

# Minimally Invasive Coronary Artery Bypass Grafting for Multivessel Coronary Artery Disease: A Prospective Longitudinal Study

VIVEK SHRIHARI<sup>1</sup>, RAMKUMAR JAYAVELAN<sup>2</sup>, KARTHICK KAVIN<sup>3</sup>, RAMKUMAR SHANMUGA SUNDARAM<sup>4</sup>, GIRISH GOPINATHAN<sup>5</sup>, PERIYASAMY THANGAVEL<sup>6</sup>

## ABSTRACT

**Introduction:** Minimally invasive coronary artery bypass grafting has been predominantly used in single vessel coronary artery disease and is gaining wider acceptance over the conventional approach. Minimally invasive surgery for multivessel coronary disease is still restricted to fewer centres due to its technical difficulty and longer learning curve.

**Aim:** To evaluate patients who underwent minimally invasive coronary artery bypass grafting surgery for multi-vessel coronary artery disease.

**Materials and Methods:** Forty three patients underwent minimally invasive beating heart coronary artery bypass grafting surgery for multi-vessel coronary artery disease. Data was analysed with inferential and descriptive statistics. Continuous or interval based variables were expressed as mean±standard deviation. Postoperative Visual Analogue Scoring (VAS) of pain (1-10) was recorded on day 1 and day 2 after surgery. They were compared using paired one-tail student t-test.

**Results:** The mean age of 43 patients was 57.88±7.91 years. Thirty three patients received two grafts. Ten patients received 3 grafts. The mean duration of ventilation was 8±3.3 hours. The length of intensive care unit stay ranged from 1 day to 3 days with a mean of 2.23±0.57 days. The mean VAS score of pain on postoperative day 1 was 3.93±2.23. It significantly reduced to 1.67±1.43 on day 2 (p<0.05). The duration of hospital stay ranged from 5 days to 18 days with a mean of 9.5±2.7 days. The duration required for the patient to resume routine physical activities was 10.35±9.13 days.

**Conclusion:** Minimally invasive coronary artery bypass grafting surgery through left anterior thoracotomy approach can be done safely for multi-vessel coronary artery disease with good and acceptable postoperative outcomes. There is a significant reduction of pain by second postoperative day. Three-fourth of the patients resumed routine physical activity within 12 days of surgery.

**Keywords:** Pain, Sternotomy, Thoracotomy

## INTRODUCTION

Percutaneous Coronary Interventions (PCIs) are indicated for focal coronary artery lesions, especially in acute ischemia [1]. The surgical revascularization with grafts provide good long-term results especially in multivessel coronary artery disease [2,3]. That being said, conventional Coronary Artery Bypass Grafting (CABG) through the midline sternotomy does come with its own share of problems. Some of these include problems related to median sternotomy such as sternal wound infections, sternal dehiscence and chronic postoperative sternal site pain to name a few. In addition, these patients require more recovery time both in the hospital, and convalescence at their homes [4-8].

A large number of patients who suffer from Coronary Artery Disease (CAD) are quite hesitant when they are given the option of conventional CABG owing to fear of the procedure itself. Consequently, surgery via left anterior thoracotomy approach has gained popularity due to the lesser tissue trauma, smaller scar, better cosmesis, shorter hospital stay and faster recovery [9,10].

Minimally invasive coronary artery bypass grafting was initially performed on patients with single vessel CAD and at present, its spectrum is being extended to multivessel CAD as well. This has been largely achieved by combining minimally invasive surgery with percutaneous coronary intervention to non-left anterior descending artery vessels. But, this hybrid multivessel revascularization can be performed in a few select centres with hybrid theatres and is associated with high economic cost [11,12].

The morbidity associated with midline sternotomy, the economic considerations and the desire of patients for a quicker return to their routine physical activities with less postoperative pain has pressurised

surgeons to achieve complete surgical revascularisation in selected multivessel coronary artery patients. However, the procedure does have a considerable learning curve for the surgeon.

Author hereby reported on their experience of 43 consecutive patients who underwent minimally invasive coronary artery bypass grafting for multivessel coronary artery disease from August 2017 to December 2018 at tertiary cardiac care centre.

