

NORMAL CORONARY ANGIOGRAMS IN PATIENTS OF SUSPECTED CORONARY ARTERY DISEASE: A SIX YEAR STUDY AT ARMY CARDIAC CENTRE LAHORE

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ABSTRACT

Objective: To assess the number of normal coronary angiographies during elective invasive coronary angiography (ICA) in patients with suspected coronary artery disease (CAD).

Study Design: Descriptive cross-sectional study.

Place and Duration: This study was conducted at Army Cardiac Centre, Lahore, from Jul 2013 to Jul 2019.

Methodology: Six-years data of patients undergoing elective invasive coronary angiography without previous percutaneous coronary intervention (PCI) or coronary artery bypass grafting surgery (CABG) was analyzed in this study. The proportion of the patients with significant coronary artery disease were defined as those with at least one lesion of $\geq 20\%$ stenosis on ICA. The rest of the patients were deemed as normal coronary angiograms. Data was entered and analyzed in SPSS-23.

Results: The study consisted of 10260 individuals and after exclusion criteria included 9788 patients, out of which 76.3% were male patients and 23.7% were females. Mean age of the patients was 64 ± 11 years, 8026 (82.4%) patients had a positive noninvasive test out of which exercise stress test was performed on 5377 (67.9%) individuals, stress myocardial perfusion imaging on 2407 (30%) and coronary computed tomography angiogram on 160 (2%) patients. About 1761 (18.1%) patients who were referred did not have any tests before. The overall rate of normal coronary angiographies was 921 (9.4%), lower among those with previous testing (81% vs. 19% without previous testing, $p=0.001$). A positive test and common risk factors were all independent predictors of obstructive coronary artery disease, with adjusted odds ratios and 95% confidence interval 1.33 (1.03–1.74) for noninvasive testing 1.04 (1.04–1.06) for age, 3.47 (2.81–4.29) for males, 1.86 (1.32–2.62) for smoking, 1.74 (1.38–2.20) for diabetes mellitus, 1.30 (1.04–1.62) for raised cholesterol levels, and 1.39 (1.08–1.80) for hypertensive patient.

Conclusions: This study serves to prove a relatively strong gatekeepers; functional tests were more often used but were outperformed by anatomic tests. The much lower rate of normal coronary angiograms is also an indirect indicator of the judicious use of invasive coronary angiography.

Keywords: Coronary angiography, Chest pain, Myocardial ischemia, Stable angina.

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INTRODUCTION

The assessment of patients with suspicion of coronary artery disease (CAD) is dependent on clinical symptoms and noninvasive tests which will be a gateway to invasive coronary angiography (ICA)¹⁻³. Coronary angiography has a pivotal role in the diagnosis of CAD. Patient selection is important to avoid any unnecessary procedural risks and costs of angiography and is critical to the high-quality care^{4,5}. The objectives of doing noninvasive testing in patients with suspected

CAD include reducing unwarranted costs and risks and stratifying patients who will get some beneficial outcome from ICA and sub-sequent revascularization. In spite of common usage of noninvasive tests, many patients undergoing ICA turn out to have normal coronary arteries or are not candidates for revascularization^{6,7}. The goal of this study was to evaluate the number of such patients who undergo ICA on suspicion of CAD but did not have any obstructive lesion in the coronaries. Rates of normal coronary angiography have been used as an indirect measure of the quality of patient selection, given that ICA in patients with a low likelihood of CAD results in higher rates of angiographic normal coronaries^{8,9}.

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Recent studies found that 39% of patients having elective angiography in hospitals in USA had normal coronaries, with some centers reporting rates in excess of 70%^{10,11}.

METHODOLOGY

This was an observational, cross-sectional study performed at a single hospital center serving a diverse population. The study population consisted of all patients referred for elective ICA for evaluation of chest pain symptoms from July 2013 to July 2019. Patients’ referral for ICA and the decision to do noninvasive testing, including which test to use, were on the discretion of attending physicians. The modalities of noninvasive pre-testing that were used were exercise electrocardiogram stress testing (ETT), stress myocardial perfusion imaging (MPI), and coronary computed tomography angiography (CCTA). The following exclusion criteria were applied: revascularization procedure or documented coronary stenosis ≥50% on previous ICA, prior CABG, negative noninvasive pre-test result and incomplete information on patients’ clinical characteristics or ICA result.

