

Original research

Risk factors to predict severity of coronary artery disease in young patients undergoing coronary artery bypass grafting: A retrospective observational study

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Abstract

Objective: The differing pattern of dyslipidemia combined with inherent insulin resistance and contribution from varying lifestyles makes Indians more vulnerable to coronary artery disease (CAD) at a younger age. Smoking and other forms of tobacco, dyslipidemia and hypertension are major risk factors in the young. Our aim of the study is to find out risk factors to predict severity of CAD in young patients undergoing coronary artery bypass surgery (CABG).

Methods: Young patients below 45 years of age consecutively admitted at our hospital and undergoing CABG were included. Demographic data are collected and analyzed. All the risk factors for early coronary artery disease and its outcome and intraoperative and immediate postoperative complications are analyzed. Early outcome analysis was done at the end of 1 year and midterm analysis was done at the end of 5 years. All routine investigations, 2D-echocardiography, electrocardiogram, and chest X-ray were analyzed at regular intervals and when required in the follow-up period also.

Results: We retrospectively evaluated 148 adult CAD patients aged ≤ 45 years, who underwent their first isolated CABG surgery at our institute. We observed that smoking was the most common risk factor followed by hypertension, altered lipid profile and diabetes. Family history of CAD and obesity were also noted in 32.4% and 21.6% of patients.

Conclusion: Our young surgical patients have a high frequency of risk factors such as smoking and dyslipidemia, hypertension and obesity which may lead to accelerated atherosclerosis and high frequency of 80% of multivessel disease in our cohort. Hypertension is the significant predictor of severe CAD in our cohort. High prevalence of CAD risk factors and LV dysfunction are associated with mortality in our cohort. Five-year survival in young Indian population after CABG is 91.8% with good functional class..

Prevention of risk factors is necessary to prevent CAD in young adults. Optimal secondary prevention with medications and strict adherence to lifestyle changes should be ensured to reduce future coronary events.

Key words: coronary artery bypass grafting, coronary artery disease, young patients

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Introduction

Old age has been reported to be a major risk factor for coronary artery disease (CAD), thus, surgical myocardial revascularization procedures are most often performed in patients with rather advanced age. Conversely, young adults represent a relatively rare and infrequent subset of ischemic heart disease (1, 2). Coronary bypass grafting is probably the most extensively studied of all surgical techniques, but the reported data on its outcome when performed in the younger population is relatively unusual (3-6).

Already published data shown that in nowadays CAD is observed at a younger age in Indians (1-4), with over 50% of CAD mortality occurring in individuals aged less than 50 years, and one-fourth of all acute myocardial infarctions (MIs) are reported in patients

below the age of 40 years (3). Projection suggested that by 2015, 62 million Indians will have CAD of which 23 million were expected to be below 40 years (5).

The differing pattern of dyslipidemia combined with inherent insulin resistance and contribution from varying lifestyles makes Indians more vulnerable to CAD at a younger age (4). Smoking and other forms of tobacco, dyslipidemia and hypertension are major risk factors in the young (6, 7). Clinical presentation of CAD in young patients may vary from multivessel disease without known risk factors to extensive ischemia in asymptomatic individuals (8). In the absence of any conventional risk factors at a young age, the occurrence of CAD makes it difficult to understand etiopathogenesis (9-11).

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Appropriate selection of medical and/or interventional strategies to improve morbidity and mortality outcomes may be difficult; however, effective risk stratification is necessary to improve outcomes (12-14).

Coronary artery bypass grafting (CABG) remains the "gold" standard for excessive CAD involving three vessels or the left main stem (15). CABG is more durable than percutaneous coronary intervention, especially when using arterial grafts only (16-18). There is an abundant literature regarding the CAD risk factors in elderly patients undergoing cardiac surgery (19-21). However, reports about younger patients undergoing CABG are sparse in comparison. D'Errigo et al. (22) recently reported the multicentre data concerning patients below 50 years of age receiving CABG with a mortality rate of 0.9% overall.

