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Early Outcomes of Using Skeletonized Left Internal Mammary Artery (LIMA) for Sequential Grafting of Multiple Left Anterior Descending Artery Lesions

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ABSTRACT

Background: In comparison to other arterial and venous conduits, the left internal mammary artery (LIMA) conduit showed superior graft patency and outstanding excellent long-term clinical outcomes. In situ LIMA grafting to the left anterior descending artery (LAD) is believed to be the "gold standard" of coronary revascularization for decades.

Objective: We aimed to compare between two surgical methods for grafting diffusely diseased LAD.

Patients and Methods: This retrospective clinical trial was carried out on 80 adult cases with diffuse LAD disease in addition to right coronary artery and left circumflex artery involvement or their branches. They were scheduled for coronary artery bypass grafting (CABG) using the cardiopulmonary bypass in Cardiac Surgery Unit of Elkasr Elaini Medical Centre, cardiothoracic Surgery Department, Cairo University, Cairo, Egypt. Patients were equally classified into two groups (A and B).

Results: Incidence of post-operative Myocardial infarction (MI), new onset AF, intra-aortic balloon pump, inotropic support and direct-current shock were significantly lower in group B compared to group A. Spontaneous recovery of sinus rhythm was significantly higher in group B compared to group A. Partial clamp time and aortic cross clamp time were insignificantly different between both groups. Total bypass time, hospital stay, and ICU stay were significantly lower in group B compared to group A. Early mediastinitis and mortality was insignificantly different between both groups.

Conclusions: It was proven that LIMA with sequential-jump anastomoses should be utilized to operate LAD diffuse coronary artery lesions and that the surgeon should avoid lengthy arteriotomy with or without endarterectomy + onlay SVG patch with a single long anastomosis due to the elevated risk of early graft occlusion.

Keywords: Multiple LAD lesions**,** Skeletonized, Sequential Grafting, LIMA.

INTRODUCTION

Usually coronary artery disease (CAD) includes the proximal section of the major epicardial coronary arteries, but not its intramural branches. It is one of the most widespread groups of chronic diseases worldwide and in developing and developed countries is a primary cause of death [1].

The operation of choice for ischemic heart disease (IHD) patients is coronary Artery Bypass Grafting (CABG) surgery which aims to elevate quality of life with longer living periods [2]. In order to secure complete myocardial revascularization, which is the primary goal of the surgery, and because of the increasing prevalence of severely diffused diseased left anterior descending (LAD) coronary arteries encountered ; CABG surgeries presents a challenge to the cardiac surgeon and require more complex manoeuvres than simple distal segment arteriotomy anastomosis [3].

In comparison to other arterial and venous conduits, the left internal mammary artery (LIMA) conduit showed superior graft patency and outstanding excellent long-term clinical outcomes. LAD In situ LIMA grafting has been believed to be the operation Of choice " of coronary revascularization for decades [4, 5]. The procedure of sequential anastomosis utilizing the LIMA conduit to graft more than one major epicardial coronary artery simultaneously was described by prior research in order to maximise the LIMA conduit benefits. By using the sequential technique in grafting coronary arteries one can do two or more distal anastomosis by the same conduit, thus providing only one proximal anastomosis for two or more distal anastomoses, which is thought to improve the total flow in the graft by augmentation of the distal run off and improving graft patency [6, 7]. Furthermore, sequential technique provide more preservation of conduits and decrease in manipulations of the ascending aorta, as well as a way to provide more anastomoses to small diameter coronary arteries thus improving survival and outcomes [8].

As a revascularization technique for a diffusely diseased LAD, coronary endarterectomy in the LAD vessel has been utilised. Although, this method still avoided by many surgeons due to the contradictory and disputed comments of numerous authors regarding its complications and patency [9]. The skeletonized harvesting method of internal mammary artery provides maximum length and enables easy sequential grafting. It has many advantages. Some of many are, skeletonization of LIMA can reduce mediastinitis risk and sternal ischemia and is better quality, longer and larger than pedicled IMA [10].

The use of saphenous vein graft as a single (sequential) graft or multiple venous grafts and in patch angioplasty of the LAD (onlay patch) with or without LIMA anastomosis, is a common technique for achieving complete revascularization of ischemic myocardial regions [11]. Sequential SVG has several advantages; first a shorter duration of procedure due to

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less time spent in operating the multiple proximal aortic anastomoses and a quicker vein harvest. Secondly, because of enhanced surgical facilitation of a minor anastomosis, more comprehensive revascularization are facilitated by the jump graft. Thirdly, enhanced graft patency has been claimed due to increased distal runoff causing higher flow rates within the within the graft [11].