Primary outcome was the number of days required to get fit for discharge from hospital. Patients were discharged when: (a) temperature and routine blood tests were normal; (b) chest X-ray film showed no evidence of pneumothorax/pleural collection requiring drainage/lung consolidation; (c) there was no evidence of infection.

Secondary outcomes were: (a) pain scores measured with a 10-cm visual analog scale on postoperative day 1 and day 2; (b) duration of postoperative ventilation; (c) duration of intensive care unit stay; (d) days required to resume routine physical activities after surgery.

## MATERIALS AND METHODS

This prospective longitudinal study was approved by the institutional ethical and research board. Written informed consent was obtained in all cases in local language. Forty three patients with multi-vessel coronary artery disease underwent minimally invasive coronary artery bypass grafting between August 2017 and December 2018 at the tertiary cardiac care center. All of them were included in the study. The participants were recruited by consecutive enumerative sampling. Patients with diagnosis of multi-vessel coronary disease following coronary angiogram were assessed for the technical feasibility of minimally invasive coronary artery bypass grafting.

Patients who had unstable angina, haemodynamic compromise, complex anatomy of the coronaries, emergency coronary bypass grafting, poor left ventricular function (Left ventricular ejection fraction <50%), grafting requirement to right coronary artery with no posterior descending artery target and chronic obstructive airway disease were excluded from undergoing minimally invasive coronary artery bypass grafting. All procedures were performed by a single cardiac surgery team.

A detailed proforma was filled for all patients. This included age, gender, New York Heart Association (NYHA) class of symptoms, associated comorbidities, echocardiography findings, number of bypass grafts, duration of ventilator support, length of Intensive Care Unit (ICU) stay and postoperative blood loss. As per the unit protocol, blood transfusion was given to patients when haemoglobin dropped below 8 g/dl.

Postoperative pain (assessed by Visual Analogue Scoring on a scale of 1 to 10) was documented on postoperative day 1 and day 2. Patients with a score  $\geq 4$  were given 1 gram intravenous paracetamol infusion over 20 minutes. Total dosage was restricted to 3 grams over 24 hours. Patients with a score  $\geq 5$  were rated as having severe pain and were treated with aliquots of 50  $\mu$ g of Fentanyl in addition to paracetamol.

Duration required for patients to resume their daily routine physical activity was recorded. Follow-up data from all patients was collected at 1 month, 3 months and 6 months postoperatively. Data pertaining to return to routine physical activities was enquired during follow-up visits and telephonic conversations. Patients who did not report for follow-up visits were contacted through telephone.

An initial pre-anaesthetic assessment of patients was done according to American Society of Anaesthesia.

### Intraoperative Technique

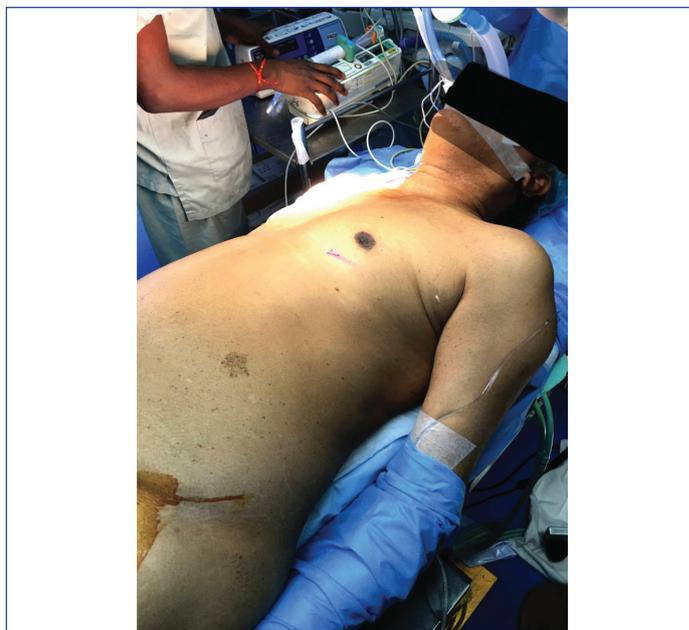
Lung isolation was achieved with double lumen tube (Portex<sup>®</sup> Endobronchial Double Lumen tube (Smith Medical, Minnesota, USA) or bronchial blocker (Copdech Endobronchial blocker tube [Daiken Medical Co., Ltd., Osaka Japan]. Pre-emptive analgesia was achieved for all patients with paravertebral thoracic (T2-T3) blockade.

