7,8] There is a lack of data on the prevalence and clinical correlated factors of CTOs[1,2,4] in Iraqi Kurdistan, although ethnicity can affect the presentation and the determinants of CAD. However, this data would be very important for health policymakers to focus on the reduction of the factors contributing to CTO according to the high economic, health, and social burden of the disease. Therefore, we investigated the prevalence of CTOs in patients with CAD and with or without prior CABG and explored the clinical risk factors associated with CTOs in the Iraqi Kurdistan population.

Materials and Methods

Study Design

The coronary angiograms and medical records of patients who visited Duhok Cardiac Center (Iraqi Kurdistan) between 1st January 2015 and 31st December 2015 were reviewed retrospectively and consecutively. The clinical information of the medical records including clinical history, comorbidities, demographic characteristics, results of cardiac catheterization, and procedural data was analyzed for this study.

Patients who underwent urgent or non-urgent coronary angiography and were diagnosed with CTO with or without prior CABG or PCI including both genders without age restriction were in included in this study. Patients with acute ST-segment elevation myocardial infarction taken for primary PCI were not included in the study. The electrocardiograms were interpreted by a cardiologist (SSM) in accordance with revised European Society of Cardiology/American College of Cardiology Foundation/American Heart Association/World Heart Federation definitions for the electrocardiographic definition of MI.[9] The patients who underwent coronary angiography were discharged between 1 and 2 days of admission whether underwent PCI or planned for elective CABG.

Ethical Considerations

The protocol of the study was approved by the scientific committee of the College of Medicine, University of Duhok, and Scientific Division of Researches from Duhok General Directorate

Table 1. Baseline and clicnial charactersictis between CTO and non-CTO pateints.

Characteristics (n=260)	CTO group (n=74, 28.46%)	Non-CTO group (n=186, 71.54%)	P-value (Two-sided)
Age (year); Mean/SD	61.30 (8.62) Range: 43-85	55.99 (10.40) Range: 25-84	<0.0001*
Gender/Male	49 (66.2)	111 (59.7)	0.328**
Occupation/Sedentary	58 (78.4)	126 (67.7)	0.089**
Residential area/Urban	33 (44.6)	132 (71.0)	<0.0001**
Catheterization Procedure Time, Min	14.93 (6.42)	13.47 (5.88)	0.092*
Renal Failure	4 (5.4)	6 (3.2)	0.477***
Cardiovascular Diseases	60 (81.1)	116 (62.4)	0.004**
Smoking			
Current Smoker	26 (35.1)	79 (42.5)	0.015**
Non-Smoker	29 (39.2)	86 (46.2)	
Ex-smoker	19 (25.7)	21 (11.3)	
Clinical characteristics			
Hypertension	57 (77.0)	117 (62.9)	0.029**
Dyslipidemia	47 (63.5)	72 (38.7)	<0.0001**
Diabetes Mellitus	38 (51.4)	60 (32.3)	0.004**
Pacemaker Presence	0 (0.0)	2 (1.1)	1.00***
Blood Urea	40.99 (10.62)	36.00 (10.23)	.001*
Serum Creatinine	1.11 (0.31)	0.96 (0.55)	.006*
Cardiac characteristics			
ECG of Patient			<0.0001**
Normal	8 (10.8)	41 (22.0)	
Old MI	33 (44.6)	36 (19.4)	
Other changes	33 (44.6)	109 (58.6)	
Exercise ECG			
Positive	10 (13.5)	67 (36.0)	<0.0001**
Negative	0 (0.0)	1 (0.5)	
Not done	64 (86.5)	118 (63.4)	
Echo LVEF			<0.0001**
EF>50%	35 (47.3)	156 (83.9)	
EF= 35-50%	35 (47.3)	30 (16.1)	
EF <35	4 (5.4)	0 (0.0)	
Vasovagal Reaction Complication	0 (0.0)	2 (1.1)	1.00*; OR: 1.40 (95% CI: 1.30-1.51)
Bleeding or Hematoma Complications	1 (1.4)	1 (0.5)	0.489**; OR: 2.53 (95% CI: 0.16-41.05)
Approach of CAG			
Right Radial	57 (77.0)	165 (88.7)	0.020**
Left Radial	8 (10.8)	5 (2.7)	
Right Femoral	9 (12.2)	14 (7.5)	
Left Femoral	0 (0.0)	2 (1.1)	
CABG	7 (9.5)	2 (1.1)	0.003**; OR: 9.61 (95% CI: 1.95-47.42)
Previous PCI	13 (17.6)	24 (12.9)	0.331*; OR: 1.44 (95% CI: 0.69-3.00)
Fluoroscopy Time/Minute	3.36 (3.00)	2.74 (2.10)	0.107***
Peripheral Artery Disease	2 (2.7)	5 (2.7)	1.00***; OR: 1.00 (95% CI: 0.19-5.30)

CAG: Coronary Angiography; LVEF: left ventricular ejection fraction; PCI: Percutaneous Coronary Intervention; ECG: Electrocardiography; MI: Myocardial Infarction; EF: Ejection Failure; OR: Odds Ratio. The bold numbers show the significant differences. *Independent t-test, ** Chi-square test, and *** Fishers' exact test were performed for statistical analyses.

of Health-Duhok registered in reference number 12072017-5 on 12th July 2017. The confidentiality of the personal information of patients was protected in this study.