The debate therefore is about the ideal way to revascularize ischemic hearts with diffuse LAD disease; using the conventional way or beating heart as well as the selection of the conduits. Also updated data regarding the results and outcome of CABG on beating heart is lacking and conflicting [12]. The hypothesis of our study was that in multiple LAD lesions, the use of jump grafts in on pump CABG would reduce the in hospital morbidity and mortality (early results). Therefore, we established this study to compare between two surgical methods of LIMA anastomosis on LAD artery in patients with severe diffuse lesions.

PATIENTS AND METHODS

This retrospective clinical trial was carried out on 80 cases of >18 years old with diffuse LAD disease in addition to involvement of right coronary artery and left circumflex artery or their branches. The patients were scheduled for CABG using the cardiopulmonary bypass in Cardiac Surgery Unit of Elkasr Elaini Medical Centre, Cardiothoracic Surgery Department in Cairo University, Cairo, Egypt from January 2017 to January 2019.

Exclusion criteria: Cases who received isolated grafting of LIMA to the Diagonal or OM to minimize surgical variability, patients with obstructed LIMA seen in coronary angiography, Octogenarians, patients with concomitant malignant tumor (to limited anticipated life expectancy), patients and/or a history of chest radiotherapy may not be suitable candidates for sequential or separate LIMA grafting, and patients with redo CABG, concomitant diseased valve.

Cases involved in our study were classified into 2 equal groups; **group A (40 patients)**, after a long arteriotomy on LAD ± endarterectomy, SVG (saphenous vein graft patch was anastomosed to the LAD as onlay patch) and the LIMA pedicled was then anastomosed to the SVG patch. In **group B (40 patients),** a small arteriotomy was performed only in nearly normal sites in the vessel's wall instead of complete opening of LAD, and in a sequential (Jump) method a skeletonized LIMA was anastomosed to these sites.

After the operation, all the patients were followed-up during hospital stay by ECG, troponin and echocardiography for assessment of early occurrence of myocardial infarction (MI).

After the procedure, routine closure was done, and to the ICU patients were transferred and then to the ward and after discharge were followed-up regularly in the clinic.

Surgical technique:

All epicardial coronary arteries size of 1.5 mm with a 50% diameter reduction in at least one angiographic view is the definition of complete revascularization whose achievement is the objective of the surgery. In group A mammary was harvested pedicled using cautery and metallic clips while in group B LIMA was harvested in skeletonized fashion using cautery and metallic clips.

