



Comparison of Clinical profile and outcome between young (≤ 45 yrs) male and female patients with coronary artery disease undergoing percutaneous coronary intervention, a single center study

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Abstract

Background -There is scarcity of data regarding CAD and the outcome following PCI in young south Indian population. We sought to analyze the clinical, coronary angiographic features and outcome in young adults (≤ 45 years of age) with CAD who underwent PCI and also to compare that between young male and female patients .

Methods- Angiographic and clinical data from total 150 patients aged ≤ 45 years of which, 110 male patients who underwent PCI from January 2014 to January 2016 were compared to age-matched 40 female patients in our centre . All patients were treated according to guidelines. 1, 6 and 12 months clinical follow-up were performed in all patients. Coronary angiography was performed only if patients were symptomatic or TMT positive.

Results -CAD risk factors were more prevalent in young male patients, Diabetes mellitus was found in 32.72%, hypertension (34.54%), dyslipidemia (36.36%), smoking (38.18%), tobacco consumption (21.81%) and hyperhomocysteinemia (23.63%) as compared to female group(17.5%,20%,12.5%,0%,5%,12.5% respectively). Family history of CAD was found to be higher in female patients as compared to males (40% vs 6.36%; $p = 0.000$). Single vessel disease was found to be common among female patients(60% vs 40.92%) and

Double vessel disease was common among male patients(44.5% vs 22.5%). The male patients had higher rate of inhospital MACE(4.54% vs 0%; $p=0.170$). Incidence of adverse events in young male patients at one year were not different from those in young females, including MI (1.81% vs 2.5%), cardiac death (1.81% vs 2.5%), TLR (7.27% vs 2.5%),TVR (1.81% vs 0%); all $p=NS$.

Conclusion - CAD risk factors and Multi vessel disease were more common in young male patients as compared to young female patients. Family history of CAD and single vessel lesions were more common in young female patients compared to young males with CAD . The in-hospital MACE was higher in young male patients and follow-up incidences of major adverse cardiac events were almost similar between the two groups.

Keywords: Percutaneous coronary intervention (PCI), coronary artery disease (CAD), major adverse cardiac events (MACE), myocardial infarction (MI),target lesion revascularization (TLR),target vessal revascularization (TVR).

INTRODUCTION

Coronary artery disease (CAD) manifests clinically in older patients predominantly and until recent years it was an uncommon clinical entity in young adults. CAD once thought as a disease of old, is now becoming increasingly common in younger generation . This has been seen as a worrying trend especially in developing countries like india and also globally.

The incidence of CAD in young Indians is about 12-16% as compared to the western population where it is <5% ^(1,2) and in two series of patients, women with CAD at <40years of age, comprised 5.6 and 11.4 percent of patients.^(3,4) In young adults the emergence of an accelerated atherosclerotic process is of particular concern, as it carries a greater impact on their lives. Their families are also affected because , many of them are still in their prime health , physically active and the sole breadwinners of their family .

Though the condition is becoming common, our knowledge of CAD in young adults and their outcome after PCI is scarce. Hence this study was performed in a tertiarycentre to analyze the clinical profile and outcome in young adults with CAD who underwent PCI and also to compare that between young male and female patients (≤ 45 years of age).

MATERIALS AND METHODS

Study design: A single center, prospective clinical study was conducted at KLE's Dr. Prabhakar Kore Hospital and MRC, Belagavi, Karnataka, India. The study was carried out for a period of 2 years i.e ,from January 2014 to January

2016. Baseline clinical and angiographic data from total 150 young (≤ 45 years) patients of which, 110 males with CAD who underwent PCI were compared to age matched 40 females in our department.