Our aim of the study is to find out the risk factors of CAD and outcomes of CABG in patients below the age of 45 years in the Indian population.

And our objectives are:

1. To identify the risk factors of coronary artery disease in patients below 45 years of age.
2. To study the nature of coronary artery disease in young patients.
3. To study the morbidity and mortality of coronary bypass.
4. To study the early and midterm outcomes of these patients.

Methods

Study designs and population

The study design is retrospective observational.

After approval from the Institutional ethics committee (UNMICRC/CVTS/2019/19), young patients below 45 years of age consecutively admitted at our hospital and undergoing CABG were included retrospectively from the period of August 2019 to August 2021 in our study. All patients provided informed consent for all procedures.

Data collection

Demographic data were collected and analyzed. All the risk factors for early CAD, intra-operative and immediate postoperative complications, and outcomes of CABG were analyzed. Early outcomes analysis was done at the end of 1 year and midterm analysis was done at the end of 5 years. All routine investigations, 2D-echocardiography, electrocardiography (ECG), and chest X-ray were analyzed at regular intervals and when required in the follow-up period also. A separate analysis was done for the patients requiring re-operation. Mortality and morbidity analysis was done as well. The number and

following type of grafts used in these patients were analyzed:

- LIMA – left internal mammary artery
- RIMA – right internal mammary artery
- LIMA-RIMA - left internal mammary artery - right internal mammary artery
- RADIAL
- SEPHANOUS VEIN

Risk factors definitions

Diabetes was defined as having a history of diabetes diagnosed and/or treated with medication and/or diet or fasting blood glucose 126 mg/dl or greater or HbA1C > 6.5. Hypertension was defined as having a history of hypertension diagnosed and/or treated with medication, diet, and/or exercise, blood pressure greater than 140 mmHg systolic or 90 mmHg diastolic on at least two occasions. Hyperlipidaemia was defined as a history of dyslipidemia diagnosed and/or treated by a physician or total cholesterol greater than 200 mg/dl, low-density lipoprotein greater than or equal to 130 mg/dl, or high-density lipoprotein <40 mg/dl.

A current smoker was defined as a person smoking cigarettes within 1 month of index admission. A positive family history of CAD was defined as evidence of CAD in a parent, sibling, or child before 55 years of age. Being overweight was defined as a body mass index (BMI) greater than 25 kg/ m². Obesity was defined as BMI greater than 30 kg/ m². A waist circumference of more than 102 cm was considered as high.

Coronary angiography

All patients were subjected to coronary angiography during the index admission or on follow-up. Significant stenosis was defined as more than 50% stenosis in any of the coronary arteries while insignificant disease as less than 50% stenosis or plaques in any of the coronary arteries.

Statistical analysis

Statistical analysis was performed using SPSS, Version 26.0 (Chicago, IL, USA). The independent sample t-test and paired sample t test used to compare continuous variables. The Chi-square test was used to compare the categorical variable. Data were presented as mean (SD) or proportion as appropriate. The logistic regression analysis was done to define predictive value of risk factors of CAD severity in young patients. The Kaplan-Meier curve was done for survival analysis. The "p" value less than 0.05 was considered to be significant.

Sample size was calculated through Rao soft software with 95% confidence interval and 5 % margin error.

Results

We retrospectively evaluated 148 adult CAD patients aged ≤ 45 years who underwent the first isolated CABG surgery at our institute during the period from

August 2015 to August 2021. Four patients were lost in follow-up. Three patients died in the immediate postoperative period and 9 died in the course of follow up (Table 1).

