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Original Article

# Use of nitroglycerin and verapamil solution by organ bath technique in preparation of left internal thoracic artery for coronary artery bypass surgery<sup>☆</sup>

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## ARTICLE INFO

### Article history:

Received 7 February 2017

Accepted 5 April 2017

Available online xxx

### Keywords:

Left internal thoracic artery (LITA)

CABG

GV solution

Papaverine solution

## ABSTRACT

**Background:** The aim of this prospective study was to compare the effect of application of nitroglycerin and verapamil solution (GV) by organ bath technique with other methods of applications and solutions on the free blood flow of LITA. The technique was not described for in situ graft before.

**Method:** The patients were randomly assigned to four groups: group I (n\_32, GV solution by organ bath technique), group II (n\_30, papaverine solution by organ bath technique), group III (n\_29, topical GV solution) or group IV (n\_29, topical papaverine solution). In each patient, pedicled LITA was harvested; thereafter applied with the randomized different methods and solutions. The free flow from the distal end of the divided LITA was measured for 15 s under controlled hemodynamic conditions after harvesting (Flow 1). The flow of LITA was measured again just prior to anastomosing the conduit (Flow 2).

**Result:** The mean blood flow in LITA was  $56.2 \pm 5.0$  ml/min before application of solutions. After application, the mean blood flow in group I:  $102.3 \pm 7.0$  ml/min, in group II:  $92.7 \pm 3.4$  ml/min, and in group III:  $88.6 \pm 2.2$  ml/min and in group IV:  $81.4 \pm 2.1$ . Proportional increases in blood flow observed in group I (82.6%) > group II (65.1%) > group III (57.6) > group IV (44.8%) ( $p < 0.05$ ).

**Conclusions:** GV solution by organ bath technique is effective and superior in comparison to use of papaverine using organ bath technique or topical spray of GV or papaverine solution.

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## 1. Introduction

Left internal thoracic artery (LITA) is the most widely used graft for anastomosis to left anterior descending artery (LAD), which is considered as gold standard in coronary artery bypass surgery (CABG).<sup>1</sup> ITA has anatomical features of a somatic artery and capable of undergoing severe spasm. It has been described in literature case reports that intractable spasm of ITA lead to transmural myocardial infarction and death.<sup>2</sup> Myocardial revascularization by CABG is a well-established surgical procedure and

yet spasm of conduits is still a debated issue by cardiac surgeons and pharmacologists. Actually, there is no a perfect vasodilator drug, because arterial spasm is often a multifactorial phenomenon modulated by different mechanism, such as mechanical stimuli, drugs, temperature, and endogenous catecholamine.<sup>5</sup>

In order to prevent LITA spasm, several vasodilatory agents, such as papaverine,<sup>7,13–15</sup> calcium-channel blockers<sup>13,17</sup> sodium nitroprusside,<sup>18</sup> nitroglycerine,<sup>17,19</sup> milrinone,<sup>19,20</sup> and phenoxibenzamine,<sup>17,21</sup> have been studied, compared, and used both topically and intraluminally to treat perioperative spasm of the arterial conduits. Papaverine is most commonly used agent,<sup>6,7</sup> which initially was proposed to be injected intraluminally. Most surgeons use this agent topically due to known adverse effects of papaverine on endothelium because of acidic pH.<sup>14,22</sup> Papaverine is the most commonly used agent for the prevention and treatment of conduit vasospasm. Glyceryl trinitrate or nitroglycerin-Verapamil (GV) solution has been an alternative to papaverine and has

<sup>☆</sup> Presented as oral presentation at the 2nd International coronary congress 2016, New Delhi, India, Nov 11–13, 2016. Presented as oral paper presentation at the 63rd Annual conference – IACTSCON 2017 at Bangalore, India, February 23rd–26th 2017.

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<http://dx.doi.org/10.1016/j.ihj.2017.04.004>

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been used by cardiac surgeons mainly for radial artery but also for ITA as glyceryl-trinitrate has a rapid onset and verapamil has a longer duration of action than papaverine in causing relaxation of vascular smooth muscles.<sup>5,13,15,16</sup>

Eleven randomized controlled trials and 2 multi-arm prospective cohort studies were found investigating the effects of topical, intraluminal and periarterial vasodilators.<sup>8</sup> These studies compared mode of administration, concentration of the drug administered and the temperature of the drug administered. We did not come across any study describing the use of organ bath technique for the prevention of spasm of left internal thoracic artery before.

We have conducted a prospective randomized controlled trial to compare the effects of nitroglycerin & verapamil solution with papaverine by organ bath technique and also compared with topical spray of these agents on the free blood flow of left internal thoracic artery (LITA) prepared for coronary artery bypass grafting (CABG).