Diagnostic and measurement principles

CAD was diagnosed as ≥50% diameter stenosis in ≥1 coronary artery. CTO was defined as total coronary artery occlusion of ≥3 months. The CTO means occlusion of 3 months or more duration, hence we depended on previous angiography (>3months) if available with occlusion this angiographically confirmed CTO. Also, we depended on history by eliciting previous myocardial infarction or angina symptoms before 3 months or more. Although sometimes coronary occlusions develop silently but if symptoms developed and angiography showed occlusion so it indicates the reason for symptoms.

Statistical Analysis

Continuous parameters were presented as a mean and standard deviation and compared using an independent t-test. Nominal parameters were presented as frequency and percentages and compared using Pearson's chi-square test or Fishers' exact tests, as appropriate. A two-sided p-value <0.05 was considered statistically significant to reject the null hypothesis. Univariate analysis of variance was performed to determine the predictors of CTO diagnosis in CAD patients. Statistical calculations were performed using SPSS version 25:00 (IBM: Corp. Chicago).

Results

During the study period, a total of 260 consecutive patients underwent coronary angiography and were diagnosed with CAD. Seventy-four (28.5%) patients have at least one CTO compared to 186 (71.5%) patients without CTO. Among the patients with CTO, 64 (24.6%) had a single vessel CTO while 10 (3.8%) had a double vessel CTO (Table 1).

Of the total 74 patients diagnosed with CTO, 33 (44.6%) had one occlusion on the left anterior descending artery (LAD), 11 (14.9%) on the left circumflex artery (LCX), 24 (32.4%) on the right coronary artery (RCA), 1 (1.4%) on LAD and LCX, 4 (5.4%) on LAD and RCA, and 1 (1.4%) on LCX and RCA.

Compared to patients without CTOs, CTO patients were more likely to have prior CABG (9.5% vs 1.5%; P=0.003), cardiovascular comorbidities (81.1% vs 62.4%; P=0.004), hypertension (77.0% vs 62.9%; P=0.029), dyslipidemia (63.5% vs 38.7%; P<0.0001), diabetes mellitus (51.4% vs 32.3%; P=0.004), and be older (61.30 vs 55.99 years; P<0.001). Furthermore, non-CTO patients were more likely to live in urban areas (71.0% vs 44.7%; P<0.0001). In addition, non-CTO patients were more likely were current smokers (42.5% vs 35.1%) while the CTO patients were more likely to be ex-smokers (25.7% vs 11.3%, P=0.015) see Table 1. Patients diagnosed with CTO were more likely to have an old myocardial infarction (44.6% vs 19.4%; P<0.0001), more likely to have a positive ECG exercise test (36.0% vs 13.5%; P<0.0001), to have a mild-to-moderate reduction in left ventricle ejection frac-

Table 2. Univariate analysis of variance of CTO predictors.

Dependent variable: CTO or non-CTO Predictors	Mean Square	F	Sig.	Partial Eta Squared (Effect Size)
Sex	0.044	0.054	0.816	0.000
Occupation	0.250	0.311	0.578	0.003
CABG	6.262	7.792	0.006	0.061
Previous PCI	0.114	0.142	0.707	0.001
Cardiovascular diseases	2.062	2.565	0.112	0.021
Peripheral Artery Disease	0.080	0.099	0.754	0.001
Smoking	0.020	0.025	0.975	0.000
Hypertension	1.174	1.461	0.229	0.012
Dyslipidemia	0.018	0.023	0.880	0.000
Diabetes mellitus	0.033	0.041	0.840	0.000
Bleeding Complication	0.554	0.689	0.408	0.006
Age	0.452	0.563	0.984	0.167
Procedure Time	0.716	0.891	0.594	0.123
Blood Urea	0.674	0.838	0.687	0.148
Serum Creatinine	0.515	0.640	0.930	0.149

Table 3. Comparison of occluded vessels among patients with previous CABG, PCI, both CABG and PCI, and medical therapy.

Study Groups	Previous therapy types CABG	PCI	Medical therapy	Both CABG and PCI	Test of Significance
CTO	6 (75.0)	12 (33.3)	55 (25.6)	1 (100.0)	0.005 Fishers' Exact Test
Non-CTO	2 (25.0)	24 (66.7)	160 (74.4)	0 (0.0)	

tion demonstrated by echocardiography (47.3% vs 16.1%; P<0.0001). The patients in two groups of the study were comparable in vasovagal reaction complication (P=1.00), bleeding or hematoma complications (P=0.489), previous PCI (P=0.331), renal failure (P=0.447), fluoroscopy time/minute (P=0.107), and peripheral artery disease (p=1.00), see Table 1.

