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RESEARCH ARTICLE
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Prevalence of Coronary Aneurysm in Patients Undergoing PCI with Stenting

Muhammad Kashif Iltaf[1]*

[1] Assistant Professor, Cardiology, Nowshera Medical College / Qazi Husain Ahmad Medical Complex.
Email: drkashifiltaf@gmail.com
Corresponding Author
Muhammad Kashif Iltaf
Assistant Professor, Cardiology, Nowshera Medical College / Qazi Husain Ahmad Medical Complex.
Email: drkashifiltaf@gmail.com

ABSTRACT

Background: Though rare, coronary artery aneurysm (CAA) is a serious potential complication of PCI (stenting). The incidence is highly variable from one population to the next, from 0.3% to 6.0%. The prevalence of drug-eluting stent associated CAA has been reported to range from 0.2% to 2.3%, and is increasing as the use of drug-eluting stents (DES) has risen. However, there is still limited data of Pakistani population.

Objective: To find the prevalence, clinical features, angiographic features, and short term outcome of coronary artery aneurysm in patients who had PCI with stenting during one-year period at Nowshera Medical College/Qazi Husain Ahmad Medical Complex hospital Nowshera.

Methodology: Prospective observational study, conducted in Department of Cardiology, Qazi Husain Ahmad Medical Complex hospital Nowshera from 01st January 2022 to 31st December 2022. In all 250 patients were enrolled who had received PCI with stenting. Luminal dimunition was considered to be luminal dilatation greater than 50% of the adjacent reference vessel diameter (RVD). All patients were clinically assessed, and had laboratory tests and follow-up coronary angiography or CT coronary angiography at 6–12 months. All the analysis of data was performed under the SPSS version 26.0.

Results: Of the 250 patients, 7 patients (2.8%) had CAA. The average age of the patients was 58.4 ± 9.2 years and male predominance (71.4%). In 85.7% of the CAA cases, drug-eluting stents were employed. The most frequent location was the right coronary artery (42.9%) followed by the left anterior descending artery (28.6%). During follow-up MACE were seen in 28.6% of CAA patients.

Conclusion: The rate of coronary artery aneurysm after PCI with stenting in our population was 2.8%, which was within the lower range of the international reports. Common factors associated with DES implantation were male gender and involvement of the RCA.Coronary artery aneurysm is a relatively rare condition, which occurs in 0.5% of cases of stenting and it is relatively uncommon in Pakistan.

KEYWORDS: Coronary artery aneurysm, percutaneous coronary intervention, stenting, prevalence, Pakistan..

INTRODUCTION

Coronary artery aneurysm (CAA) is a rare, but increasingly common, vascular anomaly defined by the local expansion of a coronary artery segment that is more than 1.5 times the diameter of the normal reference vessel.(1) If the dilated segment is present all the way around the vessel it is called a true aneurysm, if it is present in a contained way with a neck that remains attached to the arterial lumen it is called a pseudoaneurysm.(2) The incidence of coronary artery aneurysm in those undergoing coronary angiography has different prevalence in different populations and geographic region. The prevalence in large angiographic series ranges from 0.3% to 5.3%, with an estimated prevalence of 1.4% from autopsy studies.(3) The epidemiology of CAA is unique, however, when it concerns patients who have already had percutaneous coronary intervention (PCI) with stenting.(4) The occurrence of coronary artery aneurysms in association with stents is a distinct and growing iatrogenic condition, which has been increasingly reported with the widespread use of drug-eluting stents (DES).(5) The incidence of stent-related CAA after bare-metal stent (BMS) implantation has been estimated at around 0.2% while first generation DES, especially the paclitaxel-eluting stents, has been reported to have higher incidence rates of 1.0% to 3.4%.(6) However, more recent data from large implants registries indicate that the rate of CAA post-second generation DES implantation is between 0.2% and 2.3% per patient and 0.8% per lesion.(7) Mechanical factors include excessive high pressure inflation of the balloon, which creates deep injury to the arterial wall; dissection flaps that remain after the stent is in place to compromise the vessel wall; overlapping stents that cause areas of increased local stress; deployment in vessels that are excessively tortuous or heavily calcified; and the use of stents that are oversized when compared with the reference vessel diameter.(8, 9) Biological factors focus on the inflammatory reaction that occurs in response to the polymer of the stent, the drug-eluting coating, and the metal struts.(10) Endothelialization is delayed especially in DES, leaving the underlying vessel wall vulnerable to chronic inflammatory stimuli and potentially leading to vessel remodeling and aneurysmal enlargement.(11) High levels of baseline inflammatory markers, such as high-sensitivity C-reactive protein (hs-CRP > 1mg/L), have been found to be independently linked to formation of CAA after PCI.(12) Stent Associated Coronary Artery Aneurysms in the region are becoming common and gaining importance with their increasing prevalence and use, making it imperative to understand the prevalence and characteristics of these aneurysms in the region to enhance patient care and formulate region specific management guidelines.(13)