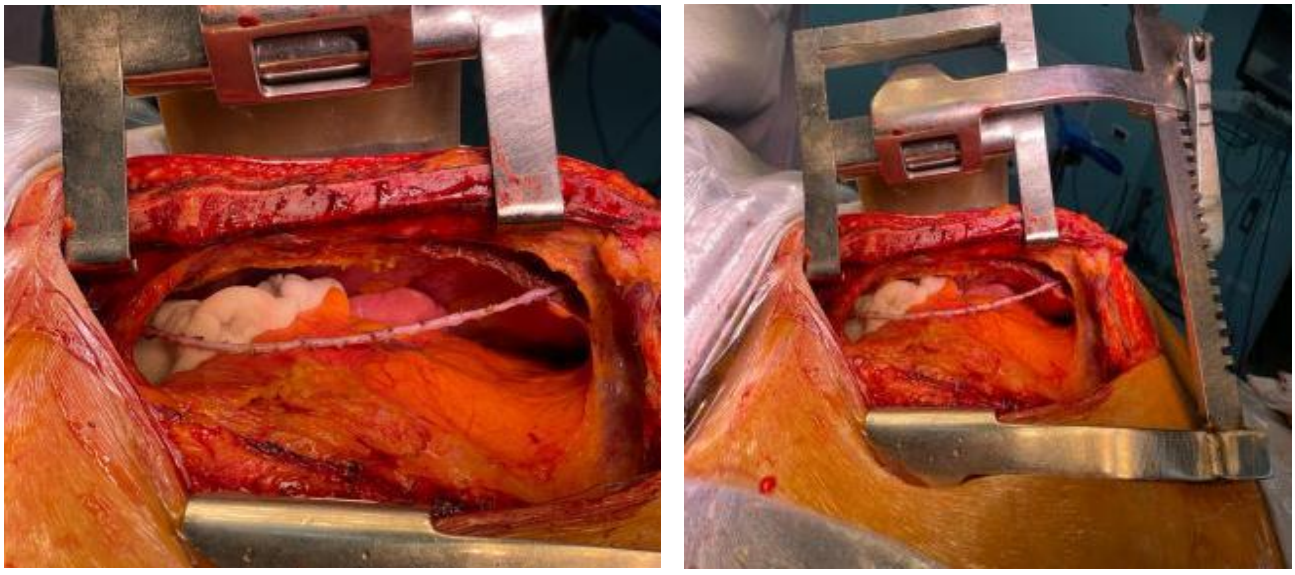

Figure (1): Harvesting of skeletonized LIMA.

In both groups, SVG was harvested from the lower limb using ligation silk sutures and surgical scissors. In group A, LIMA to SVG on lay patch to LAD 7/0 prolene after long arteriotomy ± endarterectomy+ SVG to RcA and or Cx branches while in group B Skeletonized LIMA using 08/0 prolene was anastomosed to healthy parts of these diffusely diseased LAD in jumping fashion + SVG to RCA and Cx branches. In group B in sequential LIMA grafting, the first anastomosis (a parallel-shaped anastomosis, "side-to-side fashion") was smaller than the second "end-to-end fashion".

In group A, several days of intravenous heparin were provided postoperatively. Prescribed medications included warfarin (kept with a target INR of 2.0) and aspirin low-dose (100 mg/day). Heparin was continuously administered intravenously until warfarin became effective. Warfarin medication was discontinued after 3 months. In group B aspirin was given after 12 hrs from admission to ICU in addition to clopidogrel for 6 months after surgery. In all patients in both groups for life, aspirin was then continued indefinitely.

The follow-up during hospital stay included need for use of inotropes, aortic balloon, weaning from ventilator, atrial fibrillation, chest tube drainage, reopening, MI, ICU stay and hospital stay. MI was known as a troponin I value postoperatively > 20 ng/ml accompanied with serum creatine kinase-MB elevation above normal values and > 10% of total creatine kinase, and the commencement of ECG abnormalities. All the patients underwent echocardiography at the 1st day and then after transfer to the ward from ICU. Findings such as ejection fraction (EF), and wall motion were documented.

Ethical consent:

An informed written consent was obtained from the patient or relatives of the patients. The study was done after approval from the Ethical Committee in Cardiac Surgery Unit, Elkasr Elaini Medical Centre, cardiothoracic Surgery Department, Cairo University. The Declaration of Helsinki, the World Medical Association's code of ethics for studies involving humans, guided the conduct of this work.

Statistical analysis

The data were analyzed using SPSS version 27 (IBM, Armonk, NY, USA). The data's normality was determined with the use of the Shapiro-Wilks test and histograms. Parametric quantitative data were summarized as mean ± SD and examined using an unpaired student t-test. To evaluate the non-normal distribution of the quantitative data the Mann-Whitney U-test was used and were reported as the median (IQR). Whenever applicable, the Chi-square test or Fisher's exact test was used to examine qualitative data provided as frequencies (%). In this study, statistical significance was defined as a two-tailed P value ≤ 0.05.

RESULTS

In this retrospective clinical study, 80 patients were randomly allocated into 2 groups, 40 patients in each. All allocated patients were followed-up and analysed statistically.

Age and sex were insignificantly different between two groups. Our study included 35 (43.8%) males and 5(6.3%) females in group A and 38 (47.5%) males and 2 (2.5%) females in group B. Hypertension, DM, COPD, AF, previous MI, hyperlipidemia, previous EF, and number of diseased vessels showed insignificant difference (Table 1).