Definition of risk factors and diagnostic criteria: Hypertension (HTN) is defined as systolic BP level of ≥ 140 mmHg and diastolic BP of ≥ 90 mmHg .Diabetes mellitus (DM) was diagnosed when FBS ≥ 126 mg/dl or 2-hour PG ≥ 200 mg/dl or HbA1C ≥ 6.5 %.⁽⁵⁾ Dyslipidemia - defined according to NCEP - ATP III guidelines.⁽⁶⁾ Family history of coronary artery disease was defined as evidence of coronary artery disease such as a history of myocardial infarction, coronary artery bypass surgery, angina pectoris, in a parent or sibling before 60 years of age.⁽⁷⁾ Smoking is defined as one who has quit smoking: >2 pack-years cigarette smoking but nonsmoker for >1 year; still smoking: >2 pack-years smoked and currently a smoker.⁽⁷⁾

Angiographic analysis and definitions:

Angiographic analysis was performed by experienced cardiologist, based on at least two orthogonal views .The type of lesion was classified according to ACC/AHA criteria.⁽⁸⁾ Successful procedure was defined as angiographic success (residual stenosis $\leq 20\%$, with TIMI 3 flow) and no occurrence of MACE, comprising periprocedural MI, stroke, emergency coronary artery bypass graft (CABG) and death, with relief of signs and/or symptoms of myocardial ischemia after the patient recovers from the procedure.⁽⁹⁾

Procedure

Almost all the interventions were performed using the transfemoral route. During the procedure, the choice of the material and the technique were left to the operating cardiologist discretion, as well as need of glycoprotein IIb/ III a use. Unfractionated heparin was used at the beginning of the procedure (70-100 U/kg). The MACE was defined as the occurrence of death, MI or urgent revascularization during the same admission.⁽¹⁰⁾ Stent thrombosis defined according to the academic research consortium.⁽¹⁰⁾

All patients after the procedure were treated with dual antiplatelets with (aspirin 75/150 mg and either clopidogrel 75mg od or ticagrelor 90mg bd or prasugrel 10mg od). All patients baseline demographic, clinical, procedural characteristics and in hospital outcomes were noted. Clinical follow-up was performed in all patients at 1,6 and 12 months post procedure. Patients who had chest discomfort underwent treadmill test (TMT). Coronary angiography (CAG) on follow up was done in patients with positive TMT or patients who had resting ECG changes. Study end points were MACE including MI, stent thrombosis, revascularization (TLR and TVR) and death.

Baseline demographics for both male and female patients are shown in Table 1.

Table 1 - Baseline Demographics

	Male(n =110)	Female (n =40)	p-Value
Age,yrs	39.48±4.95	41.05±4.51	0.081
Angina	105(95.45)	37(92.5)	0.476
Ejection Fraction (%)	50.63 ± 7.32	52.50 ± 7.59	0.175
Diabetes	36(32.72)	07(17.5)	0.068
Hypertension	38(34.54)	08(20)	0.088
Dyslipidemia	40(36.36)	05(12.5)	0.005*
Smoking	42(38.18)	0(0)	0.000*
Family History Of CAD	7(6.36)	16(40)	0.000*
Tobacco	24(21.81)	2(5)	0.016
Obesity	30 (27.27)	6(15)	0.120
H/O IHD	05(4.54)	05(12.5)	0.084
H/O PCI	04(3.63)	02(5)	0.706
Hyperhomocysteinemia	26(23.63)	05(12.5)	0.136

Data listed as number of patients (percent of group), mean±SD. *p* value of < 0.05 is considered significant

Mean age of male was 39.48±4.95years

Mean age of female was 41.05±4.51years

Anginal pain was predominant symptom in both groups.

The incidence of diabetes mellitus (32.72%), hypertension (34.54%), dyslipidemia (36.36%), smoking (38.18%) and tobacco consumption (21.81%) was found to be higher among males. The male group also had higher incidence of

STATISTICAL ANALYSIS

Continuous data are presented as mean ±SD and differences are compared using student *t* test. Discrete variables are expressed as counts and percentages. In two by two tables, two by three and two by four tables, differences were assessed by chi-square test. All statistical tests were two tailed. All statistical calculations were done with excel and SPSS version 20 statistical software. A *p* value of < 0.05 is considered significant.

RESULTS

Between January 2014 to January 2016 a total of 150 young patients (≤45years) underwent PCI, of which male patients were 110 and females were 40.

obesity (27.27%) and hyperhomocysteinemia (23.63%) as compared to female group.

Family history of CAD (40%) was found to be higher in females, which was statistically significant.

Clinical presentation for both male and female patients are shown in Table 2.

