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Original Article

Premature Coronary Artery Disease (PCAD) Patients Undergoing Coronary Artery Bypass Surgery At A Tertiary Care Cardiac Centre In India- Our Initial Experience Of The First 100 Cases

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Abstract

Although coronary artery disease is a well recognized clinical entity and very common in India, there is paucity of literature on the patients undergoing surgical revascularization in the form of coronary artery bypass grafting (CABG) at a young age (<40 years). The aim of this study is to analyze the details of patients with premature coronary artery disease (PCAD) who underwent CABG at a tertiary care cardiac center in India. A retrospective observational study was conducted for the present study. All patients aged <40 years with Premature Coronary artery disease (PCAD) were registered in the PCAD Registry at Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bangalore. The electronic database of case records of all patients with PCAD who underwent CABG at Sri Jayadeva Institute of Cardiovascular Sciences and Research, between April 2018 and March 2019 was analyzed. Patients were selected based on the database of PCAD registry at our institute under CTRI regulation of India (registration number CTRI/2018/03/012544), All patients were diagnosed with Coronary angiogram (CAG) and required further treatment in the form of CABG. Binary logistic regression was used to test the hypothesis (n= 100) cases, out of which LIMA was grafted in 84 cases (n=84), (odd ratio 3.55); of which LIMA to LAD was grafted in 81 cases (n=81); LIMA to RIMA –OM1 was grafted in 2 cases (n=2) , and LIMA - Radial - Y was grafted in 1 case (n=1). Off - pump CABG (OPCAB) was done in 79 cases (79%) and the remaining cases were operated On - pump. Most common conduits that were used for grafting in CABG were LIMA (84%); SVG (82%), RIMA (9%) and radial artery (1%). Mean Ejection Fraction was 51.28%, with Standard Deviation (SD) of 5.80. Carotid artery stenosis (> 50%narrowing of the internal carotid artery) was seen in 11% of the cases. Peripheral Arterial Disease (PAD) was seen in 4% of cases (odds 1.18). Mortality rate (CFR) was negatively correlated in the younger population; deaths were seen in only 2 cases (n =2). The extent of CABG characteristics was positively correlated and

statistically significant (p=0.001). In conclusion, Cardiovascular Disease (CVD) risk is more common in resource-poor and developing countries. Considering all the research findings, the present study concludes that CABG surgery can be treated with comparable components for the management of patients diagnosed to be suffering from Coronary artery disease below the age of 40 years. Relative long-term survival rate after CABG surgery, regardless of gender needs to be assessed for over a period of time at the population level.

Key words: CABG, PCAD, LIMA, CAD, mortality, survivability

INTRODUCTION

Coronary artery disease (CAD) is the most common heart disease worldwide, causing the highest number of deaths globally each year, according to the World Health Organization (WHO) report 2022 [1,2]. It is characterized by reduced blood flow to the heart muscle due to the build-up of plaque in the arteries of the heart. However, premature coronary artery disease (PCAD) affects a significant number of individuals below the age of 45, and is more prevalent in younger populations, with different studies showing varying cut-offs for the definition of PCAD, typically ranging from 45 to 65 years of age [1,2,3,4,5]. The PCAD places a significant burden on the patient and family, as well as on the healthcare delivery system of a country, particularly for people in the age group of 35–60 years, who are usually the breadwinners of the family. The prevalence of PCAD in a large survey done in German cardiac rehabilitation centres revealed 37% for men aged <55 years and women aged <65 years, while the prevalence for CAD was 67% for men aged >55 years and women aged >65 years. Risk factors for PCAD have been conventionally divided into two types: modifiable and non-modifiable[6,7]. Modifiable risk factors include smoking, hypertension, diabetes mellitus, physical inactivity, obesity, dyslipidemia, and psychological stress, as well as age, gender, ethnicity, family history of heart disease, and homocystinuria. Patients with PCAD usually present with classic symptoms of CAD such as anginal chest pain, breathlessness, and fatigue, although a proportion of asymptomatic patients may be detected to have PCAD on screening tests like TMT and CT angiography [7,8,9]. These patients are evaluated through conventional invasive coronary angiogram to determine the extent and severity of the coronary artery disease (CAD) in terms of the involved vessels, location, morphology, and percentage of lesions. The information from the angiogram guides the decision-making regarding further management, such as cardiac cath interventions or coronary artery bypass grafting (CABG) [10,11,12]. However, there is a lack of studies describing the profile of patients suffering from PCAD who were operated in the form of CABG in the Indian population. In 2019, the World Health Organization (WHO) reported that 17.9 million people died from cardiovascular diseases (CVD), accounting for 32% of all global deaths. Of these, 85% were due to heart attacks and stroke. Furthermore, over three-quarters of CVD deaths occur in low- and middle-income countries [13,14]. This study aims to compile the profile of young patients with CAD undergoing CABG at a tertiary care cardiac centre in India. Additionally, the study aims to correlate the demographic characteristics of patients with PCAD who underwent surgery for CABG and assess the risk factors and co-morbidities associated with PCAD. Lastly, the study will examine the impact of various confounding factors on the outcome of CABG.