| Table 1. Demographic and clinical and operative characteristics | | | |
|---|---------------------|------------------|-------------------|
| A. Preoperative qualitative data | | | |
| Variable | Sub variable | Frequency | Percentage |
| Gender | Male | 123 | 83.1 |
| | Female | 25 | 16.9 |
| Age groups | 21-25 | 1 | 0.7 |
| | 26-30 | 3 | 2 |
| | 31-35 | 7 | 4.7 |
| | 36-40 | 42 | 28.4 |
| | 41-45 | 95 | 64.2 |
| B. Preoperative findings | | | |
| Variable | Sub variable | Frequency | Percentage |
| Coronary artery disease | SVD | 22 | 14.9 |
| | DVD | 42 | 28.4 |
| | TVD | 84 | 56.8 |
| High cholesterol | | 58 | 39.2 |
| Diabetes | | 57 | 38.5 |
| Hypertension | | 72 | 48.6 |
| Smoking | | 78 | 52.7 |
| Obesity | | 32 | 21.6 |
| Family History | | 48 | 32.4 |
| Electrocardiography findings | CSA | 4 | 2.7 |
| | EA | 6 | 4.1 |
| | NSTEMI | 44 | 29.7 |
| | STEMI | 76 | 51.4 |
| | UA | 18 | 12.2 |
| C. Intraoperative and postoperative findings | | | |
| Intraoperative findings | Sub variable | Frequency | Percentage |
| Total arterial graft | | 83 | 56.1 |
| Functional NYHA class after 1 year of surgery | 1 | 75 | 50.7 |
| | 2 | 42 | 28.4 |
| | 3 | 13 | 8.8 |
| | 4 | 3 | 2 |
| | Lost to Follow-up | 15 | 10.1 |
| Mortality | | 12 | 8.1 |
| In -hospital mortality | | 3 | 2.02 |
| EA - exertional angina, CSA - chronic stable angina, DVD – double- vessel disease, NSTEMI - non ST- elevation myocardial infarction, STEM -ST- elevation myocardial infarction SVD - single vessel disease, TVD - triple vessel disease, UA - unstable angina | | | |

Out of the total of 148 patients, 123 were male and 25 were female. According to the data studied the youngest patient to undergo CABG was 23 years old. The mean age at presentation was 40.74 years.

Electrocardiography: Out of 148 patients 76 (51.4%) patients had STEMI, 44 had NSTEMI (29.7%), UA was seen in 18 (12.2%) patients, 6 (4.1%) had EA and 4 (2.7%) of them had CSA (Table 1).

Risk factors: In our study, we observed that smoking was the most common risk factor followed by hypertension, altered lipid profile and diabetes.

Family history of CAD and obesity were also noted in 32.4% and 21.6% of patients. (Table 1).

Extent of coronary artery disease: On angiography, triple- vessel disease was noted in 84 out of 148 double - vessel disease in 42 and single - vessel disease in 22 patients (Table 1).

Mortality analysis: In-hospital mortality in our study group was 2.02%. In the follow-up period, 9 patients died of whom one died of malignancy. In our follow-up till 11th February 2022, the overall calculated survival rate was found to be 91.9%. (Table 1) (Fig. 1).

| Case Processing Summary | | | |
|-------------------------|-------------|----------|---------|
| Total N | N of Events | Censored | |
| | | N | Percent |
| 147 | 12 | 135 | 91.8% |