Table 2: Clinical presentation

Variables	Male(n=110)	Female(n=40)	pValue
Unstable angina	20(18.18)	13(32.5)	0.061
STEMI	78(70.92)	23(57.5)	0.122
NSTEMI	7(6.36)	3(7.5)	0.805
TMT Positive	5(4.54)	1(2.5)	0.572

Data listed as number of patients (percent of group), p value of < 0.05 is considered significant

The most common clinical presentation in both male and female groups was STEMI with rates of 70.92% and 57.5 % respectively.

Baseline angiographic characteristics of both male and female patients are shown in table 3

Table 3:Baseline Angiographic characteristics

Variables	Male (n=110)	Female(n =40)	p-Value
No. Of Diseased Vessels			
SVD	45(40.92)	24(60)	0.045*
DVD	49(44.54)	9(22.5)	
TVD	16(14.54)	7(17.5)	
Lesion Location			
LM	01(0.90)	03(7.5)	0.013
LAD	84(76.36)	27(67.5)	0.513
RCA	36(32.72)	20(50)	0.126
LCX	28(25.45)	11(27.5)	0.728
D1	09(8.18)	01(2.5)	0.613
OM	15(13.63)	02(5)	0.413
RAMUS	09(8.18)	00(0)	0.185

Data listed as number of patients (percent of group), p value of < 0.05 is considered significant

Single vessel disease (SVD) was found to be common among female group(60%)and double vessel disease (DVD) was common among males (44.54%).In both male and female patients the lesion was predominantly located in Left anterior descending (LAD) artery(76.36% vs 67.5% respectively)

Type of lesion for both male and female patients is shown in Table 4.

Table 4: Type of lesion on Coronary angiography

Type of lesion	Male (n=110)	Female (n=40)	p-Value
A	89(80.90)	31(77.5)	0.257
B	10(9.10)	7(17.5)	
C	11(10)	2(5)	

Data listed as number of patients (percent of group), p value of < 0.05 is considered significant

ACC/ AHA type A lesion was predominantly present in both male and female patients with rates of 80.90 % and 77.5% respectively.

Stents used are shown in Table 5.

Table5: Stents used

Stents Used	Male(n = 110)	Female(n =40)
Everolimus(EES)	86(78.18)	30(75)
Sirolimus(SES)	9(8.18)	1(2.5)
Zotarolimus (ZES)	15(13.64)	9(22.5)

Data listed as number of patients (percent of group)

In all 150 patients drug eluting stent (DES) was commonly used, 78.18% in males and 75% in females. Everolimus eluting stent (EES) was most used.

Intracoronary medications used are shown in Table 6.

Table 6: Intracoronary medications used

Medication Used	Male(n=110)	Female(n=40)	Total(n=150)
NTG	34(30.90)	4(10)	38(25.33)
Nikorran	17(15.45)	1(2.5)	18(12)
Abciximab	20(18.18)	4(10)	24(16)

Data listed as number of patients (percent of group)

Intracoronary nitroglycerin (NTG) was administered in 38 (25.33%) patients overall. Intracoronary abciximab was used in 24(16%) patients overall and intracoronary nikoran was administered in about 18(12%) patients.

Procedural complications are shown in Table 7.

Table 7: Procedural Complications.

Variables	Male(n=110)	Female(n=40)	Total(n=150)
Slow /No reflow	17(15.45)	2(5)	19(12.66)
Dissection	7(6.36)	0(0)	7(4.66)
Perforation	0(0)	0(0)	0(0)
Tamponade	0(0)	0(0)	0(0)

Data listed as number of patients (percent of group)

Slow/ no reflow occurred in 19 (12.66%) patients overall of which 17 were males and 2 were females. Seven patients had (4.66%) coronary dissection in which all were males. None had perforation / tamponade.

The in hospital outcome is shown in Table 8 .