All the data was entered and analyzed using the statistical package SPSS version-23. Data is presented as counts (%), medians (interquartile range) or means ± standard deviation. The categorical variables were compared using Fisher's exact test. Continuous variables were compared by means of the t-test. Temporal differences during the study period in the prevalence of obstructive CAD and employment of noninvasive testing

were assessed using the chi-square test for trend. Variables that showed significant relation with obstructive CAD ($p < 0.10$) in univariate analysis were included in a binary logistic regression model to mark the independent predictors. A two-sided p -value of < 0.05 was considered to indicate statistical significance.

RESULTS

During the study period, 10260 patients underwent ICA at our hospital. After the exclusion criteria were applied (figure), 9788 patients were included in the analysis.

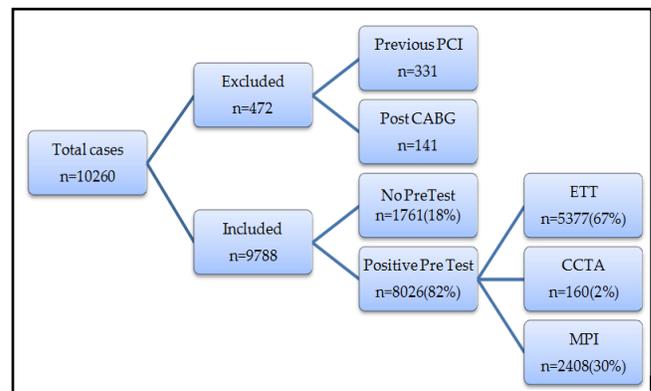


Figure: Exclusion criteria.

Males dominated the study 7439 (76.3%) whereas females were 2349 (23.7%). The demographics and risk factors are given in table. Most patients 8026 (81.8%) were referred after they had a positive noninvasive test. On ICA, the overall prevalence of normal coronary arteries was 9.4% (921 out of 9788). Single vessel, double vessel, triple vessel and left main/LAD ostial disease was identified in 2926 (33%), 4788 (54%), 351 (11%)

Table: Population characteristics and univariate analysis.

Demographics	Total Patients (n=9788)	Obstructive CAD (n=8867)	Normal Coronary Angiography (n=921)	p-value
Age, years	61 ± 11	64.7 ± 10.5	60.7 ± 11.2	<0.001
Male, n (%)	7439 (76.3%)	6916 (78%)	746 (81%)	<0.001
Female, n (%)	2349 (23.7%)	1950 (22%)	175 (19%)	
Risk Factors				
Body mass index, kg/m ²	26.0 ± 3.9	27.6 ± 3.9	28.0 ± 4.5	0.030
Hypertension	74.4%	81.3%	74.6%	<0.001
Diabetes	25.5%	32.5%	21.1%	<0.001
Smoking	31.4%	13.2%	8.9%	0.003
Hypercholesterolemia	61.2%	71.9%	65.7%	0.004

and 177 (2%) of patients, respectively. The number of normal coronary angiographies was higher in patients referred without previous noninvasive testing than in those with a positive test (68% vs. 33%, $p=0.026$). Increasing age, male gender, traditional cardiovascular risk factors and positive noninvasive testing were predictors of obstructive CAD in univariate analysis (table).

There was no important temporal difference in the rate of obstructive CAD during the study period, despite a significant rise in the number of patients undergoing noninvasive testing. Exercise stress testing 5377 (67%) and stress SPECT 2408 (30%) were the most used tests, accounting for more than 97% of noninvasive testing.

DISCUSSION

We sought to determine the rate of normal coronaries in patients undergoing elective diagnostic coronary angiography in Army Cardiac Centre Lahore. In our urban clinical setting, almost 9% of patients referred for elective ICA as a part of assessment of chest pain had obstructive coronary lesions (defined by a broad criterion of $\geq 20\%$ luminal stenosis), largely due to the fact that almost eight percent of patients had undergone prior noninvasive testing. Noninvasive pre-testing was mostly frequently used for these patients and acted as a strong independent predictor of obstructive CAD.