At univariate analysis, CTO and non-CTO patients were considered a dependent variable and clinical and general characteristics of patients as predictors. The presence of previous CABG operation was the only predictor of diagnosis with CTO during coronary angiography (P=0.006) with a variation of 6.1% compared to those not-underwent CABG, see Table 2.

Following the univariate analysis, the association of having CTO vessels in patients with previous CABG, PCI, both CABG and PCI, and non-occulted vessels was examined, as reported in Table 3. CAD patients undergone CABG surgery previously were more likely to be diagnosed with CTOs (75.0%) compared to those with previous PCI (33.3%), P=0.005.

Discussion

The overall prevalence of CTO among patients diagnosed with CAD in 2015 was 28.46%. The studies conducted on CTO reported different prevalence rates. Jeroudi *et al.*[2] reported a prevalence of CTO of 31% in patients with CAD with and without prior CABG (37% in all patients and 46% in CAD patients). They found 89% of coronary CTOs in patients with CAD and prior CABG, similarly to findings of our study (77.8%, data not shown). In a large prospective study conducted in three Canadian registries, the prevalence of CTO was 18.4% in CAD patients (defined as 50% stenosis in one vessel) without prior CABG and 54% in CAD patients with prior CABG.[1] Similarly, 22.4% in 500 patients in Egypt[10] and 33% in a German multicenter prospective registry.[4]

In this study, we found that the patients with ischemic coronary artery diseases and recognized with at least one CTO vessel have more comorbidities compared to those without CTO. Previous studies are in agreement with these findings: indeed, Jeroudi *et al.*[2] showed that CTO patients were more likely to have comorbidities, such as diabetes mellitus, CVA (Cerebrovascular accident), CHF (Congestive heart failure), MI (myocardial infarction), PCI, ex-smoker, and peripheral artery disease. Between 30 and 50% of patients with CTO have a history of MI.[11,12]

The cardiologists are more likely to refer the patients with CTO for CABG and less to PCI.[1,13,14] The choice of coronary revascularization strategy highly depends on the cardiologist's expertise and local practice patterns. We showed that previous CABG surgery was the only predictor of the future CTO in CAD patients in this region presenting a hint to the clinicians to consider PCI rather than CABG with taking into account the patients' status as well. Although the current study did not focus on the comparison of PCI and CABG, it seems that CABG is more preferred to PCI in cardiologists in this region. However, PCI techniques for CTOs have been shown to have high procedural success rates and low risk for procedural complications,[15-18] improve quality of life by the reduction in angina symptoms, an improvement in exercise capacity, improvement in left ventricular function, and reduce the need for subsequent CABG.[19,20] Although making a difference between CABG and PCI is beyond the scope of the present study, the cardiologists must select the best revascularization procedure according to the probability of better outcomes, such as quality of life, preventing future non-fatal events, or prolonging life[21] and this decision should be only in part influenced by differences among the regions.

The present study showed that the previous CABG is the only predictor of CTO in CAD patients. CTOs in patients with CAD and undergone CABG exhibit more advanced stable atherosclerosis and clinical trials have reported that atherosclerosis progresses more rapidly in grafted arteries than in non-grafted arteries.[22]

The need for repeated interventional/surgical procedures among patients following CABG is indicated by the condition of the coronary artery grafts and progressive atherosclerosis of the inherence coronary arteries. The studies have shown that within 10 years after CABG, only 60% of vein grafts and 90% of internal mammary artery grafts remain patent. The data reported in the literature have confirmed that up to 20% of autovenous grafts result in occlusion within the first postoperative year.[23] An accelerated progression of the process in the bypassed coronary artery was seen following a post-operative coronarography resulting in the progression of the stenotic lesions to total coronary occlusion. The current stenotic lesions are not reflected in the progression of the atherosclerotic process but also in changes in intracoronary circulation following the bypass insertion.[6,22] In agreement with these findings, the present study showed that the patients with a previous history of CABG were more likely to be diagnosed with CTO vessels compared to those patients with PCIs. Although this finding can be influenced by the presence of confounding factors, such as the concurrent higher burden of comorbidities in patients undergone CABG, a careful selection of the best revascularization procedure according to the current new evidence is mandatory.

Strengths and limitations of the study

The findings reported in the current study must be interpreted in light of the study design and sampling method. The patients were not followed up for a success rate of the CABG and PCI owing to the retrospective design of the study. In addition, the data of this monocentric study cannot be generalized to other settings. Duhok Cardiac Center is the only public clinical setting for cardiovascular diseases in Duhok province, strengthening the study according to the fact that the vast majority of the patients have been recruited with different degrees of complexity.

Recommendations

Since the previous CABG was determined to be the only predictor of CTO in this region, we recommend that the patients who have undergone CABG be followed for the possible CTO complications.

Conclusions

The present study determined the prevalence of CTO in patients were undergone coronary angiography in Iraq. The patients diagnosed with CTO notably tended to be older and sicker, as shown by the greater prevalence of all risk factors. They were more likely to be diabetic, ex-smoker, older, and have comorbidities such as prior CABG and PCI, cardiovascular diseases, hypertension, and dyslipidemia. The presence of prior CABG surgery was identified as the only predictor of a diagnosis of CTO.

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