Comparison of the Effect of Two Left Internal Mammary Artery Harvesting Techniques (Skeletonization and Pedicled) on Post Coronary Artery Bypass Surgery Pain and Bleeding

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Abstract

Background: Recent evidence suggests that skeletonization of the left internal mammary artery (LIMA) can improve the flow and length of the flow, reduce deep sternal infections and postoperative pain.

Objectives: The present study aimed to investigate the effect of two LIMA harvesting techniques (skeletonization and pedicled) on postoperative pain and bleeding.

Methods: This randomized double blind clinical trial study on patients undergoing LIMA harvest in Birjand was conducted during years 2012 to 2014. The patients were divided to two (skeletonization N: 30 and pedicled N: 30) groups according to the LIMA harvesting method. Their demographic information and other relevant data were collected by means of a questionnaire.

Results: In total, 60 cases, who were candidates for coronary artery bypass grafting (CABG) at the cardiac surgery department of Valiasr hospital in Birjand, were studied. In the skeletonized group, the conduit length was significantly longer (17.96 vs. 17.27, $P < 0.001$), yet there was no significant difference between early and mid-term pain scores (P values: 0.32 and 1.0, respectively) and early postoperative bleeding (782.26 vs. 903.16, $P = 0.657$).

Conclusions: The IMA skeletonized collection resulted in the reduction of postoperative pain and increased conduit length. Skeletonization could not decrease postoperative bleeding.

Keywords: Coronary Arteries, Mammary Artery, Pain, Postoperative

1. Background

Coronary artery bypass grafting (CABG) remains the gold standard for the treatment of left main coronary artery disease and multi-vessel diseases (1). Left internal mammary artery (LIMA) graft to the left anterior descending (LAD) artery has been shown to be the most important factor for survival and minimization of cardiac events in any patient undergoing coronary artery bypass grafting (2, 3). Despite these long-term benefits, some characteristics of Internal Mammary Arteries (IMAs) limit their use in specific contexts. The IMA may be subject to vasospasm and hypoperfusion in the early postoperative period, especially in the presence of vasoactive drugs (4-6). Harvesting IMA is associated with altered sternal perfusion (7, 8) and increased deep sternal wound infection (9), as well as post-operative pain (10-12). The IMAs are usually isolated from the chest wall as a pedicle, along with the surrounding vein, muscle, fat, and endo-thoracic fascia (2, 13, 14).

There are two common methods to harvest IMAs: skeletonization and pediculation. The method of skeletonization, originally described in 1987 by Keeley (15), is to collect only the IMAs without the surrounding tissue, while the traditional technique involves harvesting the tissue edge (1 - 2 cm) around IMAs. Skeletonization of the IMAs has been proposed as a solution for many problems related to the IMA harvest. Although this technique requires careful dissection and carries theoretical risk of increased arterial injury, studies to date have not demonstrated differences in microscopic injury or vascular function when skeletonized and non-skeletonized IMAs are compared (16, 17). Benefits offered include skeletonization flow (18), increased length (16), decreased sternal infection rates (19, 20) and pain reduction (21). Another advantage of using IMA skeletonization is the collateral blood supply preservation on the sternum, which allows for faster healing and reduced risk of infection (8, 22, 23).

2. Objectives

The current study aimed to determine whether the IMA skeletonization leads to differences in the length of IMAs, early and mid-term postoperative pain, and early postoperative bleeding.

3. Methods

A total of 60 patients, scheduled for elective coronary artery bypass grafting (CABG) surgery between January 2012 and November 2014, were involved in this randomized double blind clinical trial study. The study was approved by the "Birjand University of Medical Sciences ethics committee" (institutional review board of Birjand University of Medical Sciences), and all patients gave their informed written consent before surgery (Iranian registry of clinical trials (IRCT) code: IRCT2015121320112N5). The study was conducted at the cardiovascular surgery department of Birjand Valieasr hospital. American society of anesthesiology (ASA) categories II and III undergoing elective isolated CABG, requiring LIMA harvest, were screened for eligibility and were included in the study. The exclusion criteria were: emergency surgery, a history of cardiac surgery, a history of receiving medication with antiplatelet agents except ASA 80 mg/day within the previous five days, preoperative coagulation disorder, a left ventricular ejection fraction less than 20%, preoperative renal dysfunction (serum creatinine > 1.2 mg/dL), preoperative hepatic dysfunction (serum aspartate/alanine amino transferase > 60U/L), preoperative electrolyte imbalance, known hypersensitivity to HES and chronic diuretic therapy, inability to return for follow-up visits and use of intra-aortic balloon pump. Preoperative ASA 80 mg/day and atorvastatin 20 mg/day were continued for all patients. Angiotensin II receptor antagonist and angiotensin converting enzyme inhibitors were discontinued for 24 hours before surgery in all patients. The patients were randomly categorized into two groups (using a computer-based random number generator): the skeletonized harvesting method and pediculate harvesting method. Every patient in the skeletonized group was matched in every respect with a patient from the pediculate group in terms of age, gender, operation details (number of grafts, cross clamp time and pomp time) and cardiac risk factors.