METHODOLOGY

Study design

A retrospective observational study was employed for the present study. All patients with CAD who were <40 years of age were registered in the PCAD registry at Sri Jayadeva Institute of

Cardiovascular Sciences and Research, Bangalore The electronic database of case files of all patients with PCAD registered in the PCAD registry at Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bangalore between April 2018 and March 2019 was analyzed. The following exclusion and inclusion criteria were employed for the selection of patients: Patients with PCAD who have undergone CABG < 40 years of age (diagnosed by coronary angiogram) Exclusion criteria: patients suffering from terminal illness, malignancy, high-risk population (HIV/AIDS), and those who are not willing to accept the surgery were excluded from the study intervention.

Patient's selection

The patients were selected based on the PCAD registry data base at our institute under the CTRI regulation of India (registered no. CTRI/2018/03/012544). All patients were diagnosed with CAG and further required treatment in the form of CABG. Sample size

$$n = \frac{\frac{Z^2 * p(1-p)}{e^2}}{1 + \frac{Z^2 * p(1-p)}{2}} = \frac{\frac{2.58^2 * 0.50(1-0.50)}{e^2}}{1 + \frac{2.58^2 * 0.50(1-0.50)}{2}} = 260$$

( ) ( )

e N 0.05 $*425$

N = population size, z = z-score, e= margin of error, p = standard of deviation Due to paucity of cases, the sample size was restricted to (n=100) cases

In the majority of the cases, LAD was grafted (84%); all cases were taken up for CABG after routine investigations like chest X-rays, ECG, echos, and other haematological investigations. All data were gathered from bedside and registry. The study fulfilled the IBR ethical criteria and obtained consent from the patients and their caretakers.

Statistical analysis

The primary and secondary data were fed to the computer, and the analysis was done using SPSS and R statistical software. The dependent and independent variables were classified and validated by suitable data transformations (skewness data sets). Binary logistic regression, descriptive statistics, and Fisher F critical values were used to test the null hypothesis (H_0).

RESULTS

Table1:Siginificance of associated attributes

Attributes(n=100)	Mean +/-SD	odd ratio	P-value
Age (Years)	37.18±1.56	3.61	≤0.00
Gender			
Males (n=75)	36.84± 1.82	5.55	≤0.000
Females (n=25)	37.28 ± 2.15	4.78	≤0.000
Sex ratio	1:0.34		
Comordbity (n=100)			
Diabetes mellitus	38%	1.28	≤0.001
Hypertension	26%	1.11	≤0.001
Family/Ho PCAD	-	-	-
Chronic Kidney Disease (CKD)	-	-	-
Thyroid disorders	-	-	-
Smoking	24%	1.32	≤0.001
Alcoholism	12%	1.74	<0.001

Table 1 shows that out of 100 cases, males and females were (n = 75 and n = 25), respectively, with a sex ratio of 1:2. The mean age of both genders was 36.84 years with SD 1.82 in males and 37.28 years with SD 2.15 in females. The hypothesis was tested by logistic regression with respect to CABG, independent of age and gender, and was found to be statistically significant, p =0.001 (odd ratio M/F -5.55/4.78). During the study intervention, co morbidity was assessed for all recruited cases: diabetes mellitus was more prevalent (38% hazard risk), hypertension was 26% (odd ratio 1.11, Hz 2.56), smoking was 24% (odd 1.32, Hz 6.32), and alcoholism was 12% (odds 1.74, Hz 4.78). The average body mass index of all cases was 25.93 kg/m3, with a SD of 5.21 [CI 95% 15.64–36.07] and odds of 3.44. All parameters were found to statistically differ (p 0.001) with the incidence of CABG.