Table (1): Baseline characteristics and risk factors of the studied group

		Group A (n=40)	Group B (n=40)	P value
Age		52± 6	57± 6	0.510
Sex	**Male**	35 (43.8%)	38 (47.5%0	0.431
	Female	5 (6.3%)	2 (2.5%)	
DM	**NO**	16 (40.0%)	18 (45.0%)	0.821
	YES	24 (60.0%)	22(55.0%)	
Hypertension	**NO**	17 (42.5%)	20 (50%)	0.654
	YES	23 (57.5%)	20 (50%)	
COPD	**NO**	38 (95%)	40 (100%)	0.493
	YES	2 (5%)	0 (0.0%)	
AF	**NO**	37 (92.5%)	40 (100%)	0.240
	YES	3 (7.5%)	0 (0.0%)	
Previous MI	**NO**	31(77.5%)	33(82.5%)	0.780
	YES	9(22.5%)	7 (17.5%)	
Hyperlipidemia	**NO**	36(90%)	38 (95%)	0.676
	YES	4 (10%)	2 (5%)	
Preoperative EF		58± 11	57± 10	
Euroscore	**2**	9(22.5%)	17(42.5%)	P value Insignificant
	3	24(60%)	15(37.5%)	
	4	4(10%)	8(20%)	
	5	2(5%)	0(0.0%)	
	6	1(2.5%)	0 (0.0%)	

Data are presented as mean ± SD or frequency (%), DM: diabetes mellitus, AF: atrial fibrillation, MI: myocardial infarction, EF: ejection fraction.

Pleural effusion, pulmonary complications, and ventilation exploration were insignificantly different between both groups. Patients with MI had high troponin level with ECG ischemic changes. Incidence of postoperative MI, tamponade, new onset AF, IABP, inotropic support and DC shock were significantly lower in group B compared to group A (P value <0.05). Group B has significantly higher spontaneous recovery of sinus rhythm compared to group A (Table 2).

Table (2): Complications of the studied group

		Group A (n=40)	Group B (n=40)	P value
Pulmonary complications	**No**	39(97.5%)	36(90%)	0.358
	Yes	1(2.5%)	4 (10%)	
Pleural effusion	**No**	38 (95%)	37 (92.5%)	1
	Yes	2 (5%)	3 (7.5%)	
Ventilation		5.00(4-6)	4.00(4.00-6.00)	0.077
Exploration	**No**	33(82.5%)	37 (92.5%)	0.176
	Yes	7(17.5%)	3 (7.5%)	
Tamponade	**No**	36(90%)	40 (100%)	0.04*
	Yes	4 (10%)	0 (0.0%)	
Total drainage		810 (650-895)	695 (510-890)	0.054
Post MI	**No**	31(77.5%)	38 (95%)	0.02*
	Yes	9(22.5%)	2 (5%)	
New onset AF	**No**	20 (50%)	39(97.5%)	<0.001*
	Yes	20 (50%)	1(2.5%)	
IABP	**No**	32(80.0%)	39(97.5%)	0.013
	Yes	8(20.0%)	1(2.5%)	
Inotropic support	**No**	6 (15%)	33 (82.5%)	<0.001*
	Yes	34 (85%)	7 (17.5%)	
Spontaneous recovery of sinus rhythm	**No**	30 (83.3%)	6(16.7%)	<0.001*
	Yes	10(22.7%)	34(77.3%)	
Direct cardioversion shock	**No**	10(22.7%)	35(87.5%)	<0.001*
	Yes	30 (83.3%)	5(12.5%)	

Data are presented as frequency (%), DM: diabetes mellitus, IABP: Intra-Aortic Balloon Pump AF: atrial fibrillation, MI: myocardial infarction, EF: ejection fraction.

The mean aortic cross clamp time and the mean partial clamp time were insignificantly different between both groups. Total bypass time, hospital stay and ICU stay were significantly lower in group B compared to group A. (P value = 0.001). Mediastinitis occurred in one patient in group A (2.5%0 and did not occur in group B with no significant difference between both groups. Hospital stay and ICU stay were significantly lower in group B compared to group A. Number of diseased vessels was insignificantly different between both groups. Mortality was insignificantly different between both groups as occurred in 3 (7.5%) of patients in group A and did not occur in group B (Table 3).

Table (3): Aortic cross clamp time, Partial clamp time, ICU stay, and hospital stay of the studied group

	Group A (n=40)	Group B (n=40)	P value
Aortic cross clamp time	81 ±20	76 ±10	0.171
Partial clamp time	18± 4.4	17± 4	0.45
Total bypass time	128± 31.2	106±12	0.001*
Mediastinitis	1(2.5%)	0(0.0%)	1
Hospital stays	15± 3.4	8± 2	0.000*
ICU stay	4± 0.92	2± 0.41	0.000*
No of diseased vessels	3± 0.62	3±0.71	0.098
Mortality	3 (7.5%)	0 (0.0%)	0.240

Data are presented as mean ± SD

There was an insignificant difference of mean survival Time between both groups **(**Figure 2).

