Date

07/12/23

From

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To

PRS Staff

Clinicaltrials.gov

Subject: **Request for uploading study protocol and statistical plan of the trial towards registry:** *NCT06155045*

Respected Sir/ Madam,

I, Dinesh Kumar Sathanantham, Senior Resident of Cardiovascular and Thoracic Surgery the principal investigator request to upload my study protocol and statistical analysis plan on the registry number *NCT06155045 for the title* "*A COMPARATIVE STUDY BETWEEN CONVENTIONAL TECHNIQUE AND MODIFIED CARBO-DISSECTION FOR LIMA HARVESTING IN CABG PATIENTS***."**

Thanking you

Yours Sincerely

Dinesh Kumar Sathanantham

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A COMPARATIVE STUDY BETWEEN CONVENTIONAL TECHNIQUE AND MODIFIED CARBO-DISSECTION FOR LIMA HARVESTING IN CABG PATIENTS

BY

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BRIEF TITLE: Comparing a New Technique of Combining Carbon-dioxide With Electrocautery With Usual Technique of Stand-alone Electrocautery for Taking Down Left Internal Mammary Artery for Coronary Artery Bypass(CABG)

SCIENTIFIC TITLE: A COMPARATIVE STUDY BETWEEN CONVENTIONALTECHNIQUE AND MODIFIED CARBO-DISSECTION FOR LIMA HARVESTING IN CABG PATIENTS

NCT Number: *NCT06155045*
Unique Protocol ID: 95/2020
Document Date: 11/11/2020

INTRODUCTION:

CABG(coronary artery bypass grafting) is still considered the most versatile re-vascularisation procedure for CAD and often exemplary in the setting of TVD(triple vessel disease) with diabetes.[1] In the revascularization of LAD(Left Anterior Descending artery), LITA(Left Internal Thoracic Artery) or LIMA (Left Internal Mammary Artery) is the artery of prime importance, used. The dissection of the same from the surrounding fascial attachments, based on its position anterior to the endothoracic fascia and transverses thoracis is a tedious task and the venous & arterial branches are easily torn if traction is applied.[2]

Various techniques have been used for the dissection of LIMA, still studies say 40% of LITA gets damaged or has a poor flow, owing to spasm and injury.[3] To curtail this, various vaso-active agents have been studied to reduce stress and increase the flow rate of LIMA, during dissection.[2]C02, because of the hypercapnic veno-dilator properties was utilized in a few studies from 1988.[4]and proved to have promising results, though the instrumentation for the same has not been devised. We have planned to use a modified technique as per a case report done by shigu et al. (2017)[5] in a larger study; to study the efficacy of carbo-dissection for LIMA harvesting.

RESEARCH QUESTION

Does the use of modified carbodissection result in less operative time and increased flow rate in harvesting of LIMA.

AIMS &OBJECTIVES:

AIM: To study the flow rate and operative time of modified carbo-dissection for harvesting of Left Internal Mammary artery.

Objectives of the study:

1. To study the first flow in one min, operative time of conventional pedicled technique and modified carbodissection technique for harvesting LIMA

TYPE OF STUDY

Prospective comparative study

PERIOD OF STUDY : Jan 2021- Jan 2022

DURATION OF STUDY: 12 months

PLACE OF STUDY : Department of Cardiovascular and Thoracic Surgery, Government Medical College, Kottayam

STUDY POPULATION

Patients undergoing elective CABG in GMC, Kottayam with requirement of LIMA harvest in the dept. of Cardiovascular & Thoracic surgery, Govt. Medical college, Kottayam.

RESEARCH APPROACH

Quantitative

Statistical analysis:

Data will be entered into Microsoft excel data sheet and will be analyzed using SPSS 22 version software. Categorical data will represented in the form of Frequencies and proportions. Chi-square will be the test of significance. Continuous data will be represented as mean and standard deviation. Independent t test will be the test of significance to identify the mean difference between two groups. p value <0.05 was considered as statistically significant.

Sample Size:[6-9] Was estimated by using the difference in first free flow measurement in the carbon dioxide–insufflated internal thoracic arteries in Group 1 28 ± 19 mL/min and in group 2 was 60 ± 32 mL/min; from the study Mehmet O zkan et. al.[4] Using these values at 99% Confidence limit and 90% power sample size of 21 was obtained in each group by using the below mentioned formula and Med calc sample size software. With 10% non-response sample size of 21 + 2.1 ≈ 23 cases will be included in each group.