This prospective observational study was thus designed to fill this important knowledge gap. The main aim was to try to find out the incidence of CAA in patients who had received PCI with stents between now and now at Qazi Husain Ahmad Medical Complex hospital, Nowshera during 1 year period. Secondary goals were to describe clinical and angiographic characteristics of affected patients, to try and delineate possible risk factors for development of CAA, and to assess the short-term clinical results at 12-month follow-up. The generation of local data aims to guide the clinical practice, surveillance strategies, and increase the understanding of this clinically significant complication in the Pakistani population.

METHODOLOGY

Study Design and Setting: The study was a prospective observational study that was done in the Department of Cardiology of Nowshera Medical College/Qazi Husain Ahmad Medical Complex hospital in Nowshera, Pakistan. This study was conducted for one year.

Study Population: A total of 250 patients who underwent PCI with stenting during the study period were enrolled. Subjects included those who had PCI with a stent, successful procedure, and were ≥18 years old and received PCI for any reason (stable angina, unstable angina, NSTEMI or STEMI). Individuals who had a previous history of coronary artery bypass grafting, prior history of Kawasaki disease, congenital coronary anomaly and the ones who did not give informed consent were excluded.

Inclusion and Exclusion Criteria

Inclusion Criteria:

Patients 18 years of age or older at time of index procedure.

Patients who had completed percutaneous coronary intervention (PCI) with at least one coronary stent (drug-eluting stent or bare-metal stent) for any clinical indication (stable angina, unstable angina, non-ST-elevation myocardial infarction [NSTEMI] or ST-elevation myocardial infarction [STEMI]).

Those patients who had signed informed consent forms to participate in the study and to have their clinical data collected and analyzed.

Patients who were followed at 6-12 months after any PCI to assess for the development of a coronary artery aneurysm by undergoing coronary angiography or a CT coronary angiography.

Exclusion Criteria:

Patients who had undergone a prior coronary artery bypass grafting (CABG).

Patients who have a known diagnosis of Kawasaki disease, congenital coronary artery abnormalities, or connective tissue disorders (e.g., Ehlers-Danlos syndrome, Marfan syndrome) that put them at risk for coronary artery ectasia or aneurysm formation without iatrogenic causes.

Patients who were previously receiving PCI in the same target vessel (repeat stenting) which might have affected the evaluation of aneurysm formation.

Patients with severe valvular heart disease or cardiomyopathy who are undergoing surgery which may affect the clinical outcome and follow-up.

Patients with active malignancy or other life-threatening conditions (with estimated life expectancy <1 year).

Women who are pregnant or breastfeeding.

Patients who did not want to give informed consent or did not show up for imaging at the 6-12 month time point.

Patients who had insufficient or incomplete angiographic/cardiological data to make a proper evaluation of the coronary artery aneurysm.

All patient data included demographic data (age, gender, and comorbidities), clinical presentation, and procedural details (type of stent, number of stents, target vessel, stent diameter and length). Baseline laboratory tests such as complete blood count, renal function tests, lipid profile, and high-sensitivity C-reactive protein (hs-CRP) were done.

The definition for Coronary Artery Aneurysm (CAA) was defined as luminal dilatation more than 50% of the diameter of the adjacent normal reference vessel. At 6–12 months after PCI, all patients had follow-up coronary angiography or CT coronary angiography performed to look for the development of CAA.

Follow-up and Outcomes: All patients were followed up for at least one year. Clinical endpoints evaluated were all-cause death, non-fatal myocardial infarction, target vessel revascularization, stent thrombosis and major adverse cardiovascular events (MACE), a composite of all-cause death, non-fatal myocardial infarction and target vessel revascularization.

Data analysis: All data were analyzed using SPSS 26.0 (IBM Corp., Armonk, NY, USA). Means ± standard deviations were used for continuous variables and frequencies and percentages were used for categorical variables. Independent t-test was used for continuous variables and chi-square test was used for categorical variables to compare CAA group with non-CAA group. A P value <0.05 was deemed significant.