Table2: Siginificance of associated attributes on haematological parameters

Haematological	Mean +/-SD CI-95%	Odd ratio	P-value parameters
HDL (mg/dL)	30.28±6.71 [CI 95% 17.00-43.30]	4.76	
LDL (mg/dL)	107±23.16 [CI 95% 61.63-152.42]	3.34	≤0.000
TG (mg/dL)	201±26.55 [CI 95% 148.87-253.34]	2.98	≤0.000
			≤0.000
Non-HDL (mg/dL)	135±34.56 [CI 95% 67.74-203.22]	3.63	≤0.000
VLDL (mg/dL)	37.58±2.21 [CI 95% 33.20-41.86]	4.11	≤0.000
Cholesterol to HDL Ratio	5.75±3.81 [CI 95% -1.72-13.21]	3.87	≤0.000
CK	156±39.63 [CI 95% 148.59-63.87]	3.77	≤0.000
CK-MB	19.02±2.36 [CI 95% 14.36-23.61]	3.98	≤0.000
Creatinine	1.01±0.83 [CI 95% 0.62-2.62]	2.78	≤0.000
RBS	157±19.62 [CI 95% -133.25-168.28]	2.14	≤0.000
TFT	100%	-	1.00
HB (gram per decilitre)	13.16±2.13[CI 95% 8.93-17.28]	5.77	≤0.000

All haematological parameters with different follow-ups were taken, and the data was analyzed by multinomial logistic regression. High density lipoprotein (HDL) mean was 30.28 (mg/dL) with SD 6.71. [CI 95% 17.00–43.30] odds of 4.76. The average observed absolute value of Low Density Lipoprotein (LDL) (107 ±23.16 mg/dL) with a [CI 95% 61.63–152.42] odds ratio was significantly different at 3.34; the Triglycerides (TG) absolute mean was 201, SD 26.55 mg/dL. [CI 95% 148.87253.34] The odds ratio was 2.98; non-HDL was 135; SD was 34.56 mg/dL. [CI 95% 67.74–203.22] odds were 3.63; Very Low Density Lipoprotein (VLDL) 37.5, SD 82.21 (mg/dL) [CI 95% 33.20– 41.86] odds were 4.11. The mean ratio was 5.75 ± 3.81 [CI 95% ;1.72-13.21] with significant odds of 3.77; the Creatine Kinase (CK) mean was 156 ±39.63. [CI 95% 148.59–63.87] significant odds were 3.77; the creatine kinase myocardial band (CK-MB) mean was 19.02 ± 2.36 [CI 95%14.36- 23.61] odds of 3.98. Creatinine was significantly associated ($p<0.01$) with mean 1.01±0.83 mcro/dL. The [CI 95% 0.62-2.62] odds ratio is 2.78. Random Blood Sugar (RBS) 157±19.62 [CI 95% 133.25168.28] odds 2.14, TFT 100%, and Haemoglobin (HB) (gram per deci liter) 13.16±2.13 [CI 95% 8.93-17.28] odds 5.77; all parameters were statistically significant, p= 0.001.