The operating instrument cart had long minimally invasive instruments. Patients were then positioned at a 15° to 30° right lateral decubitus position [Table/Fig-1]. The patient was draped to allow access to the left groin and bilateral thigh and leg for saphenous vein harvesting. A 4- to 6-cm incision was made in the left fifth intercostal space (left anterior thoracotomy). A rib spreader was inserted [Table/Fig-2]. Rultract retractor systems (Medtronic, 710, Medtronic Parkway Minneapolis, Minnesota, 55432-5604, USA) were used to gain exposure following thoracotomy. An incision on the pericardium was made 2 cm anterior to the left phrenic nerve, extending cephalad to the level of the left atrial appendage and caudally towards the diaphragm. Pericardial traction sutures were inserted to mobilise the left ventricular apex. Coronary artery targets were assessed.

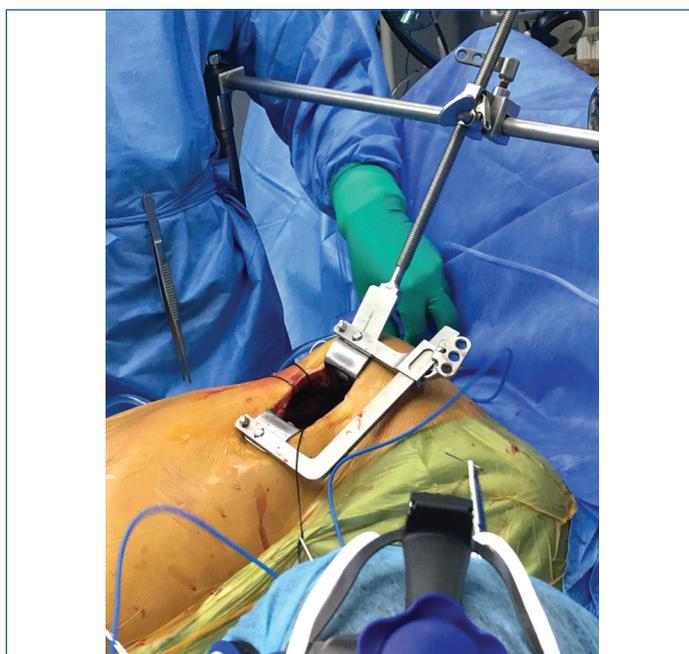
With the use of long minimally invasive instruments and a long electrocautery blade, the Left Internal Mammary Artery (LIMA) was harvested from the first rib down to its bifurcation [Table/Fig-3]. Heparin 2 mg/kg body weight was given intravenously before division of the internal mammary artery.

LIMA was anastomosed with the Left Anterior Descending (LAD) coronary artery using 8-0 polypropylene continuous sutures with the help of an epicardial stabiliser (Octopus NS, Medtronic, Minneapolis, Minn). The harvested saphenous vein graft was then anastomosed proximally to the ascending aorta by using 6-0 polypropylene sutures after the application of an aortic side-biting clamp.

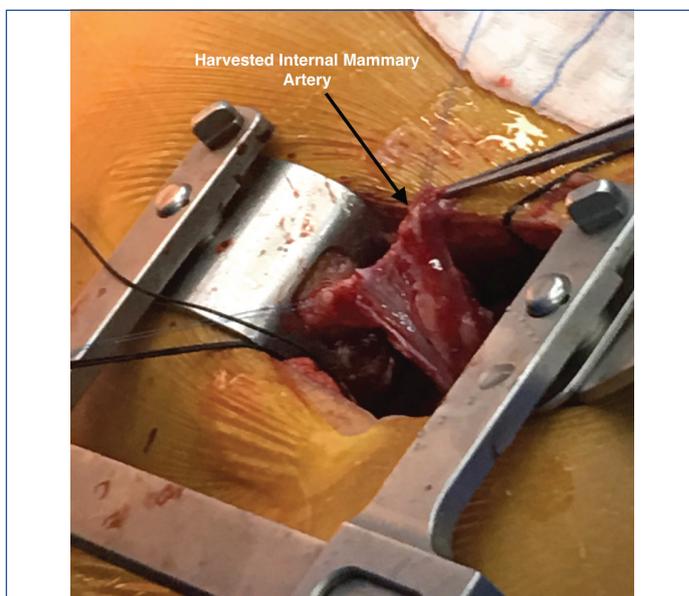
For visualisation of the posterior descending branch of the right coronary artery, retraction of the left ventricular apex toward the patient's left shoulder is done; for visualisation of the obtuse marginal branches of the circumflex coronary artery retraction of the apex