Ethical considerations: Study was approved by the Institutional Review Board of Nowshera Medical College/Qazi Husain Ahmad Medical Complex hospital. All participants gave written informed consent before entering the study.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics

Characteristic	Total (N=250)	CAA Group (n=7)	Non-CAA Group (n=243)	p-value
Age (years), mean ± SD	56.2 ± 10.4	58.4 ± 9.2	56.0 ± 10.5	0.42
Male Gender, n (%)	168 (67.2)	5 (71.4)	163 (67.1)	0.81
Diabetes Mellitus, n (%)	98 (39.2)	3 (42.9)	95 (39.1)	0.84
Hypertension, n (%)	142 (56.8)	4 (57.1)	138 (56.8)	0.99
Dyslipidemia, n (%)	112 (44.8)	3 (42.9)	109 (44.9)	0.92
Smoking, n (%)	87 (34.8)	3 (42.9)	84 (34.6)	0.65
Family History of CAD, n (%)	65 (26.0)	2 (28.6)	63 (25.9)	0.87
BMI (kg/m²), mean ± SD	27.4 ± 4.2	28.1 ± 4.5	27.3 ± 4.2	0.56
hs-CRP (mg/L), mean ± SD	4.8 ± 6.2	8.6 ± 7.8	4.6 ± 6.1	0.04*

Statistically significant (p<0.05); CAD: Coronary Artery Disease; BMI: Body Mass Index; hs-CRP: High-

sensitivity C - reactive protein

Table 2: Angiographic and Procedural Characteristics

Characteristic	CAA Group (n=7)	Non-CAA Group (n=243)	p-value
Target Vessel, n (%)			
- LAD	2 (28.6)	98 (40.3)	0.52
- LCx	1 (14.3)	52 (21.4)	0.65
- RCA	3 (42.9)	67 (27.6)	0.37
- LMCA	0 (0)	8 (3.3)	0.62
- Multivessel	1 (14.3)	18 (7.4)	0.48
Stent Type, n (%)			
- Drug-Eluting Stent (DES)	6 (85.7)	189 (77.8)	0.62
- Bare-Metal Stent (BMS)	1 (14.3)	54 (22.2)	0.62
Number of Stents, mean ± SD	1.7 ± 0.8	1.4 ± 0.6	0.21
Stent Diameter (mm), mean ± SD	2.9 ± 0.4	3.1 ± 0.5	0.34
Stent Length (mm), mean ± SD	24.3 ± 8.2	20.7 ± 7.6	0.18
Lesion Length >33 mm, n (%)	3 (42.9)	52 (21.4)	0.17
Chronic Total Occlusion, n (%)	2 (28.6)	31 (12.8)	0.22
Post-dilatation performed, n (%)	4 (57.1)	98 (40.3)	0.37

LAD: Left Anterior Descending; LCx: Left Circumflex; RCA: Right Coronary Artery; LMCA: Left Main Coronary Artery

Table 3: Clinical Outcomes at 12-Month Follow-up

Outcome	CAA Group (n=7)	Non-CAA Group (n=243)	p-value
All-cause Mortality, n (%)	1 (14.3)	8 (3.3)	0.12
Non-fatal Myocardial Infarction, n (%)	1 (14.3)	6 (2.5)	0.08
Target Lesion Revascularization, n (%)	1 (14.3)	9 (3.7)	0.16
Stent Thrombosis, n (%)	0 (0)	3 (1.2)	0.77
MACE (Composite), n (%)	2 (28.6)	18 (7.4)	0.04*
Heart Failure, n (%)	1 (14.3)	12 (4.9)	0.28
Rehospitalization for Cardiac Causes, n (%)	2 (28.6)	24 (9.9)	0.10

Statistically significant ($p<0.05$); MACE: Major Adverse Cardiovascular Events

DISCUSSION

The current study aimed to assess the prevalence, clinical features, and prognosis of coronary artery aneurysm in 250 patients that received PCI with stenting at Qazi Husain Ahmad Medical Complex hospital Nowshera during a year. In our cohort, the prevalence of CAA was 2.8% which is in the lower range of the globally reported incidence (0.3% to 6.0%).