Sample Size Estimation Formula:

$$\text{Sample size} = \frac{2SD^2(Z_{\alpha/2} + Z_{\beta})^2}{d^2}$$

SD – Standard deviation = From previous studies or pilot study

$Z_{\alpha/2} = Z_{0.05/2} = Z_{0.025} = 1.96$ (From Z table) at type 1 error of 5%

$Z_{\beta} = Z_{0.20} = 0.842$ (From Z table) at 80% power

d = effect size = difference between mean values

So now formula will be

$$\text{Sample size} = \frac{2SD^2(1.96 + 0.84)^2}{d^2}$$

Table 2: The normal deviates for Type I error (Alpha)

Alpha	Zα (One tailed)	Zα/2 (two tailed)
0.20	0.84	1.28
0.15	1.04	1.44
0.10	1.28	1.64
0.05	1.64	1.96
0.01	2.33	2.58
0.001	3.09	3.29

Table 3: The normal deviates for statistical power

Power	$Z_{1-\beta}$
0.70	0.52
0.75	0.67
0.80	0.84
0.85	1.03
0.90	1.28
0.95	1.64
0.99	2.33

Sample Size For Comparing Two Means

Input Data

Confidence Interval (2-sided)	99%
Power	90%
Ratio of sample size (Group 2/Group 1)	1

	Group 1	Group 2	Mean difference[1]
Mean	28	60	-32
Standard deviation	19	32	
Variance	361	1024	

Sample size of Group 1	21
Sample size of Group 2	21
Total sample size	42

[1] Mean difference= (Group 1 mean) - (Group 2 mean)

Randomization:

Computer generated randomization using www.randomization.com for the allotment of case between two groups, details as mentioned below.

A Randomization Plan

from

http://www.randomization.com

1. B
2. B
3. A
4. B
5. B
6. B
7. A
8. A
9. A
10. A
11. B
12. A
13. B
14. B
15. B
16. A
17. A
18. B
19. A
20. A
21. A
22. B
23. B
24. A
25. B
26. A
27. A
28. A
29. B
30. A
31. B
32. B
33. A
34. B
35. A
36. B
37. A
38. B
39. B
40. A
41. A
42. B
43. A
44. B
45. B
46. A

46 subjects randomized into 1 block
To reproduce this plan, use the seed 29386
along with the number of subjects per block/number of blocks
and (case-sensitive) treatment labels as entered originally.
Randomization plan created on 12/2/2020, 11:36:59 PM

HYPOTHESIS:

Use of modified carbodissection for harvesting will result in better flow rate and less operative time.

MATERIALS AND METHODS

STUDY PROCEDURE

After taking informed consent, patients with CAD with indication for CABG and satisfying the inclusion criteria will be admitted, data will be collected on predefined proforma.

Methodology

Following consultation to our department, after a detailed history and clinical examination,patients with CAD, being planned for CABG, will be subjected to a detailed pre-op Echocardiogram and coronary angiogram. After necessary pre-op assessment, patient will be taken up for the surgery. Invasive monitoring will be done. After median sternotomy, pericardiectomy, LIMA dissection will be done by the planned method as in: The modified carbodissection technique is performed using an improvised instrument that combines an electrocautery pencil (Valleylab™ Force FX electrocautery Pencil, Covidien, USA) with a CO2 mister blower (PerfX® Heart Lung pack Blower/Mister Kit, B L lifesciences, Noida,India) that is routinely used in off-pump CABG. The instruments are fixed together using silk ties. The electrocautery is used in the coagulation mode at a setting of 10 to 15. The CO2

flow is set at 2 to 3 liters/minute. Saline flow is adjusted to a level where it does not hinder the effective coagulation but still prevents drying and desiccation of the tissues.[5]

Following dissection of LIMA by the above mentioned technique, flow of blood from the harvested LIMA, for one whole minute is noted. The operative time required for the dissection of LIMA will be noted and entered.

STUDY TOOLS

Structured Proforma

Instruments –

1. Gas blower/mister (PerfX® Heart Lung pack Blower/Mister Kit, B L lifesciences, Noida, India)
2. Electrocautery (Valleylab™ Force FX electrocautery Pencil, Covidien, USA)
3. C02 supply

INCLUSION CRITERIA

1. Elective CABG
2. Hemodynamically stable CAD patients

EXCLUSION CRITERIA

1. Re-operation, previous sternotomy (where LIMA is already dissected)
2. concomitant valve operation, ventricular aneurysm resection
3. other additional major cardiac procedures
4. Patients with chronic obstructive pulmonary disease

DATA MANAGEMENT AND STATISTICAL ANALYSIS

Data will be coded and entered in Microsoft Excel and analyzed using IBM SPSS software Qualitative data will be presented using percentage and 95% CI, and analyzed with chi square test of independence. Quantitative data will e presented using mean and standard deviation.

Independent t-test will be used for comparison between groups. Pearson's correlation coefficient will be used to test the relationship between parameters. A p value < 0.05 is used as threshold for significance.