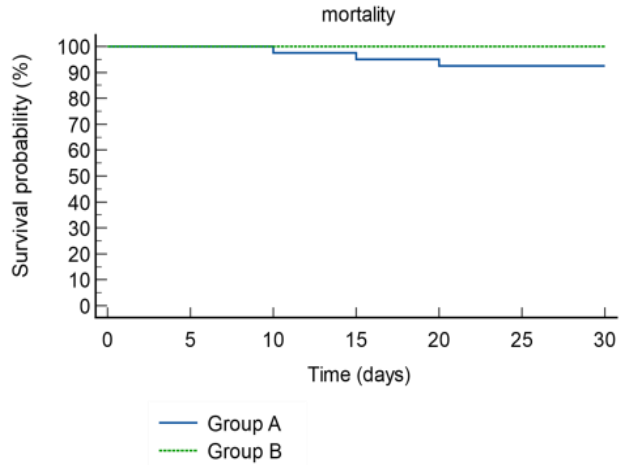

Figure (2): Kaplan Meier for mortality among the studied groups.

DISCUSSION

Globally, CAD is the major cause of death. Not all diseased vessels can be effectively Revascularized by simple CABG. . For cases with diffuse coronary artery stenosis, incomplete revascularization represents an independent predictive risk factor [13, 14]. In instances with diffuse disease in the LAD, revascularization is unsuccessful and a substantial risk factor for postoperative major adverse cardiac events (MACE) [15].

Although the associated high risk and difficulties with CABG, a worse prognosis will happen for cases with diffuse CAD if they do not have this procedure [16]. By developing congestive heart failure 5.8 % of cases who were denied CABG due to diffuse CAD died, 37.2 % died of acute MI and 39.2 % died of cardiac causes, according to a follow-up survey [17].

There are several studies comparing different approaches to these lesions. In some of these, long arteriotomy and conduit anastomosis even on diseased regions are advised [8, 18]. Other studies are against this and suggest alternatives such as arterial endarterectomy or multiple anastomoses on these lesions [19, 20].We compared two surgical techniques of LIMA anastomosis on LAD artery in patients had severe diffuse lesions in this research.

Our findings revealed that regarding complications between the two methods, incidence of tamponade, post-operative MI, new onset AF, IABP, inotropic support were significantly lower in group B compared to group A. Spontaneous recovery of sinus rhythm was significantly higher in group B compared to group A. Total bypass time, hospital stay, and ICU stay were significantly lower in group B compared to group A. Also, 3 (7.5 %) patients in group A died, whereas no patients in group B died. These findings can be attributed to the intra-operation surgical technique where in long arteriotomy and long anastomosis, the surgeon is obliged to use larger calibre prolene sutures in order to decrease the chance of suture disruption or needle breakage. Coronary endarteryctomy (CE) is associated with high propensity for de novo thrombogenesis and embolization from atheromatous debris causing MI and eventual death, which explain the poor outcomes and patency with endarterectomy method and increased MI incidence and mortality as reported by many papers [21].

Also, several factors can affect graft patency, involving the conduit type, diameters of reconstructed artery and distal native artery, prior MI in the territory of endarterectomized vascular, flow in the endarterectomized channel, intraoperative graft flow and antithrombotic medication utilization [22]. Endarterectomy in particular causes denudation of the coronary endothelium, which increases thrombogenesis and releases inflammatory mediators' cascade, involving matrix metalloproteinases, interleukin-1B, and homocysteine [23]. This mechanism not only results in oxidative stress causing extended consumption of endogenous antioxidants, but it also promotes the generation of nitric oxide (NO) synthase inhibitors, hence decreasing NO availability. Thus, CE may cause not only enhanced proliferation of vascular smooth muscle cell and eventual endarterectomized conduit re-occlusion, but also systemic oxidative stress, which may affect the late luminal patency of other coronary grafts [23].