Table 8: In hospital outcome

Variables	Male(n = 110)	Female(n =40)	p-Value
In-Hospital MACE	5(4.54)	0(0)	0.170
Death	1(0.90)	0(0)	0.545
Stent Thrombosis	2(1.81)	0(0)	0.391
TLR-PCI	2(1.81)	0(0)	0.391

Data listed as number of patients (percent of group), *p* value of < 0.05 is considered significant

The male patients had higher rate of inhospital MACE (4.54% vs 0%; *p*=0.170). Two (1.81%) male patients had stent thrombosis and two (1.81%) male patients underwent TLR -PCI. One male patient died due to non cardiac cause.

One year follow up outcome is shown in Table 9.

Table 9 : One year follow up outcome.

Variables	Male(n=110)	Female(n=40)	p-value
MACE	14(12.72)	4(10)	0.649
MI	2 (1.81)	1 (2.5)	0.792
Cardiac death	2 (1.81)	1 (2.5)	0.792
TLR - PCI	8 (7.27)	1(2.5)	0.276
TVR - PCI	2 (1.81)	0	0.391
CABG	0(0)	1(2.5)	0.096

Data listed as number of patients (percent of group), *p* value of < 0.05 is considered significant

The 1year follow up MACE was almost similar between 2groups. Two (1.81%) male patients had MI and 1 (2.5%) female had MI. Eight (7.22%) males and 1(2.5%) female patient underwent TLR-PCI. Two (1.81%) male patients underwent TVR-PCI. One (2.5%) female patient underwent CABG. Total 3 patients died, out of which, 2 (1.81%) were males and 1(2.5%) was female patient.

DISCUSSION

In developing countries, the burden of cardiovascular disease is rapidly increasing, mainly due to lifestyle changes along with increase in incidence of risk factors among younger population. In India in the last three decades^(11,12) the prevalence of the cardiovascular risk factors including DM, HTN, smoking, dyslipidemia etc has markedly increased especially in the younger population.

In our study, smoking history was present in 28% of patients, in which all were male patients, which was comparable with study done by Jayachandra et al.⁽¹³⁾ which reported positive smoking history in 22% of young subjects (<45 years). In our study, hypertension was found in 34.54% of male patients and 20% of female patients. In a study done by Franklin H et al.⁽¹⁴⁾ reported 19% of male patients and 32% of female patients were hypertensive. In our study, diabetes was noted in 32.72% of male patients and 17.5% of female patients which was higher than previous study by Jayachandra et al.⁽¹³⁾ with rates of 8% in young males and 11% in young females. This is because our study group included only patient with documented CAD.

In the present study, the family history of CAD was more common in young females which was found in 40% of patients compared to 6% in young males. Compared to study by Franklin et al.⁽¹⁴⁾ which was higher than the present study with rates of 58% in male and 55% in females. This difference is due to difference in sample size. The Dyslipidemia is well known risk factor involved in the pathogenesis of CAD⁽¹⁵⁾, which is responsible for premature CAD specially in Asian Indians. In present study, Dyslipidemia was found in 30% of the total patients, of which 36% were males and 12.5% were females. In contrast to our study, a study done by Jayachandra et al.⁽¹³⁾ showed that 12% of males and 11% of females had Dyslipidemia.

Angiographic characteristics were compared between male and female patients. SVD, DVD and TVD were present in 41%, 44.5%, and 14.5% of males and 60%, 22.5% and 17.5% of females respectively. Where as Jason H. et al⁽¹⁶⁾ reported

SVD, DVD and TVD in 55%, 27%, 15% of young males and 60%, 24.5% and 12.8% of young female patients respectively.

Complications following PCI occurred at a low frequency. Overall in hospital MACE rate was 3.33%, in hospital mortality was 0.9% in young males and 0% in young females. This was almost similar compared to study done by V.S. Srinivas et al⁽¹⁷⁾, where in hospital mortality was 0.70% in young males and 0.22% in young females. Overall 1 year mortality in young patients in our study was 2%, which was not very different from that reported by Alhaddad ZI et al.⁽¹⁸⁾ where the mortality was 3.6%. There was no difference in mortality between young male (1.81%) and young female (2.5%) patients.

CONCLUSION

CAD risk factors and Multi vessel disease were more common in young male patients as compared to young female patients. Family history of CAD and single vessel lesions were more common in young female patients compared to young male patients with CAD. The in-hospital MACE was higher among young male patients and follow-up incidences of major adverse cardiac events were almost similar between two groups.