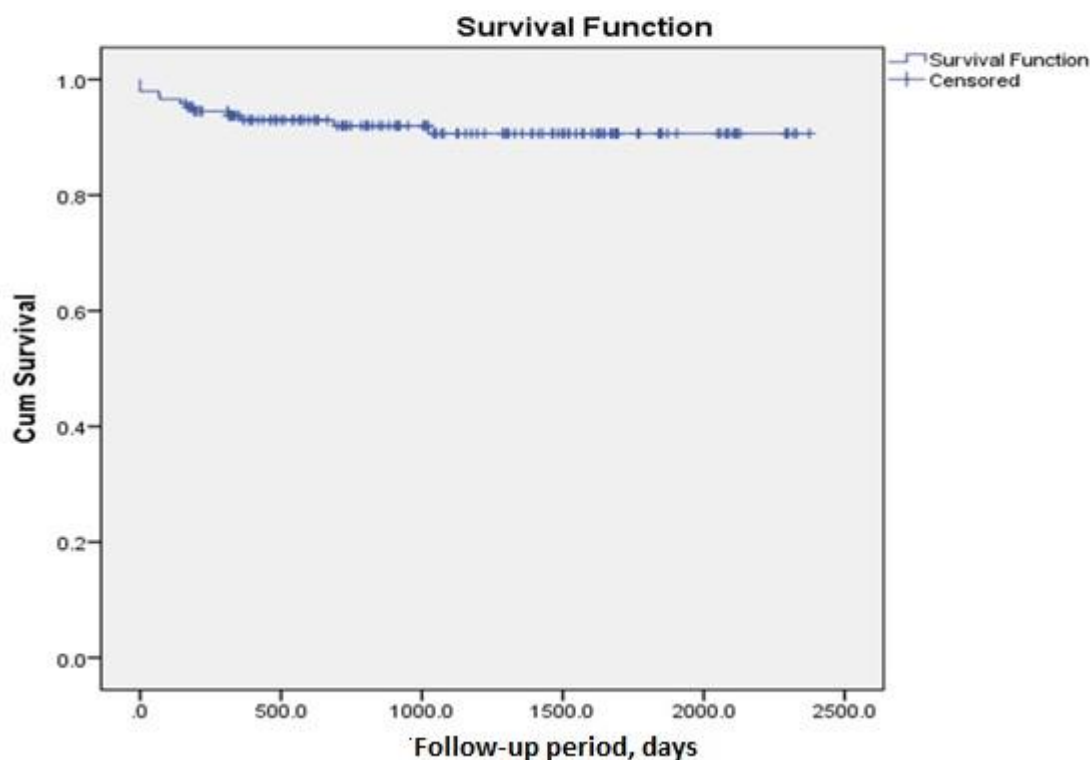


Figure 1. Kaplan-Meier survival curve of young patients during follow-up period

Risk factors in deceased patients: Of the 12 patients that died in the postoperative period hypertension, diabetes and dyslipidemia was noted in half of the patients. History of smoking was present in 5 patients, 4 of them had a positive family history and 2 were morbidly obese. Severe left ventricular (LV) dysfunction was noted in 8 out of 12 (66.66%)

patients that died, and mild to moderate LV dysfunction was seen in 2. The results of our study confirmed that LV dysfunction was a strong factor associated with death among young patients who underwent CABG.