3.1. Surgery

All patients were pre-medicated with 5 mg of intramuscular morphine two hour before the surgery. Anesthesia was induced with etomidate (2 mg/kg), midazolam (0.01 mg/kg), sufentanil (1.5 μg/kg) and cisatracurium (0.2

mg/kg). Anesthesia was maintained with a continuous infusion of sufentanil (0.2 - 0.3 μg/kg/hour), cisatracurium (2 μg/kg/minute), and isoflurane (0.6 - 1.5%) in 100% oxygen and propofol (25 - 100 μg/kg/minute) during CPB, based on patients Bispecteral Index (BIS), which was being kept between 40 - 60. The priming solution also included NaHCO3 7.5% (45 mEq), 20% mannitol (5 mL/kg), heparin (10 mg/L) and ringer lactate for both groups and 500 milliliter of 6% hydroxyethyl starch 130/0.4 (Voluven, Fresenius Kabi, Bad Homburg, Germany). During surgery and at the intensive care unit, colloid solutions were not used. Heparin (primary bolus 3 mg/kg) was administered before the establishment of CPB. After inducing the anticoagulation with heparin, activated clotting time (ACT) was kept over 380 seconds. The CPB was established with a membrane oxygenator (Terumo System 1™, Terumo, Leuven, Belgium) with target flow rates of 2.4 to 2.8 L/min/m² for all patients. Leukocyte-depleted packed red blood cells (PRBCs) were given when hemoglobin was < 7 g/dL. Moderate hypothermia to 32°C and cold (4 - 8°C) cardioplegia concentrations were the same (K$^+$ 20 mmol/L for arrest induction and 10 mmol/L for maintenance) in all patients. Furthermore, α-stat acid-base gas managing was used, and the goal range for PaO$_2$ was 200 - 300 mmHg. Throughout CPB, norepinephrine or nitroglycerine were used to maintain arterial pressure between 60 - 80 mmHg. Heparin was reversed with protamine sulfate (1 mg per 1 mg of heparin). Before weaning out from CPB, all patients were rewarmed to 36°C.

All IMA harvesting procedures were performed by the same surgeon. After standard median sternotomy, the left hemisternum was raised using the IMA retractor. The left pleura were cut longitudinally. When the IMA was harvested as a pedicled conduit, the generous pedicled containing the IMA, accompanying veins, fat, fascia and lymph, were mobilized using a moderate voltage (15 - 20 v) unipolar electrocoagulation. The pedicle was isolated from the epigastric bifurcation near to the origin of the IMA. When the IMA was isolated from a skeletal way, a longitudinal incision in the fascia endothoracic was performed at the boundary between the artery and vein of the internal support; this incision was made with a very low voltage (5 - 10 v) unipolar electrocautery to prevent thermal damage to the arterial wall. The branches of the IMA were dissected and exposed using the tip of the electrocautery, and its proximal and distal portions were ligated by clips and cut by a pair of scissors. Once the branches got separated, the surrounding medial and lateral tissues were removed. Dissection was performed until the length of the IMA was mobilized from its most proximal portion to its distal bifurcation, generally to the sixth intercostal space (24).

After surgery, all patients were moved to the intensive care unit (ICU) where their lungs were mechanically ven-

tilated. Tracheal extubation was done when hemodynamics was stable and there was an acceptable spontaneous breathing (Pao$_2$ > 70 mmHg with Fio$_2$ 0.4, respiratory rate < 15/min) with blood gas parameters being at a normal range. Postoperatively, fluid therapy was used to keep the central venous pressure between 7 and 10 mm Hg and urine output above 1 mL/kg/hour. An anesthesiologist who was blinded to the patients' group managed all patients, postoperatively.

3.2. Postoperative Assessments

All post-operative assessments were performed by the medical staff, who were blinded to the group of the patients. Patients were generally transferred to the ward on the second or third postoperative day, and their discharge and early post-operative bleeding were evaluated through the drainage of draining tubes in the first 24 hours, postoperatively. Each patient's pain was assessed by visual analogue scoring (VAS) at the time of discharge from the hospital and at one-year follow-up (25). Post-operative pain was managed by an auto-fuse 100 mL Morphine-Apotel pump (Darman Gostar, Iran), with an infusion speed of 5 mL/hour and a bolus dose of 0.5 mL and a locking time of 15 minutes with 0.5 mg/kg morphine. In addition, 40 mg/kg Apotel (Razi Pharmaceuticals) was administered by dilution with 100 mL normal saline and if a VAS of > 4 was reported 1 mg bolus morphine was also administered to the patients.