BIBLIOGRAPHY

1. Zimmerman FH, Cameron A, Fisher LD, Ng G. Myocardial infarction in young adults: angiographic characterization, risk factors and prognosis (coronary Artery Surgery Study registry). *J Am Coll Cardiol* 1995;26(3):654-61.
2. Jalowiec DA, Hill JA. Myocardial infarction in the young and in women. *Cardiovasc Clin* 1989; 20:197-206
3. Cole JH, Miller JI 3rd, Sperling LS, Weintraub WS. Long-term follow-up of coronary artery disease presenting in young adults. *J Am Coll Cardiol* 2003; 41:521.
4. Fournier JA, Sánchez A, Quero J, et al. Myocardial infarction in men aged 40

- years or less: a prospective clinical-angiographic study. *Clin Cardiol* 1996; 19:631.
5. American Diabetes Association. Standards of medical care in diabetes—2016. *Diabetes Care*. 2016;39(suppl 1):S1-S106
 6. Third report on national cholesterol education program (NCEP). Expert Panel on Detection, Evaluation, and Treatment of High Blood cholesterol in Adults (Adult Treatment Panel III), Executive summary.
 7. A Positive Family History of Premature Coronary Artery Disease Is Associated With Impaired Endothelium-Dependent Coronary Blood Flow Regulation Volker Schaechinger, MD; Martina B. Britten, MD; Mathias Elsner, MD; Dirk H. Walter, MD; Inge Scharrer, MD; Andreas M. Zeiher, MD. *Circulation*. 1999;100:1502-1508.
 8. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, Jacobs AK, Kern MJ, King SB, et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI writing Committee to Update 2001 Guideline for Percutaneous Coronary Intervention). *Circulation*. 2006;113(7):e166-286.
 9. ACC/AHA Guidelines for Percutaneous Coronary Intervention (Revision of the 1993 PTCA Guidelines)—Executive Summary *Circulation*. 2001; 103:3019-3041.
 10. Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials—a case for standard definitions. *Circulation*. 2007;115:2344–51.
 11. Kasliwal R, Kulshreshtha A, Agrawal S, Bansal M, Trehan N. Prevalence of cardiovascular risk factors in Indian patients undergoing coronary artery bypass surgery. *JAPI*. 2006;54:371-5.
 12. Gupta R. Meta-analysis of prevalence of hypertension in India. *Indian heart journal*. 1996;49(1):43-8.
 13. Jayachandra S, Agnihotram G, Rao RP, Murthy CV. Risk-factor profile for coronary artery disease among young and elderly patients in Andhra Pradesh. *Heart India*. 2014;2(1):11.
 14. Franklin H, Zimmerman , Cameron A, Fisher LD, Grace N. Myocardial infarction in young adults: angiographic characterization, risk factors and prognosis (Coronary Artery Surgery Study Registry). *Journal of the American College of Cardiology*. 1995;26(3):654-61.
 15. Klag MJ, Ford DE, Mead LA, He J, Whelton PK, Liang K-Y, et al. Serum cholesterol in young men and subsequent cardiovascular disease. *New England Journal of Medicine*. 1993;328(5):313-8
 16. Jason h. Cole, Joseph I. Miller, Sperling LS, Weintraub WS. Long-term follow-up of coronary artery disease presenting in young adults. *Journal of the American College of Cardiology*. 2003;41(4):521-8.
 17. V.S. Srinivas, MBBS, Sangeeta Garg, MD, Abdissa Negassa, PhD, Ji Yon Bang, MS, E. Scott Monrad, MD . Persistent Sex Difference in Hospital Outcome following Percutaneous Coronary Intervention: Results from the New York State Repo . Volume 19 - Issue 6 - June, 2007
 18. Zayd I. Alhaddad, Rawan A. Hammoudeh, Rinad R. Tabbalat, Yousef Khader, Imad A. Alhaddad, Ayman J. Hammoudeh. One year prognosis of young Middle Eastern patients undergoing percutaneous coronary interventions. *Int J Res Med Sci*. 2017 Jan;5(1):257-263.