Table 3:Correlation of CABG with different attributes

Attributes(n=100)	(%)	odd ratio	P-value
LIMA to LAD	84%	3.55	≤0.000
LIMA –RIMA-OM1	2%	1.25	<0.01
LIMA –Radial- RAMUS D1	1%	0.63	>0.001
Most common Conduits LIMA SVG RIMA Radial artery	 84% 82% 9% 3%	 2.56 3.11 1.85 1.25	 <0.001 <0.001 <0.001 <0.001
OPCAB	79%	2.14	≤0.000
LAD 1-1.5 1.5-1.75 1.75-2.0 2.0-2.5	 14% 74% 10% 02%	 1.55 3.98 1.87 <1	 ≤0.000 ≤0.000 ≤0.000 >0.001
LCX/OM 1-1.5 1.5-1.75 1.75-2.0	 44% 18% 06%	 4.89 1.58 2.44	 ≤0.000 ≤0.000 ≤0.000
2.0-2.25 Nil	04% 12%	2.12 <1	≤0.000 >0.001
RCA/PDA/PLV 1-1.5 1.5-1.75 1.75-2.0 2.0-2.25 Nil	 29% 16% 05% 06% 43%	 5.74 3.88 2.69 1.85 <1	 ≤0.000 ≤0.000 ≤0.000 ≤0.000 ≤0.000 >0.001
Ejection Fraction (Mean±SD)	51.28±5.80	6.74	≤0.000
Carotid artery stenosis (>50% narrowing of internal carotid artery) Yes(B/L) No	 11% 89 %	 2.74 <1	 >0.001
Peripheral arterial disease (PAD) Yes No	 04% 96%	 1.18 <1	 ≤0.000 ≤0.000
Death Yes No	 02% 98%	 <1	 >0.01

Table 3 shows the correlation of CABG with different attributes. The binary logistic regression was employed to test the hypothesis, and out of 100 cases, 84% were grafted with LIMA as a conduit (odd ratio 3.55); Binary logistic regression was used to test the hypothesis of which LIMA was grafted to LAD (n=81); LIMA to RIMA–OM1 (n=2), LIMA to Radial Y (n=1). OPCAB was (79%).Most common conduits that were used for CABG were LIMA (84%); SVG (82%), RIMA (9%) and radial artery (3%). Mean Ejection Fraction (EF) was 51.28%, with SD 5.80 and carotid artery stenosis (> 50% narrowing of internal carotid artery) at 11%. Analysis of various sizes of

shunts that were used during the surgery was done LAD shunt size; it was seen in different dimensions: 1-1.5 (14%), 1.5-1.75 (74%), 1.75-2.0 (10%), and the least expression was seen in 2 cases. The LCx/OM was correlated with CABG; the size of shunt between 1-1.5 was seen as the highest percentage (44%) followed by 1.5–17.5 (18%), 1.75-2.0 (0.6%) and 2.0-2.25 (04%). The shunt used for RCA/PDA/PLV was seen as - 1–1.5 (29%), 1.5–1.75 (16%), 1.75 - 2.0 (5%) 2.0-2.25 (6%) The mean ejection fraction was 51.28% with SD 5.80 and carotid artery stenosis (> 50% narrowing of internal carotid artery) at 11%. Peripheral artery disease (PAD) was seen in 4 cases (odds 1.18). The case fatality rate (CFR) was negatively correlated in the younger population; only 2 cases were found to be deaths (2%) The magnitude of CABG attributes was positively correlated and found to be statistically significant (p= 0.001). The survivability was estimated by using receiver operating characteristics analysis, with age as the dependent variable and the rest of the parameters as independent variables. The results showed that the good specificity on survivability (95.68%), the sensitivity (81.36%) the PPV (0.76), the NPV (0.52), and the AUC was (@1% level 0.98) (Fig. 1), and a similar statistical method was employed for the age and different types of grafting. Both variables were statistically significant at the 1% level of significance, with good specificity (84.94%) and sensitivity (65.38%). PPV (0.66), NPV (0.45), and (AUC@5% 0.78). The survivability strongly correlated with different types of grafting and the age of the patients (<40years) (Fig. 2).

