

Original Research Article


A Study of the Conventional Risk Factors and Early Outcomes of Coronary Artery Bypass Grafting in Patient with Early Onset of Coronary Artery Disease (Age <45 Years): A Five Year Retrospective Study

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Abstract

Introduction: Coronary Artery Disease (CAD) is a significant cause of morbidity and mortality in the Indian population. We have been very few studies comparing the Indian population who develop CAD at an early age, arbitrarily defined as less than 45 years with those who develop it at a later. Very few studies compare the conventional risk factors in the patients with early onset CAD and those who present later.

Aim: To study the conventional risk factors in patient who presented with early onset of coronary artery disease (age < 45 years) planned for CABG and to study the immediate outcome and perioperative morbidity (within 30 days of surgery) in these patients.

Materials and methods: Between January 2016 to December 2020, data was collected for 100 patients below age of 45 years who underwent coronary artery bypass grafting in NIMS hospital. We retrospectively analyzed the perioperative data and evaluated patient outcome.

Results: The mean age was 42 years, majority was males - 80 while females - 20. Smoking - 33, Hypertension - 50, Diabetes - 35, Hypercholesterolemia - 38, were the most frequent risk factors. Impaired left ventricular function (EF < 40%) in 15, indication for surgery was triple vessel disease in -79, double vessel disease in - 15, and single vessel disease in - 6, LMCA was affected in 10, the mean hospital stay was 7.97+/- 1.97 days, there were 8 deaths (within 30 days). Post-operative ICU stay was 4.13+/-1.81 days. Use of IABP in 14 patients, inotropes required for more than 48 hours in 87 patients, complications like renal dysfunction 5, and no cerebral stroke was observed.

Conclusion: We are getting considerable number of young patient with coronary artery disease as there is early age onset of risk factors and most of them land up with a triple vessel disease, however, as they are young the post-operative morbidity is low and duration of ICU hospital stay is less.

Key words

Conventional risk factors, Early outcome, Coronary artery bypass grafting, CABG, Coronary artery disease.

Introduction

Coronary Artery Disease (CAD) is a significant cause of morbidity and mortality in the Indian population [1]. Studies have shown that Indian subpopulation may be at a greater risk of CAD developing at a younger age than the western population [2]. There have been very few studies comparing the Indian population who develop CAD at an early age, arbitrarily defined as less than 45 years with those who develop it at a later. Very few studies compare the conventional risk factors in the patients with early onset CAD and those who present later [3]. Similarly, there are very few studies which compare the perioperative Coronary Artery Bypass Grafting (CABG) surgical outcomes in patients with early onset CAD versus those who undergo the procedure at a later age [4]. The early onset patients might have lesser exposure to Diabetes mellitus, have better lung function or be fitter, however, the nature of disease might be different than that of the older population, presence of micro vascular disease and variability in incidence of Myocardial Infarction [5] are certain conditions which might influence the surgical outcome.

The present study was a retrospective study to compare the clinical profile and outcomes of CABG in patients with early onset CAD and those with the conventional presentation of CAD.

Materials and methods

This study was a retrospective study conducted at NIMS, Hyderabad from 2016-2020. Study group was 100 patients less than 45 years of age who undergo CABG for CAD. This group was compared to the control group by selecting the patient aged more than 45 years listed in order for surgery immediately after the study patient. With the approval from Institutional Ethics Committee and information was obtained from case records and discharge records, including telephonic calls.

Inclusion criteria

- All patients with CAD undergoing CABG at age <45 years form the study group
- All patients listed to undergo surgery immediately after the early onset CABG patients as per medical records form the control group.

Exclusion criteria

- Patients with concomitant procedures
- Patients with preoperative cerebral stroke and renal dysfunction
- Patients undergoing emergency surgeries

Operative Technique

A full median sternotomy was performed. cardiopulmonary support was used in most of the cases, off pump CABG was taken as alternative.

Total Arterial Revascularization (TAR)

After a full median sternotomy the LIMA harvested in no touch technique with minimal trauma as pedicle graft and treat with papaverine solution prior to use.