[Table/Fig-1]: The patient is positioned at 15° to 30° angle in right lateral decubitus position.



[Table/Fig-2]: The intraoperative placement of the rib retractor with rib cage elevator.



[Table/Fig-3]: The harvested Internal mammary artery (arrow mark).

inferiorly toward the right hip is done. Saphenous vein graft was anastomosed to the coronary artery by using 7-0 polypropylene sutures. At the end of procedure, a left pleural chest tube was placed through a separate incision. The left lung was re-inflated and all grafts were inspected. The thoracotomy incision was closed with a No. 1 Vicryl suture around the intercostal space. The anterior pectoralis muscle was closed with No. 1 Vicryl. The subcutaneous tissue and skin were closed in layers.

All patients were extubated on the same day of surgery. Chest drains were removed on postoperative day 1. Postoperative VAS of pain (1-10) was recorded on day 1 and day 2 after surgery.

All patients were administered dual antiplatelet drugs, beta-blockers and anticholesterol drugs.

## STATISTICAL ANALYSIS

Data was analysed with inferential and descriptive statistics. Continuous or interval based variables were expressed as mean±standard deviation. The variables analysed were duration of ventilation, ICU and hospital stay. Postoperative VAS of pain (1-10) was analysed on day 1 and day 2 using paired one-tail student t test. The p-value <0.05 was considered significant. Duration of convalescence was also analysed. Statistical analysis was done using MEDCALC version 18.

## RESULTS

The mean age of patients was 57.88±7.91 years (range 42-77). Most of the operated patients were male (88.4%). There were 38 male and 5 female participants. Thirty seven patients presented with NYHA class II and 6 patients with NYHA class III symptoms. Ten patients had triple vessel disease. Twenty eight patients had double vessel disease. Four patients had left main with double vessel disease. One patient had left main with triple vessel disease. 58.1% of patients had diabetes mellitus, 46.5% had systemic hypertension and 11.6% had hypothyroidism [Table/Fig-4]. All the patients included in the study had good left ventricular ejection fraction. The mean preoperative ejection fraction was 57.79%±1.03.

Characteristics of the study population (n=43)	Number (%)
Triple vessel disease	10 (23.25%)
Double vessel disease	28 (65.11%)
Left main with double vessel disease	4 (9.30%)
Left main with triple vessel disease	1 (2.32%)
Diabetes	25 (58.13%)
Systemic hypertension	20 (46.51%)
Hypothyroidism	5 (11.62%)

**[Table/Fig-4]:** Characteristics of study population who underwent minimally invasive coronary bypass Grafting.  
Notes: pes of implan

All patients underwent left internal mammary artery to left anterior descending artery anastomosis. Saphenous vein grafts were used for anastomosing the remaining coronary artery targets. Thirty three patients received two grafts. Ten patients received 3 grafts. The duration of ventilation ranged from 3 hours to 16 hours with a mean of 8±3.3 hours. The length of intensive care unit stay ranged from 1 day to 3 days with a mean of 2.2±0.6 days. The average perioperative blood loss was 219.5±66.4 mL [Table/Fig-5]. One patient underwent re-exploration for bleeding, 6 patients needed blood transfusion. The length of hospital stay ranged from 5 days to 18 days, with a mean of 9.5±2.7 days. The median duration of hospital stay was 5.7 days.

The mean VAS score of pain on postoperative day 1 was 3.93±2.23. It significantly reduced to 1.67±1.43 on day 2 (p<0.05).

The overall duration required for the patient to return to his/her daily routine physical activities was 10.35±9.1 days. Thirty two (74.4%) patients resumed their routine activities within 12 days of surgery [Table/Fig-6]. There were no cerebrovascular events or mortality in the study.