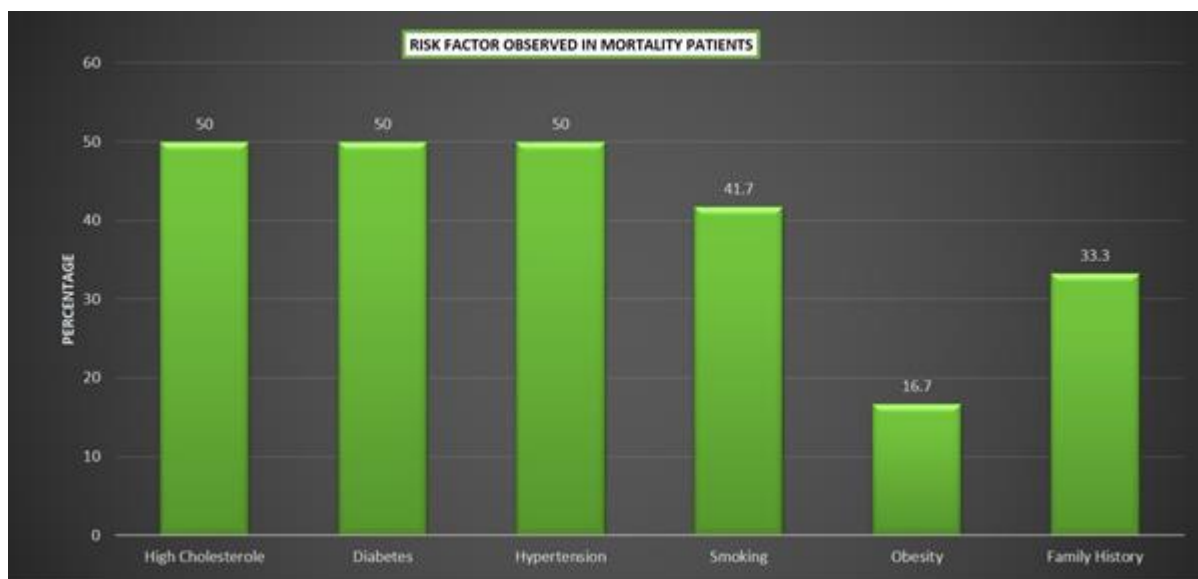


Figure 2. Risk factors for coronary artery disease in mortality group of young patients undergoing coronary artery bypass surgery

Coronary artery endarterectomy and outcomes:

Overall, 13 patients underwent endarterectomy, 6 out of these 13 patients were in NYHA class I at follow-up. Two patients died. Both patients had severe LV dysfunction. One of the patients died of severe biventricular dysfunction with sepsis, MODS and sternal dehiscence. The above- mentioned patient

was intra-aortic balloon pump dependent. Another patient died at the home of acute myocardial infraction. Patient was a known case of hypertension, diabetes, obesity and hyperlipidemia with a positive family history. One patient is in NYHA class IV. He is a smoker and has a known case of hypertension and hyperlipidemia with a positive family history.

Table 2. Postoperative functional class in young patients who underwent coronary endarterectomy

| NYHA class | Number of patients | Percentage |
|------------|--------------------|------------|
| I | 6 | 46.2 |
| II | 3 | 23.1 |
| III | 1 | 7.7 |
| IV | 1 | 7.7 |
| Died | 2 | 15.4 |

Left ventricular function before and after CABG: In our study, we observed and compared the LVEF of the operated patients. We noted an improvement in the LVEF in the follow-up period. The mean preoperative

EF of the patient was 42.59%, while the mean postoperative EF was 45.34%. This showed significant clinical improvement in young patients undergoing CABG (p <0.0001) (Table 3).

Table 3. Left ventricular ejection fraction (LVEF) before and after surgery

| Variables | Mean | Standard Deviation | Minimum | Maximum | p |
|-----------------------|-------|--------------------|---------|---------|---------|
| Pre-operative LVEF % | 42.59 | 10.54 | 20.00 | 60.00 | <0.0001 |
| Post-operative LVEF % | 45.34 | 10.77 | 15.00 | 60.00 | |

Table 4. Risk factors analysis the severity of coronary artery disease

| | B | Wald | OR(95% CI Lower, Upper) | p |
|---|--------|-------|-------------------------|--------|
| High cholesterol | -0.568 | 1.256 | 0.57(0.21,1.54) | 0.2624 |
| Diabetes | -0.615 | 1.393 | 0.55(0.2,1.51) | 0.2379 |
| Hypertension | 1.268 | 5.717 | 3.56(1.26,10.06) | 0.0167 |
| Obesity | -1.238 | 4.921 | 0.29(0.1,0.87) | 0.0265 |
| Family history of coronary artery disease | 0.701 | 1.420 | 2.02(0.64,6.39) | 0.2334 |

The above Table 4 shows that in young patients, hypertension and obesity were significant predictors of severe coronary artery disease in our patients ($p=0.0167$ and $p=0.0265$, respectively).

Discussion

CAD in young adults is increasing in prevalence due to changing lifestyles. Risk factor profile remains similar to those of elderly patients but conditions like hyperhomocysteinemia, hypercoagulable states, cocaine use, etc. may be specific to the younger population and should be evaluated in CAD cases.

The prevalence of CAD is more in males as compared to females. In our study among young patients undergoing CABG, 80% were males. This is consistent with the study conducted by Aggarwal et al., who found CAD prevalence of 94.94% ($n=75/79$) and 86.75% ($n=72/83$) in periods 2001-2002 and 2009-2010 respectively (23). Other reports also suggest a higher CAD prevalence in young Indian males than females (24).