Combined Venous And Arterial Revascularization

Usually use the LIMA and the saphenous vein as grafts. The LIMA was most frequently anastomosed to the LAD or D1, whereas the saphenous used for rest of diseased vessels. The venous only revascularization achieved using the saphenous vein as aortocoronary bypass anastomize to ascending aorta as standardize. CPB instituted with cannulation of ascending aorta and a single two stage right atrial cannulation. Standard bypass management included membrane oxygenators, arterial line filters, and non-pulsatile flow with a mean arterial pressure greater than 50 mm Hg. The myocardium was protected by using intermittent antegrade cold blood cardioplegia or crystalloid solution. Anticoagulation achieved using 300U/Kg of heparin. If required heparin supplement to maintain the activated clotting time above 400 sec. and fully reverse with protamine at the end of the procedure. Patient received nitroglycerin infusions for the first 24 hours if feasible. Inotropic agents were chosen by the hemodynamic state. Other routine medications included daily Aspirin and resumption of cholesterol lowering agents and B-blockers unless contraindicated beginning during the early postoperative course.

All data of Patient demographics, Diagnosis, Surgeries Performed, OT records and follow up record collected and analyzed in excel spread sheet. Continuous data presented was Mean and Standard Deviation, categorical data as percentages.

Statistical Analysis

Patient characteristics were described by using frequencies and percentages for categorical variables, and means and standard deviations for continuous variables. The primary outcome measure was death within 30 days. Secondary outcome measures included ICU stay, post-operative hospital stays, renal dysfunction, cerebral stroke. To describe central tendencies we have used mean, to find out difference between groups T test was used and to find association between variables Chi square test and Fischer's exact test had been used.

Results

In our study, majority of the study participants belonged to the age groups of 41-50 years and 35% belonged to the age groups of 31-40 and a meager of 3% belonged to the age group of 20-30. Majority of the patients with CAD who underwent CABG were male (80%).

Most common risk factor found among the patients of CAD is hypertension in 50%. Whereas, the next most common risk factors observed were hypercholesterolemia, DM, alcohol consumption and smoking (**Table – 1**).

In majority of the patients three vessel diseases was observed (79%), whereas 15% had a double vessel disease (15%) and a minority of 6% had a single vessel disease (**Figure – 1**).

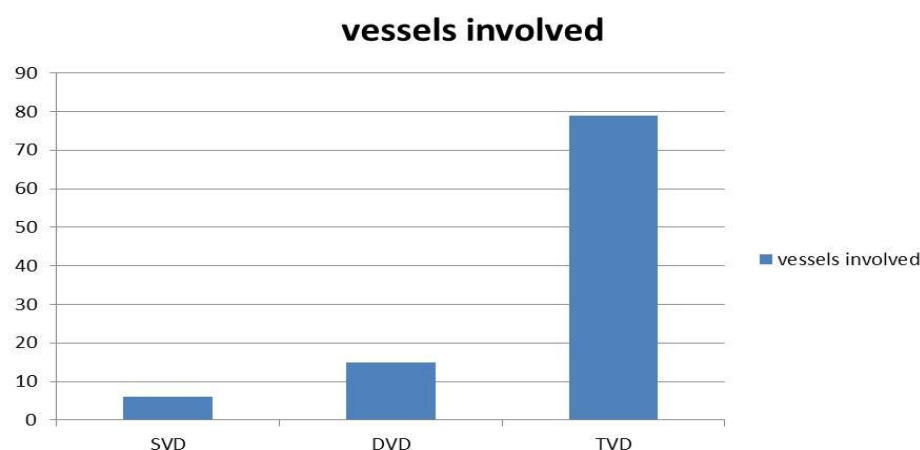
CABG alone was employed in majority of the patients, whereas additional procedures like mitral valve repair and repair of ventricular septal defect has been employed in a meager of 8% of the patients.

In Majority of the patients (94%) the technique employed was Del nido Cardioplegia during surgery, whereas off pump technique was employed in a single patient. Majority of the study participants who underwent CABG required 3-4 grafts (82%), whereas a very few patients needed a single graft (4%) and a meager needed more than 5 grafts (2%) as per **Table - 2**.

Table - 1: Age-wise distribution of the study participants.

Age	Frequency	Percentage
20-30	3	3%
31-40	35	35%
41-50	62	62%
Total	100	100%
Gender		
Male	80	80%
Female	20	20%
Risk factors		
Hypertension	50	50%
Hypercholesterolemia	38	38%
DM	35	35%
Alcohol dependency	34	34%
Tobacco usage	33	33%
Family history	26	26%
Sedentary lifestyle	17	17%

Figure – 1: A bar chart depicting frequency distribution of patients depending on the number of vessels involved.