Postoperative variable	Value
Duration of ventilation (hrs)	8±3.35
Length of intensive unit care stay (days)	2.23±0.57
Mean perioperative blood loss (mL)	219.53±66.37
Postoperative Hospital stay (days)	9.49±2.66
Pain on Postoperative Day 1 (VAS score) vs. Pain on Postoperative Day 2 (VAS score)	3.93±2.23 vs. 1.67±1.43 (p <0.05)
Resumption of daily activities (days)	10.35±9.13

**[Table/Fig-5]:** Postoperative variables of patients who underwent minimally invasive coronary artery bypass grafting.

Days (in range) required to resume daily routine physical activities after surgery	Number of patients (%) (N=43)
Day 1 to 4	10 (23.26%)
Day 5 to 8	17 (39.53%)
Day 9 to 12	5 (11.63%)
Day 13 to 16	6 (13.95%)
Days >16	5 (11.63%)

**[Table/Fig-6]:** Days required for patients to resume their daily routine physical activities.

## DISCUSSION

This study showed that good and acceptable postoperative outcomes can be achieved by minimally invasive coronary artery grafting for multivessel coronary artery disease. Following midline sternotomy, the incidence of sternal wound complications such as dehiscence of sternum or superficial sternal wound infections and deep sternal wound infections ranges from 0.3% to 8% [13,14]. These complications following sternotomy leads to about 10% to 40% increase in morbidity and mortality [15].

The most appealing benefit of embracing minimally invasive surgery is avoidance of these dreaded sternal wound complications. The length of postoperative stay in present study ranged from 5 days to 18 days with a mean of 9.5±2.7 days. Two patients had superficial thoracotomy wound infection and one patient developed left sided pleural collection warranting intercostal drainage. It leads to their prolonged hospital stay. These three patients skewed the mean hospital stay data. Surgical site infections after minimally invasive surgery are usually superficial. It occurs mostly in obese female patients due to pressure necrosis of the skin edges by the retractor blades [16,17]. Although the study had just two patients (0.04%) with superficial wound infection which resolved after daily dressings, it prolonged their hospital stay.

An accurate comparison with conventional sternotomy approach is difficult because of the inherent tendency of surgeons to choose patients with lower risk for minimally invasive coronary artery bypass grafting. Rogers CA et al., conducted a randomised study (STET trial) of 93 elective CABG patients undergoing off-pump coronary artery bypass grafting via median sternotomy and anterolateral thoracotomy approaches. They noted a shorter intubation time (4.26 hrs vs. 5.35 hrs) and similar ICU stay (22.4 vs. 23 hrs) in thoracotomy group [18]. In the index study, the mean duration of ventilation was 8±3.3 hours. The length of intensive care unit stay ranged from 1 day to 3 days with a mean of 2.2±0.6 days.

Birla R et al., compared off-pump CABG to minimally invasive CABG. They noted shorter duration of ventilation (5.04 hrs vs. 5.35 hrs) and ICU stay (38.36 hrs vs. 47.87 hrs) in the minimally invasive group. The present study noticed a similar trend for the minimally invasive surgery [19].

Lapierre H et al., compared 150 sternotomy off-pump CABG to minimally invasive CABG. They found lower hospital stay (5.4 days vs. 7.2 days) in the minimally invasive group [20]. The index study showed a similar result with a median duration of hospital stay of 5.7 days.

Ruel M et al., conducted a dual center study of 91 patients who underwent minimally invasive CABG. Twenty (23%) patients needed

postoperative blood transfusion [21]. McGinn Jr JT et al., reported a dual center experience of 450 patients who underwent minimally invasive CABG. A total of 96 patients (21.3%) required perioperative blood transfusion [16]. In the present study, only 6 (13.9%) patients required blood transfusion.

Meyerson J et al., evaluated post-sternotomy pain in 318 patients based on visual analogue scale (VAS, 0-100 mm). Forty-one patients (13%) reported maximum pain intensity  $\geq 30$  mm and 14 of these patients (4%) scored  $\geq 54$  mm (severe pain). This prospective study showed a high overall incidence (28%) of non-cardiac pain after sternotomy [8]. In the present study, sternotomy was avoided. The pain of minimally invasive thoracotomy was assessed with VAS score (Range 1-10). There was a significant reduction in the mean VAS score on postoperative day 2 in comparison with postoperative day 1 which facilitated early ambulation of patients and easier performance of breathing exercises. Almost 75% of the patients resumed their daily routine physical activities within 12 days of surgery.