The outcome of a diagnostic test relies on the pretest probability of the patients in whom it is done and on the way the test changes that probability. In an ideal situation, a positive noninvasive test should raise the likelihood of obstructive coronary disease to the point that upholds performing ICA, and a negative test should decrease that probability to the point where obstructive coronary disease can be reliably excluded. Although ICA will always be carried out in few patients without obstructive CAD, the 2011 standards for catheterization laboratory accreditation from the Accreditation for Cardiovascular Excellence organization proposes that the incidence of non-obstructive CAD in patients undergoing elective ICA should be $<40\%$. Extravagant rates

are not desirable because they are not in favor of both individual patients and of overall healthcare cost-effectiveness. Lately, Genders *et al*¹², conducted a multicenter study involving 11 European hospitals and described 58% rate of obstructive CAD (ranging from 39.4% to 75.5%). In the United States, Patel *et al*⁶, described an overall 41% rate of patients with obstructive coronary disease in the National Cardiovascular Data Registry, however there was a great difference in this rate in different centers and ranged from 23 to 100%¹¹.

Although the CAD risk and rates of normal coronaries in our hospital compared with other hospitals may represent differences in the clinical threshold for coronary angiography, it is also possible that these findings simply reflect differences in the population served. Although the median age of the retired patients undergoing angiography is similar to that observed in the community practice, the retired army population is predominantly men with a high prevalence of comorbid conditions. Thus, a higher Framingham risk among patients undergoing angiography in our patients may reflect population differences rather than patient selection.

Although normal coronary rates indirectly reflect patient selection, this measure lacks a quality improvement target to support proper patient selection, and the optimal rate of normal coronaries is unknown. As a result, it is unclear if the lower normal coronary rate in Army Cardiac Centre, as compared with other hospitals, reflects relative procedural underuse from overly restrictive patient selection in our setup or potential overuse in other countries.

As an alternative to normal coronary rates, pre-procedural measures of patient selection may afford avenues for quality improvement. For example, the consistent evaluation of pre-procedural risk of significant CAD has been emphasized as an effective approach to ensure optimal patient selection¹³. In our study, higher use of pre-procedural stress testing suggests the potential benefit of a patient selection strategy emphasizing CAD risk. However, this approach fails to

consider the treatment implications of the angiographic findings for highly symptomatic patients when pre-procedural evaluation of CAD risk is low¹⁴. Moreover, higher use of noninvasive stress testing among patients with a low-probability of CAD may inadvertently lead to higher rates of normal coronary angiography due to diagnostic evaluation of false-positive tests¹⁵⁻¹⁸. An alternative approach evaluates patient symptoms, global CAD risk, stress test findings, and the implications of the angiographic results in assessing the procedural indication. Recently published Appropriate Use Criteria (AUC) for diagnostic coronary angiography guidelines apply this procedural indication framework and may support high quality selection for angiography through identification of patients in which the procedural risk outweighs the potential diagnostic benefit.

CONCLUSION

Among patients undergoing elective coronary angiography in Army Cardiac Centre, approximately 10% patients had normal coronaries. This is a much lower average rate of normal coronaries as compared with previous findings from other international hospitals. Future emphasis on procedural indication, with ongoing monitoring of normal coronary rates as an indirect measure of effect, may assist quality improvement efforts to achieve consistent patient selection as a part of high quality care.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