SVD: Single Vessel Disease, DVD: Double Vessel Disease, TVD: Triple Vessel Disease

In majority (95%) of the patients they needed a usage of 2 to 3 ionotropes, which were a combination of dopamine, adrenaline and nor adrenaline. Very meager needed a usage of 4 ionotropes (**Table – 3**).

Overall, the mean duration of stay in the ICU was 4.13+/-1.81 days and the mean hospital stay was 7.97+/- 1.97 days, there were 8 deaths (within 30 days) and the length of duration of hospital stay was found to have a statistically significant association with factors like the surgical technique employed and the drugs used for ionotropic support. More complicated the

surgery and more the number of ionotropes used more was the length of ICU and the hospital stay (**Table – 4**).

Among the patients who underwent surgery, no statistically significant association had been observed between the pump time and length of a patients stay in the ICU during the post-operative period. But, a weakly positive correlation had been observed between the mean pump time and the duration of hospital stay, by which we can say that as the mean duration of pump times increases the mean duration of length of ICU as well as hospital stay also increased (**Figure – 2**).

Table - 2: Frequency distribution based on the surgical procedure employed.

Surgery done	Frequency	Percentage
CABG	77	77%
CABG+IABP	13	13%
CABG+MVR	7	7%
CABG+VSDR	3	3%
Technique employed		
BCP	5	5%
DNCP	94	94%
Off pump	1	1%
No. of grafts		
1	4	4%
2	12	12%
3	56	56%
4	26	26%
5	2	2%

CABG: Coronary Artery Bypass Graft, IABP: Intra Aortic Ballon Pump Device, MVR: Mitral Valve Repair, VSDR: Ventricle Septal Defect Closure, BCP: Blood Cardioplegia, DNCP: Del Nido Cardioplegia.

Table - 3: Frequency distribution based on the ionotropes used.

Ionotropes used	Frequency	Percentage
1 (A)	3	3%
2(A+B)	51	51%
3(A+B+C)	44	44%
4(A+B+C+D)	1	1%
4(A+B+C+E)	1	1%

A: DOPAMINE INJ. **B:** ADRENALINE INJ. **C:** NORADRENALINE INJ. **D:** VASOPRESSIN INJ. **E:** DOBUTAMINE INJ.

Table - 4: Mean duration of ICU and hospital stay based on various factors.

Factor		Mean duration (in days)			
		ICU		Hospital	
Age	<40	4.13±1.89	0.99	8.11±1.74	0.54
	>40	4.12±1.77		7.87±2.11	
Gender	Male	4.01±1.41	0.19	7.93±1.87	0.76
	Female	4.6±2.93		8.1±2.36	
Diagnosis	DVD	3.33±1.23	0.13	7.4±1.45	0.
	SVD	3.67±2.66		7.83±2.64	
	TVD	4.32±1.81		8.08±2.01	
LVD	Good	3.47±1.61	0.13	7.16±1.12	0.14
	Moderate	4.18±1.69		8.16±1.74	
	Severe	4.53±2.05		8.17±2.6	
Surgical procedure	CABG	3.89±1.73	0.02	7.56±1.77	0.01
	CABG+ABP	5±1.91		8.92±2.06	
	CABG+MVR	4.43±1.27		9±1.73	
	CABG+VSD	6.33±2.52		11.67±1.15	
Inotropic support	<2	3.28±0.92	<0.0001	7.22±0.98	<0.0001
	>2	5.11±2.1		8.76±2.42	

Figure - 2: Correlation between pump time and stay in ICU.