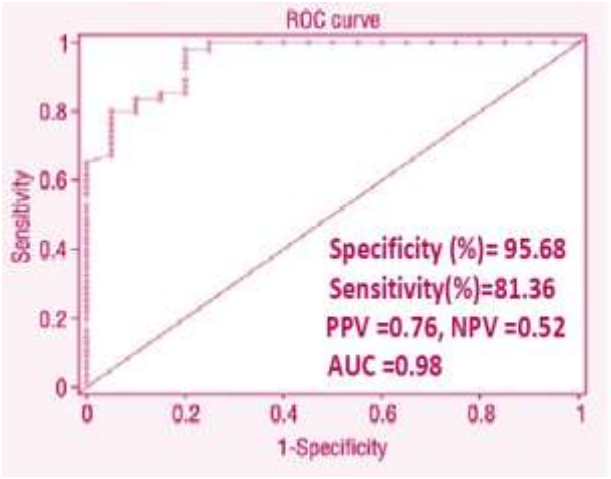

Figure 1: CABG final outcome (survivability)

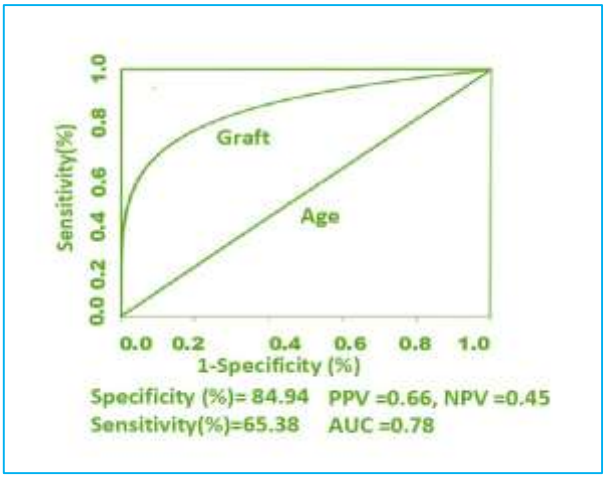

Figure 2: Grafting correlation with age

Table 4: Correlation of various grafts with repsect to age and gender

CABG attributes	(%) Male(n=75) /Female(n=25)	Mean age±SD	Odd ratio	P-value
LIMA-LAD (n=81)	81%	38.68+/-1.85	4.98	≤0.000
LIMA-RIMA-OM1	02%	36.55+/-0.85	3.62	≤0.000
LIMA –Radial- RAMUS D1	01%	37.85+/-1.25	2.22	≤0.000
SVG (Male/F)	82%	37.57+/-2.66	3.28	≤0.000
SVG-LAD (Male/F) -16/3	16%	37.11±4.09	1.22	≤0.000
SVG-DIAGONAL(M/F)	02%	39.63±0.11	1.32	≤0.000
SVG-OM(M/F)	03%	37.55±0.16	1.11	≤0.000
SVG TO RAMUS(M/F)	18%	36.2±0.95	1.89	≤0.000
SVG-RCA (Male /F)	10%	39.11±0.12	1.38	≤0.000
SVG-DISTAL RCA (Male /F)	08%	36.25±0.33	1.14	≤0.000
SVG-PDA(Male /F)	22%	38.25±2.18	1.63	≤0.000
SVG->PLV (M/F)	03%	40.00±0.01	1.62	≤0.000
RIMA-OM1(M/F) 6:1	07%	40.00 +/-0.0	<1	>0.001
LIMA TO RIMA(M/F) -2:0	02%	38.55+/-0.25	1.54	≤0.000
Radial artery - OM (M/F) - 3:0	03%			
Death (Male=2)	01%	37.50+/0.85	<1	>0.001
LIMA - LAD, SVG TO OM, SVG TO PDA	01%			
LIMA-RADIAL Y TO RAMUS & D1	02			
Co morbidity (yes) Hypertension-01, Diabetes Mellitus (DM)-01				

The LIMA and LAD correlation was done in multivariate logistic regression, and the absolute observed prevalence (LIMA-LAD) was seen in 81% with a mean age of 38.68, SD 1.85. SVG was 82%, SVG-LAD 16%, **SVG-DIAGONAL(M/F)** 02%**, SVG-OM(M/F)** 03%**, SVG TO RAMUS(M/F)** 18%**, SVG-RCA (M/F)** 10%**, SVG-DISTAL RCA (M/F)** 08%**, SVG-PDA (M/F)** 22%**, SVG->PLV (M/F)** 03%. Two cases of death with a mean age of 37.50 years (associated mortality: hypertension and diabetes mellitus) All CABG-associated parameters, including LIMALAD and OPCAB, were found to be statistically significant (p = 0.001).