In the same context with **Fayad and Amr** [24] who enrolled 275 cases performed reconstruction of extensively diseased LAD from 2015 to 2019. They were classified into 2 groups: gp 1 (n = 138) involved cases performed plaque exclusion and patching, and gp 2 (n = 137) involved cases performed endarterectomy and patching and reported that endarterectomy is associated with LAD's intimal lining disruption resulting in early graft thrombosis due to coagulation cascade stimulation. Preventing these dreaded consequences necessitates prompt, vigorous anticoagulation treatment after surgery.

In a previous meta-analysis that examined the coronary endarterectomy effect on MI incidence and early death following CABG, it was discovered that endarterectomy enhance renal failure, pulmonary complications, postoperative ventricular arrhythmias, and inotrope, 30-day mortality use were significantly higher in cases performed adjunct CE, and that the procedure is associated with poorer long-term graft patency[24]. **Takanashi *et al.*** [25] discovered that the death rate of endarterectomy patients was 2.7%, which is comparable to other studies. The considerably greater mortality associated with endarterectomy in comparison with standard CABG may be due to concomitant risk factors and comorbidities rather than endarterectomy use. The appropriate technique for endarterectomy still a contentious topic [26].

There are two surgical procedures known as open and closed procedures. The closed technique is performed by endarterectomized intima traction via a tiny arteriotomy. Although anastomosis of the graft is quick and simple, there are a number of potential disadvantages [27]. These disadvantages involve that inadequate endarterectomy may result in the distal end of the lumen becoming obstructed by thrombus or dissection and probabilities that septal perforators and diagonal branches may be torn off despite gentle traction. Alternatively, although the open procedure (long arteriotomy and entire plaque removal under direct visualization) takes longer time, using this approach, the side branch apertures and LAD distal end can be directly visualised and endarterectomized with confidence.

Also, in a prior meta-analysis, postoperative renal complications, MI, and death were found to be higher in high-risk cases or those with diffuse LAD disease who underwent endarterectomy with CABG as compared to those who underwent isolated CABG [28]. This comes in line with **Zarrabi *et al.*** [29] who conducted a study on 40 patients to compare between long arteriotomy on LAD, by the same length the LIMA posterior surface was opened and was anastomosed along the LAD course via diseased and normal parts (gp A) and jump method (gp B) and discovered that group B exhibited significantly superior outcomes in terms of the increase in ejection fraction and the functional class improvement. In terms of post-operative haemorrhage, infection, early mortality, pericardial and pleural effusion, the two groups had comparable outcomes. In group A, there were two incidences of MI and 1 death after 18 months, but there was no MI reported in group B which is similar to our findings.

In addition, in some areas especially larger plaques, the surgeon have to insert the needle in LAD artery farther than the vessel free edge or even in some cases from the vessel base [30]. This caused a great volume of suture material being lodged in anastomosis area and leads to accelerated vessel occlusion. Moreover, plaque fracture may lead to imminent dissection in the anastomosis area and further occlusion [31]. Also, **Kaya *et al.*** [32] found that in the second method diffuse lesions are managed by using small arteriotomies in seemingly normal LAD artery areas or anterolateral wall with fewer plaque densities and then side to side LIMA anastomosis and multi-segment jump anastomosis are performed. Additionally, a multicentre propensity-matched research of sequential vein grafting of the heart performed by **Skov *et al.*** [33] found that jump grafts were related with decreased postoperative haemorrhage durations as well as shorter bypass (as our study) and Cross clamp time. Their results were anticipated due to the time-saving qualities of the jump grafts, and they are consistent with those of earlier experiments [34].

Less anastomoses of the central aorta, and thus a decreased possibility of an improperly performed anastomosis, can account for a substantial portion of the lower amount of bleeding. Moreover, the shorter Cross Clamp and total bypass times seen in this study constitute a benefit of the jump approach, despite the fact that the difference in Cross Clamp time is only 2 minutes.

Our research had some possible limitations. First, this was a single-center study with a small sample size. Further studies are needed with longer duration of follow-up to investigate long-term outcomes need longer observation to confirm this result.

CONCLUSIONS

It was proven that LIMA with sequential-jump anastomoses should be utilized to operate LAD diffuse coronary artery lesions and due of lower chance of long-term patency ; long arteriotomy with single long anastomosis with or without endarterectomy and using saphenous vein patches should be avoided as possible by surgeons. Our jumping technique is preferred due to its superiority in lowering the Incidence of Postoperative MI, new onset AF, use of intra-aortic balloon pump, Inotropic support and DC shock total bypass time, ICU stay and hospital stay

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