Jideus L et al., followed-up 97 patients who developed sternal wound infection. They concluded that sternal wound infection after cardiac operations is a serious problem. They leave physical, cosmetic and mental scar. Consequently, they have a low quality of life [4]. In our study, only two patients developed superficial wound sepsis which resolved completely at the time of discharge. To avoid the potential dreaded complications of midline sternotomy, a cosmetically acceptable small left lateral thoracotomy scar was opted.

Despite the advantages, minimally invasive multi-vessel coronary artery bypass grafting encounters technical difficulties. It is overcome gradually with a prolonged learning curve. Its execution requires highly trained surgical skills. Consequently, minimally invasive multivessel coronary artery bypass surgery has succeeded in only low numbers and at specialised centres.

## LIMITATION

There is a selection bias in this study because of the tendency of surgeons to choose patients with a lower risk and a better anatomy of target coronary arteries for minimally invasive surgery. Present study is observational with a small sample size taken from single-centre experience. The findings of the study need to be reconfirmed in future prospective longitudinal studies with larger sample size.

## CONCLUSION

Despite higher technical difficulty, minimally invasive coronary artery bypass grafting surgery via left anterior thoracotomy approach can be done safely for multi-vessel coronary artery disease with good and acceptable postoperative outcomes. There is a significant decrease in the postoperative pain by second postoperative day enabling early rehabilitation of the patients. Three-fourth of present study's patients resumed routine physical activity within 12 days of surgery. By avoiding the conventional midline sternotomy approach, the known complications of sternal wound dehiscence and chronic postoperative sternotomy pain was also avoided.