The results of our study are similar to some international studies. A Korean study of second generation DES implantation showed a 1.02% per patient implantation rate, lower than the prevalence we observed.(14) This difference could be attributed to variations in study populations, stent types and follow-up methods. A study in

the United States evaluating STEMI patients who underwent PCI, however, showed a prevalence of only 0.17%, which is much lower than our results. This difference may be due to the fact that we studied all-comers who underwent PCI and not only STEMI patients, and because CAA might be more common in elective follow-up angiography.(15) There has been 0.2% to 2.3% incidence of CAA after DES implantation reported, and our prevalence is slightly higher than that. This could be due to the greater percentage of DES use in our patient population (85.7% in CAA group compared to 77.8% overall) and the fact that we had a longer follow-up period for late developing aneurysms.(16) Furthermore, a systematic review showed that the range for the incidence of DES-associated CAA was 1-3.4% in clinical registries, consistent with our results. Concerning distribution of CAA, the RCA was the most common vessel involved (42.9%), followed by the LAD (28.6%). This is in line with the earlier report indicating RCA is a predilection site for the formation of CAA.(17) The mechanism of the RCA's predominance may relate to the mechanical properties of the vessel, such as vessel tortuosity, and a greater prevalence of calcific lesions in the RCA.(18)In terms of risk factors, patients who developed CAA had significantly higher baseline hs-CRP levels compared to those without CAA (8.6 ± 7.8 mg/L vs. 4.6 ± 6.1 mg/L, p=0.04).(19) This finding is consistent with previous research which showed that high baseline inflammatory status, defined as hs-CRP > 1 mg/L, predicted CAA formation after STEMI. Delayed endothelialization and remodeling of the vessel wall following stent implantation can lead to aneurysmal dilatation as a result of the inflammatory response.(20)However, we noted that at least some of these procedural characteristics occurred more frequently in the CAA group, with lesion length >33 mm (42.9% vs. 21.4%) and CTO (28.6% vs. 12.8%).(21) The results are similar to the previously described risk factors, including lesion length >33 mm and chronic total occlusion. This may be because of the small number of cases in this study that were diagnosed as CAA.(22) Results of 12-month clinical outcomes showed the CAA group had significantly higher MACE rates than non-CAA group (28.6% vs. 7.4%, p=0.04). This is similar to the in hospital MACE rate of 14.3% and follow up MACE rate of 38.1% at 18.9 months in the Coronary Artery Ectasia and Aneurysm Registry (CAESAR).(23) The international coronary artery aneurysm registry (CAAR) also found that 37.1% of patients experienced MACE at a median of 44.8 months after taking part in the study. This is a clinically important complication and should be monitored particularly in CAA patients who had a higher MACE rate.(3)Patients with CAA have an estimated 71% 5-year survival rate. This increased mortality rate in the CAA group (14.3% vs 3.3%) is a concerning trend, which needs to be investigated by further longer follow-up.(24) The mechanisms of stent-associated CAA are complex. Residual dissection, deep arterial wall injury, and/or aggressive post-dilatation during stent deployment, can cause weakened vessel wall and lead to aneurysmal dilatation. The inflammatory reaction induced by the delivery of the stent polymer and elution of the drug also may play a role in vessel wall remodeling.(25) The higher incidence of CAA in patients with elevated hs-CRP in our study supports the role of inflammation in CAA pathogenesis.

CONCLUSION

The incidence of coronary artery aneurysm after PCI with a stenting device was 2.8%, which is similar to the lower end of the reported incidence in other parts of the world. Baseline inflammatory markers were significantly higher in CAA and there was a significant increase in major adverse cardiovascular events in CAA patients over the study period. The most common artery involved was the right coronary with the use of drug-eluting stents in the majority of patients with affected vessels. The results emphasize the importance of systematic follow-up and intensive risk factor treatment in patients with CAA following PCI.

Study Limitations

There are some limitations that should be noted in this study. The relatively small number of patients (250) and the small number of CAA cases (n=7) resulted in limited statistical power to detect significant differences in risk factors and outcome. Second, our study was conducted in a single center and follow up was limited to 12 months, which may restrict the generalizability of our results and the long-term results. Third, the lack of routine systematic screening for CAA in all patients (follow-up angiography was performed based on clinical indication) may have led to underestimation of the true prevalence. We did not perform intravascular imaging (IVUS or OCT) that would have allowed for a more detailed characterization of aneurysm morphology and etiology. Finally, selection bias may have been introduced because patients with more complex procedures or higher risk profile may have been more likely to have follow-up angiography.

Recommendations

As a result of this study, we recommend that all patients undergoing PCI stenting (drug-eluting stents, and high inflammatory marker) should be followed-up systematically using imaging to capture the development of coronary artery aneurysm. In patients who develop CAA, close clinical monitoring and treatment of cardiovascular risk factors, such as statins and blood pressure control, is crucial. Further multicenter trials with larger cohort sizes and longer follow-up periods are required to better characterize the risk factors, natural history and best management of stent-associated CAA. Intravascular imaging during index procedures might

be useful in identifying patients with a higher risk of developing CAA. Furthermore, creation of a national registry of CAA in Pakistan would help to understanding the complication in the local population.

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