3.3. Statistical Analysis

For the sample size, with an $\alpha = 0.05$ and a $\beta = 0.01$ and 99% power and allowable difference $\mu_2 - \mu_1 = 0.26$, the sample size was calculated from the Equation 1:

$$n_1 = n_2$$
$$= \frac{2\left(z_{\frac{\alpha}{2}} + z_\beta\right)^2 \sigma^2}{(\mu_1 - \mu_2)^2} \qquad (1)$$

Thus, n1 and n2 were calculated as 20, which gave us a total sample size of 40. To be more precise, the final sample size was decided to be 60 (30 in each case and control groups) (26).

Demographic information and data concerning early bleeding volume and pain score at discharge and one-year follow-up were collected by a questionnaire and analyzed using SPSS (version 18). Results were expressed as mean ± standard deviation, and as the results were normally distributed, according to the Kolmogorov-Smirnov test, analyses were performed using the t-test. P values less than 0.05 were considered significant.

4. Results

In the current study, after the inclusion and exclusion criteria were applied, 60 isolated CABG cases were studied (Figure 1). In the S group (n = 30), harvested LIMA was performed according to skeletonization technique, and in group P (n = 30), the pedicled technique was used.
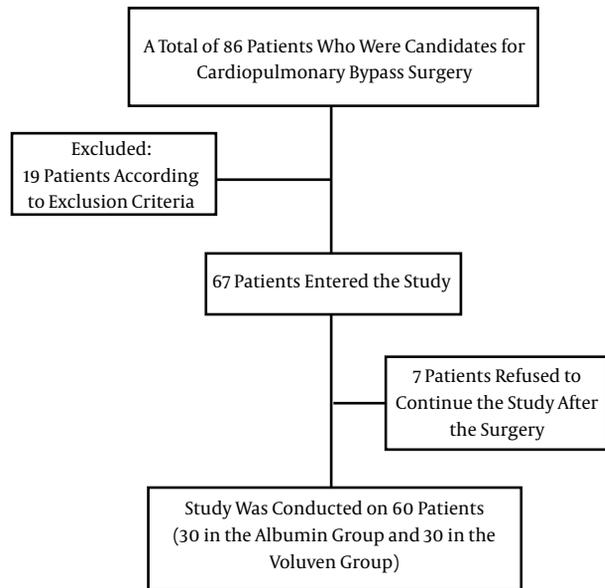

Figure 1. Flowchart of the Study Participants

Patients' demographic information and cardiovascular risk factors are recorded in Table 1. Mean (± SD) age of the study participants was 63.9 (± 8.9) and 62.9 (± 9.7) in the skeletonized and pedicled groups. As the table shows, there was no statistically significant difference between the groups regarding age, gender, cardiovascular risk factors, number of grafts, cross clamp time, and pomp time.

As illustrated in Table 2 (showing early mean bleeding volume, and mean early and midterm postoperative pain scores), there were no significant differences between the two groups in the early and mid-term pain scores (postoperative and after one year of follow-up). However, there was a significant difference in LIMA length between the groups (17.96 ± 0.50 vs. 17.27 ± 0.33, P < 0.001).

5. Discussion

This study aimed to evaluate the bleeding volume (during the first 24 hours postoperatively), as well as the conduit length and postoperative pain after CABG in two

Table 1. Comparison of Demographic and Cardiovascular Perioperative Risk Factors in the Patients[a]

Variable	Skeletonized	Pedicled	P Value[b]
Age, y	63.93 ± 8.99	62.90 ± 9.76	0.67
Gender, %m	55	55	1.00
Number of distal anastomoses	4.3 ± 0.70	4.2 ± 0.66	0.57
Cross Clamp time, min	74.566 ± 12.08	68.833 ± 16.33	0.12
CPB time, min	121.93 ± 25.25	114.83 ± 21.776	0.43
Clamp time, min	74.56 ± 12.08	68.83 ± 16.33	0.24
Pump time, min	121.93 ± 25.25	114.83 ± 21.77	0.36
Risk Factors			
DM	43.3	46.6	0.79
DLP	36.6	23.3	0.26
HTN	63.3	46.6	0.19
COPD	3.3	3.3	0.99
CVA	0	3.3	0.31
Smoking	16.6	13.3	0.72

Abbreviations: COPD, chronic obstructive pulmonary disease; CVA, Cerebral vascular accident; DLP, dyslipidemia; HTN, hypertension; DM, diabetes mellitus.