## REFERENCES

- [1] Le May MR, So DY, Dionne R, Glover CA, Froeschl MP, Wells GA, et al. A citywide protocol for primary PCI in ST-segment elevation myocardial infarction. *N Engl J Med*. 2008;358:231-40.
- [2] Daemen J, Boersma E, Flather M, Booth J, Stables R, Rodriguez A, et al. Long-term safety and efficacy of percutaneous coronary intervention with stenting and coronary artery bypass surgery for multivessel coronary artery disease: a meta-analysis with 5-year patient-level data from the ARTS, ERACI-II, MASS-II, and SoS trials. *Circulation*. 2008;118:1146-54.
- [3] Bair TL, Muhlestein JB, May HT, Meredith KG, Horne BD, Pearson RR, et al. Surgical revascularization is associated with improved long-term outcomes compared with percutaneous stenting in most subgroups of patients with multivessel coronary artery disease: results from the Intermountain Heart Registry. *Circulation*. 2007;116(suppl 1):I226-31.
- [4] Jideus L, Liss A, Stahle E. Patients with sternal wound infection after cardiac surgery do not improve their quality of life. *Scand Cardiovasc J*. 2009;43:194-200.
- [5] Jarvinen O, Saarinen T, Julkunen J, Huhtala H, Tarkka MR. Changes in health-related quality of life and functional capacity following coronary artery bypass graft surgery. *Eur J Cardiothorac Surg*. 2003;24:750-56.
- [6] Speziale G, Bilotta F, Ruvolo G, Fattouch K, Marino B. Return to work and quality of life measurement in coronary artery bypass grafting. *Eur J Cardiothorac Surg*. 1996;10:852-58.
- [7] Lahtinen P, Kokki H, Hynynen M. Pain after cardiac surgery: a prospective cohort study of 1-year incidence and intensity. *Anaesthesiology*. 2006;105:794-800.
- [8] Meyerson J, Thelin S, Gordh T, Karlsten R. The incidence of chronic post-sternotomy pain after cardiac surgery: a prospective study. *Acta Anaesthesiol Scand*. 2001;45:940-44.
- [9] Reser D, Holubec T, Caliskan E, Guidotti A, Maisano F. Left anterior small thoracotomy for minimally invasive coronary artery bypass grafting. *Multimed Man Cardiothorac Surg*. 2015;2015. pii: Mmv022.
- [10] Balaguer JM, Umakanthan R, Leacche M, Byrne JG. Minimally invasive cardiac surgery. *Curr Probl Surg*. 2012;49(9):529-49.
- [11] Reeves BC, Angelini GD, Bryan AJ, Taylor FC, Cripps T, Spyt TJ, et al. A multi-centre randomised controlled trial of minimally invasive direct coronary bypass grafting versus percutaneous transluminal coronary angioplasty with stenting for proximal stenosis of the left anterior descending coronary artery. *Health Technol Assess*. 2004;8:01-56.
- [12] Murphy GJ, Bryan AJ, Angelini GD. Hybrid coronary revascularization in the era of drug-eluting stents. *Ann Thorac Surg*. 2004;78:1861-67.
- [13] Losanoff JE, Jones JW, Richmann BW. Primary closure of median sternotomy: techniques and principles. *Cardiovasc Surg*. 2002;10:102-10.
- [14] Negri A, Manfredi J, Terrini A, et al. Prospective evaluation of a new sternal closure method with thermoreactive clips. *Eur J Cardiothorac Surg*. 2002;22:571-75.
- [15] Shih CC, Shih CM, Su YY, Lin SJ. Potential risk of sternal wires. *Eur J Cardiothorac Surg*. 2004;25:812-18.
- [16] McGinn Jr JT, Usman S, Lapierre H, Pothula VR, Mesana TG, Ruel M. Minimally Invasive Coronary Artery Bypass Grafting-Dual-Center Experience in 450 Consecutive Patients. *Circulation*. 2009;120:S78-S84.
- [17] Chan V, Lapierre H, Sohmer B, Mesana TG, Ruel M. Handsewn proximal anastomoses onto the ascending aorta through a small left thoracotomy during minimally invasive multivessel coronary artery bypass grafting: a stepwise approach to safety and reproducibility. *Semin Thorac Cardiovasc Surg*. 2012 Spring;24(1):79-83.
- [18] Rogers CA, Pike K, Angelini GD, Reeves BC, Glauber M, Ferrarini M, et al. An open randomized controlled trial of median sternotomy versus anterolateral left thoracotomy on morbidity and health care resource use in patients having off-pump coronary artery bypass surgery: The Sternotomy Versus Thoracotomy (STET) trial. *J Thorac Cardiovasc Surg*. 2013;146:306-16.e1-9.
- [19] Birla R, Patel P, Aresu G, Asimakopoulos G. Minimally invasive direct coronary artery bypass versus off-pump coronary surgery through sternotomy. *Ann R Coll Surg Engl*. 2013;95:481-85.
- [20] Lapierre H, Chan V, Sohmer B, Mesana TG, Ruel M. Minimally invasive coronary artery bypass grafting via a small thoracotomy versus off-pump: A case-matched study. *Eur J Cardiothorac Surg*. 2011;40:804-10.
- [21] Ruel M, Shariff MA, Lapierre H, Goyal N, Dennie C, Sadel SM, et al. Results of the minimally invasive coronary artery bypass grafting angiographic patency study. *J Thorac Cardiovasc Surg*. 2014;147:203-09.

### PARTICULARS OF CONTRIBUTORS:

1. Senior Resident, Department of Cardiothoracic Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.
2. Senior Consultant, Department of Cardiothoracic Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.
3. Consultant, Department of Cardiothoracic Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.
4. Consultant, Department of Cardiothoracic Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.
5. Consultant, Department of Cardiothoracic Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.
6. Professor and Head, Department of Cardiothoracic Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

### NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Ramkumar Jayavelan,  
5, Jayanthi Street, Dr. Seethapathy Nagar, Velachery, Chennai, Tamil Nadu, India.  
E-mail: drramkumarj@gmail.com

### AUTHOR DECLARATION:

- Financial or Other Competing Interests: No
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

### PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Aug 16, 2019
- Manual Googling: Sep 04, 2019
- iThenticate Software: Sep 09, 2019 (18%)

### ETYMOLOGY: Author Origin

Date of Submission: **Aug 15, 2019**  
Date of Peer Review: **Aug 27, 2019**  
Date of Acceptance: **Sep 05, 2019**  
Date of Publishing: **Oct 01, 2019**