## 2. Materials & methods

### 2.1. Patient selection and data collection

The study consisted of 120 patients who underwent harvesting of LITA prepared for elective off pump CABG between August 2016 and December 2016 in Department of Cardiovascular & Thoracic Surgery, Lokmanya Tilak Municipal Medical College & Sion Hospital, and Mumbai, India. We routinely use off pump CABG. The surgery was done by a single surgeon. The surgeon was blinded for the vasodilating solutions. The study was approved by the local Ethics Research Committee and each patient included in the study gave a written consent.

All the patients were randomly assigned to one of the four groups: group I (n = 32), treatment with GV solution by organ bath technique; group II (n = 30), treatment with papaverine solution by organ bath technique; group III (n = 29), treatment with topical GV solution; group IV (n = 29), topical papaverine solution.

### 2.2. Surgical technique

All patients were anesthetized with standard general anesthesia using fentanyl and pancuronium. Continuous blood pressure monitoring via radial or femoral arterial lines, heart rate, and central venous pressure was constantly monitored. After median sternotomy, pedicled LITA was harvested from the subclavian vein to beyond LITA bifurcation by a single surgeon using low-power electrocautery. Major branches of LITA were ligated with hemoclips. LITA dissection time was recorded starting after opening the pleural space and tracing till the dissection was completed. The artery was divided distally following systemic administration of heparin.

After harvesting, the free flow from the distal divided end of the LITA was measured for 15 s in a heparin tinged open beaker under controlled hemodynamic conditions; free flow (ml) per minute was calculated accordingly (Flow 1). The measured blood was transfused back to the patient through central line. Afterward, following the randomization, LITA was treated with the appropriate solution and method.

The two solutions used in this study were: GV solution consisted of nitroglycerin 2.5 mg; verapamil 5 mg; 8.4% NaHCO<sub>3</sub>, 0.2 ml; heparin, 500 units; and Ringer's lactate solution, 300 ml and the second solution was papaverine solution (1 mg/ml 0.9% normal saline). The two methods used for application of the solutions were: organ bath technique: the harvested graft was placed in a 20 cc syringe blocked with a tip cap containing either GV or papaverine solution. The syringe was placed in pleural cavity and the graft was allowed to dilate in solution bath (Fig. 1). The syringe was removed from the pleural cavity immediately prior to using it for anastomosis, topical method: The solution was sprayed onto the LITA pedicle throughout its whole length with 25 gauge needle attached to a syringe after harvesting. LITA pedicle was wrapped in the same topical solution-soaked gauze piece.

Just before the anastomosis, the flows of LITA were measured again (Flow 2). The flow rate before and after applications of solution were compared amongst all the groups and analyzed.

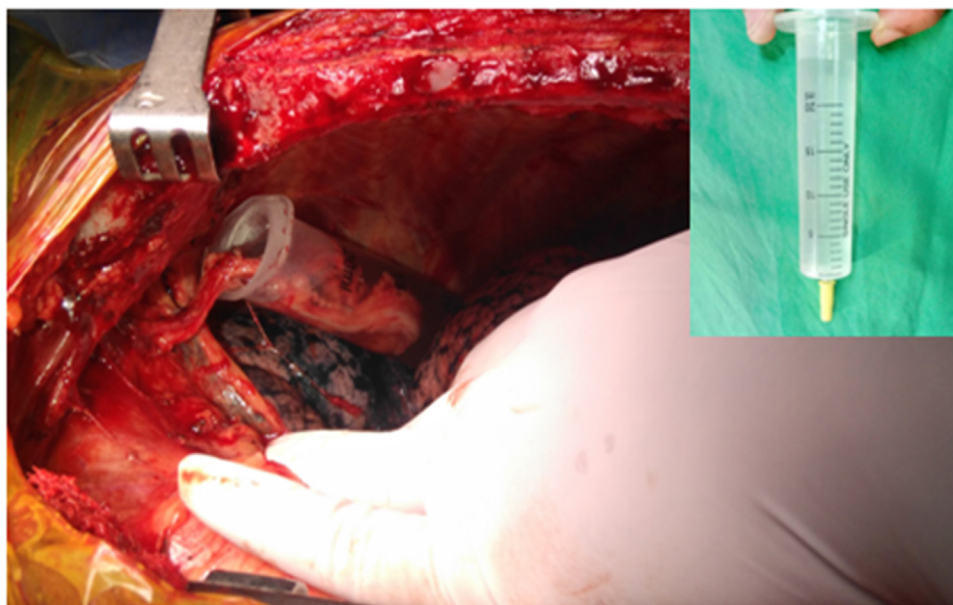


Fig. 1. LITA was placed in a 20 cc syringe with GV solution or papaverine and placed in the pleural cavity.

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