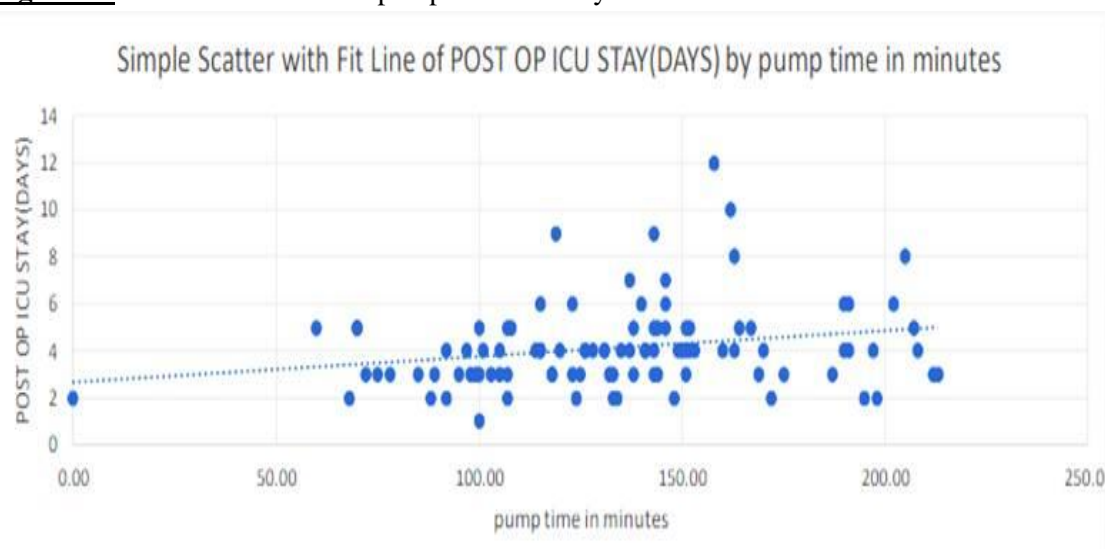


Table - 5: Renal dysfunction in comparison with various factors.

Factor		Renal dysfunction		P value	Statistical significance
		Yes	No		
Age	<40	2	36	0.93	NS
	>40	3	59		
Gender	Male	3	77	0.58	NS
	Female	2	18		
Diagnosis	DVD	1	14	0.4	NS
	SVD	1	5		
	TVD	3	76		
LVD	Good	0	19	0.7	NS
	Moderate	3	47		
	Severe	2	28		
Surgery employed	CABG	2	75	0.003	Significant
	CABG+IABP	0	13		
	CABG+MVR	1	6		
	CABG+VSD	2	1		
Inotropic support	<2	1	53	0.18	NS
	>2	4	42		
Total cholesterol levels	<200	2	60	0.53	NS
	>200	3	35		
CKD	Yes	0	2	1	NS
	No	5	93		

Among the patients who underwent surgery, renal dysfunction was seen in 5% of the subjects and it was found to have a statistically significant association with the surgery done. More complicated the surgery, renal dysfunction is seen in them (Table – 5).

Among the patients who underwent surgery, Mortality was seen in 8% of the patients. A statistically significant association of mortality

was seen among factors like female gender, severe left ventricular dysfunction and the no of inotropic drugs used. Mortality rate among female was more. A severe left ventricular dysfunction had a negative impact on survival of the patients and when more number of inotropic drugs were used, more was the mortality observed (Table – 6).

Table - 6: Association of mortality in comparison with various factors.

Factor		Mortality		P value	Statistical significance
		Yes	No		
Age	<40	3	35	0.7264	NS
	>40	5	57		
Gender	Male	4	76	0.026	Significant
	Female	4	16		
Diagnosis	DVD	0	15	0.31	NS
	SVD	0	6		
	TVD	8	71		
LVD	Good	1	18	0.02	Significant
	Moderate	1	50		
	Severe	6	24		
Surgery employed	CABG	7	70	0.85	NS
	CABG+ABP	1	12		
	CABG+MVR	0	7		
	CABG+VSDR	0	3		
Inonotroic support	2(A+B)	0	54	0.001	Significant
	3(A+B+C)	8	38		
Total cholesterol levels	<199	5	57	0.13	NS
	200-239	1	30		
	>240	2	5		
CKD	Yes	0	2	1	NS
	No	8	90		

Discussion

The present study has been conducted among 100 patients posted as an analytical cross sectional study to undergo CABG in a tertiary care centre, with the objectives to:

- To study the conventional risk factors in the patients who present with significant Coronary Artery Disease planned for treatment by Coronary Artery Bypass Grafting
- To study the immediate and 30 day mortality and perioperative morbidity in patients with early onset of CAD undergoing CABG Surgery.

Socio demographic characteristics

In the present study, majority of the study participants belonged to the age groups of 41-50 years and 35% belonged to the age groups of 31-40 and a meagre of 3% belonged to the age group of 20-30. Majority of the patients with CAD who underwent CABG were male (80%).