DISCUSSION

This study has shown an alarmingly higher rate of PCAD in India as compared to earlier studies conducted at national and worldwide levels. Majority of the patients received the left internal mammary artery (LIMA) to the left anterior descending (LAD) artery as a standard graft, with the radial artery and saphenous vein being the next alternative conduits. (Radosław Zwoliński1 et al. 2012)[10]. The long-term outcomes of CABG surgery in young women are positive, particularly with regard to their quality of life. However, a significant decrease in patients' professional activity was observed postoperatively, which was largely due to a subjective feeling of illness, rather than any medical reasons. The main factor contributing to an unsatisfactory clinical outcome after CABG in younger population is continued cigarette smoking. Additionally, the study population was

significantly affected by the onset of menopause before the age of 45 years. (Cohen et al., 1986)[11] The likelihood of failure for CABG surgery in young individuals increased with the presence of cardiac risk factors. Given the high rate of long-term failure for CABG surgery in young patients, it is necessary to reassess its use in this group in comparison to current aggressive medical therapy for angina.(Arslan et al., 2015)The isolated coronary artery bypass surgery can be performed on young patients, and the early postoperative results are similar to those of middle-aged patients. Therefore, we believe that age does not significantly affect the early postoperative outcome of this procedure. The age of PCAD presentation in the current study is much younger than the mean age for Zahrni et al., and is comparable to Prashanth et al., 2010, Ilir Balaj et al., 2023. Coronary endarterectomy allows revascularization in end-stage CAD when the myocardium is still viable. The use of dual Antiplatelet therapy after Coronary endarterectomy for at least six months seems to improve mid-tolong-term patency rates and survival, and reduced the incidence of major adverse cardiac and cerebrovascular events. (Balaj et al.,2023)[1]. Imaging after coronary surgery is considered the best test of postoperative graft function. However, it was only available in 48.50% of surviving patients due to patients refusal and financial issues , although proposed by us to all patients .Other outcomes such as low cardiac output syndrome , Myocardial infarction and cardiac cause mortality would indirectly indicate graft failure .In this present study , the correlation of grafting is significantly associated with younger aged population with ignorable CFR (mortality) which is 2% .The study, in accordance with Tahir et al. and Badran et al., showed a significant difference in the prevalence of diabetes mellitus between premature and mature CAD. Unlike Badran et al., however, it showed no significant gender difference of prevalence of diabetes mellitus in the PCAD. Besides, the study showed a significantly higher incidence of dyslipidemia in PCAD that is similar to what Penida et al. found. Takanshi et al., reported a 30 days mortality of 1.10% and a Perioperative Myocardial infarction rate of 95 in patients after Coronary endarterectomy of the LAD and left internal thoracic artery (LITA) grafting . Although coronary artery endarterectomy remains rare in current practice , it has continued to be used as a bail out option in patients presenting with end stage diffuse coronary artery disease undergoing coronary artery bypass grafting with acceptable short to long term survival outcomes, Mäkikallio et al., 2016[8].

CONCLUSION

In the current scenario, CVD risk is more common in resource-poor and developing countries. As per all the research findings, the present study concludes that CABG surgery can be performed with comparable attributes for treating the patients with coronary artery disease who underwent surgery at <40 years of age. Relative long-term survivability after CABG surgery, irrespective of gender needs to be evaluated over a longer duration of time to derive further conclusions The present study will serve as a clinical guide for cardiologists. There was also a trend for improved disease-specific survival for younger patients in the Indian context. CABG continues to be the standard form of treatment for revascularisation in this subset of patients.

Limitations of the study

The present study was conducted as a sample-based observational study with a single center. The naive or control population was not grouped to compare the efficacy of the grafting; due to the limited intervention on the patients selection, we only considered registry data for follow-up of the cases. Those possibilities of selection bias call for an increase in the random error for testing the hypothesis.

Conflict of interest

There is no conflict of interest between any funding agency and an institutional authority.

Ethical clearance

The primary data sets were collected from the institutional registry, and clearance was obtained by IBR.

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