- Gibbons J, Abrams J, Chatterjee K. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina-summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Chronic Stable Angina). *Circulation* 2003; 107(1): pp.149-58.
- Fox K, Garcia MA, Ardissino D, Chatterjee K, Daley J, Prakash C, et al. Guidelines on the management of stable angina pectoris: executive summary: the task force on the management of stable angina pectoris of the European Society of Cardiology *Eur Heart J* 2006; 27(11): pp.1341-81.
- Wijns W, Kolh P, Danchin N, Di-Mario C, Falk V, Folliguet T, et al. Guidelines on myocardial revascularization *Eur Heart J* 2010; 31(20): pp.2501-55.
- AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2012; 60(): e44-64.
- Patel MR, Bailey SR, Bonow RO. ACCF/SCAI/AATS/AHA/ASE/ASNC/HFSA/HRS/SCCM/SCCT/SCMR/STS 2012 appropriate use criteria for diagnostic catheterization: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society for Cardiovascular Angiography and Interventions, American Association for Thoracic Surgery, American Heart Association- Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2012; 59(22): 1995-27.
- Patel MR, Peterson ED, Dai D, Brennan M, Redberg RF, Anderson V, et al. Low diagnostic yield of elective coronary angiography. *N Engl J Med* 2010; 362(1): pp.886-95.
- Genders TS, Steyerberg EW, Alkadhi H. A clinical prediction rule for the diagnosis of coronary artery disease: validation, updating, and extension *Eur Heart J* 2011; 32(11): pp.1316-30.
- Bashore TM, Bates ER, Berger PB, Clark DA, Cusma JT, Dehmer GJ. American College of Cardiology/Society for Cardiac Angiography and Interventions clinical expert consensus document on cardiac catheterization laboratory standards. A report of the American College of Cardiology task force on clinical expert consensus documents. *J Am Coll Cardiol* 2001; 37(8): 2170-14.
- Douglas P, Iskandrian AE, Krumholz HM, Gillam L, Hendel R, Jollis J, et al. Achieving quality in cardiovascular imaging: proceedings from the American College of Cardiology Duke University Medical Center Think Tank on Quality in Cardiovascular Imaging. *J Am Coll Cardiol* 2006; 48(10): 2141-51.
- Patel MR, Peterson ED, Dai D, Brennan M, Redberg FR, Anderson V, et al. Low diagnostic yield of elective coronary angiography. *N Engl J Med* 2010; 362(1): 886-95.
- Douglas PS, Patel MR, Bailey SR, Dai D, Kaltenbach L, Brindis RG, et al. Hospital variability in the rate of finding obstructive coronary artery disease at elective, diagnostic coronary angiography. *J Am Coll Cardiol* 2011; 58(8): 801-09.
- Cole JH, Chunn VM, Morrow JA, Buckley RS, Phillips RM. Cost implications of initial computed tomography angiography as opposed to catheterization in patients with mildly abnormal or equivocal myocardial perfusion scans. *J Cardiovasc Comput Tomogr* 2007; 1(1): pp.21-26.
- Batchelor WB, Mark DB, Knight JD, Granger CB, Armstrong PW, Califf RM, et al. Development and validation of a simple model to predict severe coronary artery disease after myocardial infarction: potential impact on cardiac catheterization use in the United States and Canada. *Am Heart J* 2003; 145(2): 349-55.
- Patel MR, Dehmer GJ, Hirshfeld JW, Smith PK, Spertus JA. ACCF/SCAI/STS/AATS/AHA/ASNC/HFSA/SCCT 2012 appropriate use criteria for coronary revascularization focused update: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, American Society of Nuclear Cardiology, and the Society of Cardiovascular Computed Tomography. *J Am Coll Cardiol* 2012; 59(1): 857-81.

15. Diamond GA, Kaul S. Low diagnostic yield of elective coronary angiography *N Engl J Med* 2010; 363(93): 94-95.
 16. Santos MB, Ferreira AM, de Araújo Goncalves P, Raposo L, Campante R, Almeidaet TM, et al. Diagnostic yield of current referral strategies for elective coronary angiography in suspected coronary artery disease-an analysis of the ACROSS registry. *Rev Port Cardiol* 2013; 32(6): 483-88.
 17. Wijeysondera HC. Impact of system and physician factors on the detection of obstructive coronary disease with diagnostic angiography in stable ischemic heart disease. *Circulation: Cardiovascular Quality and Outcomes* 2014; 7(1): 648-55.
 18. Gašenok OV, Martsevich Slu. Determination of indications for coronary angiography in asymptomatic patients and patients with stable angina. *Kardiologija* 2014; 54(10): 57-62.
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