In the study conducted by Arif M, et al. [6], among young adults undergoing CABG, the mean age of the patients was 36.5 ± 3.17 years and the male were more 62% and this finding is in concordance with the present study.

In the study conducted by Legare JF, et al. [7], among elderly population with a mean age of 63 ± 10.1 years, a male preponderance was seen even in the advanced age groups, which could be probably because of the presence of excessive risk factors for CAD among male patients.

In the study conducted by Shapira, et al. [8], the mean age of the patients has been observed to be 66 ± 10 years and the majority of the patients were male and this finding is in consonance with the present study.

Risk factors for CAD

Most common risk factor found among the patients of CAD is hypertension in 50%. Whereas, the next most common risk factors observed are hypercholesterolemia (38%), DM

(35%), alcohol dependency (34%) and present tobacco usage (33%), positive family history (26%), sedentary lifestyle in 17%.

In the study conducted by Arif M, et al. [6], the risk profile observed by them displayed that increased BMI was the major contributor for cardiovascular disease. Following obesity, hypertension (49.5%), diabetes (29.9%) and dysfunctional lipids (14.7%) were commonly seen, while smoking and positive familial history were also found to have relation with CAD. And these findings similar to the observations made in the present study.

In the study conducted by Legare, et al. [7], hypercholesterolemia has been found to be the most common risk factor among the patients studied and this can be because the mean BMI was observed to be higher when compared to the mean BMI observed in the patients of the present study. Next common risk factor being hypertension in 60% of the patients, diabetes in 36%, peripheral vascular disease in 15.3% and cerebrovascular disease in 8% and renal failure has been seen in a meagre of 2.7% and these observations are in near concordance with the present study.

In the study conducted by Shapira, et al. [8], hypertension is seen in 80% of the patients, DM in 42% of the patients, peripheral vascular disease in 36% of the patients and COPD in 24% of the patients and CRF in 15% of the patients. In this study HTN is the most common risk factor and this finding is in consonance with the present study. But, the prevalence of the CAD risk factors observed is slightly more than that observed in the present study, which could be because the mean age of the patients in this study was higher than the mean age of the patients in the present study.

Disease profile of the patients

In majority of the patients three vessel disease was observed (79%), whereas 15% had a double

vessel disease (15%) and a minority of 6% had a single vessel disease.

In a similar study conducted by Legare, et al. [7], among 300 patients, SVD was observed in 8% of the patients, DVD in 18% whereas the triple vessel disease is seen in a majority of 74% of the patients and these observations were in concordance with the present study.

In the study conducted by Shapira, et al. [8], SVD is seen in 1.3% of the patients and DVD is seen in 17% and the majority had three vessels involved which is in 81.5%, a finding which is in strict concordance with the present study findings.

Surgical procedures and techniques employed

CABG alone was employed in majority of the patients, whereas additional procedures like mitral valve repair and repair of ventricular septal defect has been employed in a meager of 8% of the patients. In Majority of the patients (94%) the technique employed was Del Nido Cardioplegia during surgery, whereas off pump technique was employed in a single patient.

In the study conducted by Habib, et al. [9], on the outcomes of CABG, the off pump technique has been employed in 1.8% of the patients and this finding is in concordance with the present study.

No. of grafts

Majority of the study participants who underwent CABG required 3-4 grafts (82%), whereas a very few patients needed a single graft(4%) and a meager needed more than 5 grafts (2%).In majority (95%) of the patients they needed a usage of 2 to 3 ionotropes, which were a combination of dopamine, adrenaline and nor adrenaline. Very meager needed a usage of 4 ionotropes.

In the similar study conducted by Shapira, et al. [8], average number of grafts required per patient

were found to be 3.7 ± 1 , and this finding is in strict consonance with the present study.

In the study conducted by Nathone HM, et al. [10], the mean number of grafts per patient was 2.6 in the on-pump group and 2.4 in the off-pump group.

Post-operative ICU and hospital stay and the factors associated with the length of the stay

Overall, the mean duration of stay in the ICU is 4.13 ± 1.81 days and the mean hospital stay was 7.97 ± 1.97 days, there were 8 deaths (within 30 days) and the length of duration of hospital stay was found to have a statistically significant association with factors like the surgical technique employed and the drugs used for inotropic support. More complicated the surgery and more the number of inotropes used more was the length of ICU and the hospital stay.