Among CAD types in young Indian population undergoing STEMI was found to be the most common form of presentation in young adults. Bhardwaj et al., also reported acute MI almost exclusively in young males ($n=123/124$) (6).

Classic cardiovascular risks factors such as hypertension, hyperlipidemia, obesity, diabetes and smoking are highly prevalent among young Indian CAD patients undergoing CABG in our study that is in agreement with previously published (24). In the study of Kelly et al. (25), their young coronary patients were more likely to have a positive family history, hypercholesterolemia and to be smokers compared with their control group. These patients probably have

the more aggressive atherosclerotic disease. Several risk factors including dyslipidaemia and pro-coagulant disorders may be associated with disease progression in these patients. Furthermore, vein graft patency is decreased in patients with hypercholesterolemia and diabetes which are commonly seen in young patients with CAD.

Obstructive as well as non-obstructive pathologies prevail in young individuals. Search for causes like coronary dissection, myocardial bridging, coronary anomalies, aorto-arteritis etc., is necessary in cases where causes remain unidentified. Investigations like exercise stress testing, stress echocardiography, and coronary angiography can help identify young individuals at higher risk of CAD. In our study, among young patients undergoing CABG multivessel disease was found in 80%, including triple-vessel in more than half – 56%. Predictors of coronary artery disease severity in our patients were hypertension and obesity: probability of severe CAD was 3.5 times higher in patients with hypertension, while obesity had protective effect.

An association between LV dysfunction and worse long-term prognosis after CABG has been demonstrated previously (26, 27). The results of our study confirmed that LV dysfunction was a strong factor associated with death among young patients who underwent CABG. Hypertension, dyslipidemia, diabetes, smoking and positive family history were the most common risk factors seen in patients who died in the course of our study.

In our study 75 out of 148 patients (50.7%) were NYHA class I at subsequent follow-up, showing a good midterm outcome and symptom-free survival of young patients undergoing CABG. Survival was 91.8%.

Optimal medical management can be helpful in non-obstructive CAD. For obstructive CAD, PCI with stenting should be preferred if available and affordable. For complex coronary lesions, multivessel disease or LV dysfunction, especially when associated with diabetes CABG can be a method of choice. Preference to total arterial grafting should be given. In our study we found that patients undergoing total arterial grafting had better symptom-free survival. Occlusion of saphenous vein grafts has prompted the use of internal mammary arteries as the conduits of choice (28). Several studies have shown the superiority of mammary grafts over saphenous vein grafts in maintaining patency and improving the 10-year survival rate (28-32). Loop et al. (31) found that patients who had vein grafts had 1.61 times greater risk of death throughout the 10 years compared with those who received internal mammary artery conduits.

Study limitations

This is the retrospective observational study and we collected the data consecutively from the database. To make more results stronger we needed to collect the data from healthy individual to compare the risk factors.

Conclusion

Our young surgical patients have a high frequency of risk factors such as smoking and dyslipidemia, hypertension and obesity which may lead to accelerated atherosclerosis and high frequency of 80% of multivessel disease in our cohort. Hypertension is the significant predictor of severe CAD in our cohort. High prevalence of CAD risk factors and LV dysfunction are associated with mortality in our cohort. Five-year survival in young Indian population after CABG is 91.8% with good functional class.. Prevention of risk factors is necessary to prevent CAD in young adults. Optimal secondary prevention with medications and strict adherence to lifestyle changes should be ensured to reduce future coronary events.

Ethics: Informed consent was obtained from patients before all procedures. The study protocol was approved by the Ethics Committee of the institute (UNMICRC/CVTS/2019/19)

Peer-review: External and internal

Conflicts of interest: None to declare

Authorship: K.B., M.S., N.P., H.P., A.P., C.D. equally contributed to study and manuscript preparation

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