[a] Values are expressed as mean ± SD or %.

[b] P values were calculated using Students' T-test or Mann-Whitney Test as appropriate.

Table 2. Comparison of Early Postoperative Bleeding and Early and Mid-Term Pain Scores Between the two Groups

Variable	Skeletonized	Pedicle	P Value[a]
Drainage, cc	782.2 ± 453.0	903.1 ± 518.2	0.65
Early pain score	2.77 ± 0.43	2.87 ± 0.34	0.32
Mid-term pain score	1.17 ± 0.37	1.17 ± 0.37	1.00
LIMA length	17.96 ± 0.05	17.27 ± 0.33	< 0.001

[a] P values were calculated using Students' T-test.

groups of patients with different LIMA harvesting techniques.

In our study, the two groups (skeletonized and pedicled) did not significantly differ in terms of bleeding during the first 24 postoperative hours. However, Calafiore et al. (27), Takami and Ina (18) and Bonacchi et al. (28) stated that LIMA harvest postoperative bleeding was significantly reduced with the skeletonized method. It seems that appropriate hemostasis at IMA harvest and the fact that the operations were done by the same surgeon can justify why bleeding was similar in both methods.

In our study, postoperative pain at discharge and at one-year follow-up was evaluated by VAS. No significant dif-

ference was observed between the two groups in terms of early and one-year pain scores. On the contrary, Boodhwani (25) simultaneously compared patients with both pedicled and skeletonized techniques in a double-blind study. After three months of follow-up, postoperative pain was less in the skeletonization than the pedicled group (P = 0.002). Nonetheless, in a study on post-CABG operation pain by Bar-El et al. (29) there was no significant difference between the groups. Chronic pain after bypass coronary artery operation may come from ischemic damage to intercostal nerves (29). Regarding this, our one-year follow-up insignificant pain difference corresponds with this finding. In addition, discharge pain was less in the S group in our study, which may be due to less traumatic damage in the skeletonized technique

In our study, the length of the harvested conduit was significantly more in S than in the P group (P < 0.001), which is in line with the findings of Calafiore et al. (27). In Boodhwani, the difference was not significant although conduit length was more in the skeletonized technique (P = 0.09) (25). In the majority of studies, IMA was longer in the S technique as a result of IMA harvest alone, ignoring surrounding tissues including fascia, muscles and veins. This is in line with our study.

In this study, the focus was only on 24-hour postoperative bleeding, discharge and one year follow-up pain. Several studies, however, have indicated the preference of skeletonization in reducing respiratory and pulmonary complications. Uzun et al. demonstrated that LIMA harvest with the pedicled technique reduced FVC significantly more than the skeletonization technique (P = 0.001) (30). Furthermore, LIMA harvest with the skeletonization technique with or without polar dissection has shown to reduce respiratory problems more than the pedicled technique in the two studies. In their study on the effect of bilateral IMA harvesting on respiratory performance, Bonacchi et al. divided patients to the following groups: 82 patients were treated with the skeletonization technique and without polar dissection, 186 patients with the pedicled technique and polar dissection, and 31 patients with the skeletonization technique and polar dissection. Postoperative respiratory complications were similar in all of the groups with dissected polar irrespective of the LIMA harvest technique. In the group where LIMA was harvested using the pedicled technique, patients in need of long-time ventilation, one-way plural effusion, post-operative thororacosynthesis and atelectasia were significantly more than in the skeletonization group (28, 31).

Our study did not have a large sample size. Nevertheless, all the operations are carried out by the same surgeon and the same technique at one single center, reducing operation technique and skills bias. In addition, potential

detrimental factors to the study were eliminated as far as possible since the two groups were matched for age, gender, cardiovascular risks and coagulation conditions.

In conclusion, given the increased conduit length and reduced early pain in patients in the skeletonization technique, this technique can be preferred over the pedicled technique.

Footnote

Authors' Contribution: Study concept and design: Pooya Derakhshan; acquisition of data: Mahmood Hosseinzadeh Maleki; analysis and interpretation of data: Amir Rahmanian Sharifabad; drafting of the manuscript: Hamid Reza Mashreghimoghadam; critical revision of the manuscript for important intellectual content: Mahmood Hosseinzadeh Maleki; statistical analysis: Amir Rahmanian Sharifabad; administrative, technical and material support: Tooba Kazemi; study supervision: Pooya Derakhshan.

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