In a study conducted by Michalopoulos A, et al. [11], the result of logistic regression analysis showed that the usage of the number of inotropes was the most important determinant of stay in the ICU and this finding was in consonance with the findings made in the present study. The possible reasons found for prolonged stay in the ICU where the inotropes were not used are found to be hypoxaemia, atrial fibrillation, their combination and mental disturbances

Among the patients who underwent surgery, no statistically significant association has been observed between the pump time and length of a patient's stay in the ICU during the post-operative period. But, a weakly positive correlation has been observed between the mean pump time and the duration of hospital stay, by which we can say that as the mean duration of pump times increases the mean duration of length of ICU as well as hospital stay also increased.

In a similar study conducted by Tunc, et al. [12], the ICU stay of ≥ 48 h was observed in 20.1% of the patients. Diabetes mellitus and low ejection fraction, long aortic cross clamp,

cardiopulmonary bypass time and intra-aortic balloon pump requirement, arrhythmia, myocardial infarction, renal dysfunction and need for hemodialysis, use of ≥ 2 inotropic agents, infection, sepsis and respiratory complication were found to prolong the ICU stay.

Factors associated with mortality and morbidity post CABG

Among the patients who underwent surgery, renal dysfunction was seen in 5% of the subjects and it was found to have a statistically significant association with the surgery done. More complicated the surgery, renal dysfunction is seen in them.

In the study conducted by Puskas, et al. [13], renal failure has been observed in nearly 2% of the patients who underwent CABG, and this has been found to be nearly in concordance with the present study.

In the study conducted by William JB, et al. [14], renal failure has been shown to be more in the subjects where the surgery done was complex and the number of inotropes used were more.

Among the patients who underwent surgery, Mortality was seen in 8% of the patients. A statistically significant association of mortality was seen among factors like female gender, severe left ventricular dysfunction and the no of inotropic drugs used. Mortality rate among female was more. A severe left ventricular dysfunction had a negative impact on survival of the patients and when more number of inotropic drugs were used, more was the mortality observed.

In the study conducted by Arif, et al. [6], it was observed that though significant difference has been observed over the groups, but a less mortality has been observed in age group less than 40 and this finding made was similar to the present study, which was opined to be because of increased percutaneous preference as compared to the coronary revascularization and they have

also opined that a positive family history had an impact on the morbidity status of the CAD patients in the younger age groups which were in relation to metabolic and genetic risk factors.

In the study conducted by Tunc, et al. [12], Intra-aortic balloon pump requirement, use of ≥ 2 inotropic agents, post-operative myocardial infarction and need for post-operative hemodialysis are independent risk factors for patients undergoing open heart surgery and these observations made are similar to the present study findings.

Whereas, in the follow up study conducted by Cohen DJ, et al. [15], among patients of various age groups from younger to older over a period of 13 years with 5 year follow up, they have observed that event free survival was worst among the patients belonging to younger age groups. This morbidity increased with the presence of cardiac risk factors. They have also opined that the young patients need to be re-evaluated relative to current aggressive medical therapy for angina.

In the study conducted by Binacari, et al. [16], they have also observed that the 5 year mortality is not influenced by the CAD risk factors but by the complexity of the surgical procedure which is in concordance with the findings of the present study. And they have also made a conclusion that 5 year follow up will be shorter and it needs a longer follow up to observe the mortality and morbidity patterns in younger patients.

Conclusion

The mean age was 42 years, majority were males - 80 and females - 20. Smoking - 33, Hypertension - 50, Diabetes - 35, Hypercholesterolemia - 38, were the most frequent risk factors. Impaired left ventricular function ($EF < 40\%$) in 15, indication for surgery was triple vessel disease in - 79, double vessel disease in -15, and single vessel disease in - 6, LMCA was affected in 10, the mean hospital stay was 7.97 ± 1.97 days, there were 8 deaths

(within 30 days). Post-operative ICU stay was 4.13 ± 1.81 days. Use of IABP in 14 patients, inotropes required for more than 48 hours in 87 patients, complications like renal dysfunction 5, and no cerebral stroke was observed.

We are getting considerable number of young patient with coronary artery disease as there is early age onset of risk factors and most of them land up with a triple vessel disease, however as they are young the post-operative morbidity is low and duration of ICU hospital stay is also less.

Limitations of study

The sample size of the study is less, and the results of the study can't be generalized. This is only a retrospective study. Further randomized prospective studies need to be done to have a more reliable data.

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