LIMITATIONS OF STUDY:

Small sample size

Skill dependent

PRINCIPAL INVESTIGATOR:.Dinesh Kumar Sathanantham

REVIEW OF LITERATURE

Over the period of years, the internal thoracic artery or internal mammary artery has become the main conduit of choice for coronary artery bypass grafting; based on its superior patency rates and longer survival period.[4] A proper functioning LIMA grafted to LAD, provides a patency rate of 98% at 1 year and 94% at 7 years, compared to a patency rate of only 75% at 5 years for saphenous vein graft.[1] The operative technique used for the dissection of ITA, might affect the flow capacity[4] Different techniques have been tried over the period of years for LIMA dissection and most commonly used are the pedicled, skeletonised/semi-skeletonised technique. But still studies have shown a failure rate of LIMA failure is high at 40%.[3] Nevertheless, the thoracic wall damage and sternal infection are present.

To counter-act this reduced flow rates due to spasm and injury, various vaso-active agents have been used in the yester years. The most commonly used is a topical (or) intra-luminal vaso-dilator namely papaverine. Use of gaseous vaso-dilators, has not been studied in detail and the safer of all is Carbon dioxide(C02), due to its easy diffusion and non inflammable properties, has more vaso-dilatory properties Both *in vitro* and *in vivo* studies have demonstrated a rightward shift of the oxygen–hemoglobin dissociation curve after administration of CO_2. Sakai *et al.* described this as an "artificial Bohr-effect". This was responsible for the increased partial pressure of oxygen and the decreased pH.[7]

A few studies have combined the use of C02 insufflation in LIMA dissection, as a gaseous vaso-dilator to avoid injury. In 1988, Myles Edwin Lee, used the C02 insufflation technique called carbo-dissection and in this technique, C02 is injected into the endothoracic fascia to form subpleural emphysema bleb, to aid in the dissection of LIMA. Methodology used was Cardiac pacing lead introducers (8F to 12F), initiallymodified by placing four to six side holes within a centimetre of the tip, are now used as obtained from themanufacturer but with the tip flattened to give an ellipticalcross-section for easy passage through tissue. An **8F**introducer, now our standard, is attached to a commerciallyavailable gas delivery system (Gish Biomedical,Santa Ana, CA), which includes a Luer lock connector,0.6-cm (%-inch) polyvinylchloride tubing, and a 0.45-kmgas filter (Model No., Gas-1) (Fig l), all of which are brought to the operative field with the pump tubing andconnected to a tank of C02 by the perfusionist. A small incision is made in the endothoracic fascia medial to the ITA pedicle and adjacent to the superiorborder of a costal cartilage. The incision should bejust long enough to accommodate the introducer andnot allow gas leaks into the atmosphere. A flow of 4 to 6L/min suffuses the chest wall for distances of 10 cm laterally,superiorly, and inferiorly, in approximately 2 seconds. In another study conducted by ozakan et al,

employed the use of subpleural emphysema with 24G needle, thereby forming a bleb to clearly dissect. The study was done on 28 consecutive patients and had no incidence of complications.

An another descriptive study by O¨ zkan et al, described the use of carbo-dioxide insufflations in 350 patients and no incidence of complications was reported.[8] As this technique seems tedious and injury to LITA, due to the insufflate needle is still present. An improvised technique as described by shigu et al[5], published in 2017, which uses a modified technique on carbo-dissection : technique is performed using an improvised instrument that combines an electrocautery pencil with a CO2 mister blower. The instruments are fixed together using silk ties. The electrocautery is used in the coagulation mode at a setting of 10 to 15. The CO2 flow is set at 2 to 3 liters/minute. This method is relatively easier to perform, with no excessive use of resources. Therefore this was taken to be used in own study of dissection of LIMA.

In study by O¨ zkan et al, done in 2003, showed significantly high flow rates of 68+/ _ 46 mL/min in carbondioxideinsufflated group, compared to 53+/ _ 32 mL/min in the conventional group and lesser operative time in carbon insufflated group.[4]

REFERENCES

1. Talal Al Atassi, Hadi D Toeg, Vincent Chan, Marc Ruel. *Coronary Artery Bypass Grafting,* In: Selke Frank W, Del Nido Pedro, Swanson, Scott J. Sabiston& Spencer surgery of the chest.(19ed.);2016. P 1551-2.

2. Lee ME.Carbodissection of the internal thoracic artery. J ThoracCardiovasc Surg. 2005 May;129(5):1203-4;
3. Blake KL, Watt PAC, Smith JMT, De Souza AC, Spyt T J, Thurston H. Randomized comparison of ultrasonic aspiration versus conventional electrocautery for dissection of the human internal thoracic artery. J ThoracCardiovascSurg 1996;111: 1194-9).
4. Ozkan M[1], Koramaz I, Ulus AT, Tavil Y, Filizlioglu H, Baykan EC, Eryilmaz S, Inan B, Katircioglu SF, Ozyurda U. Effect of carbon dioxide insufflation on free internal thoracic artery flows: is it a vasodilator?
5. Gilbert S, Singh D, Sivakumar MK. Modified carbodissection: A new technique for harvesting the internal mammary artery. *Multimed Man Cardiothorac Surg*. 2017;2017:10.1510/mmcts.2017.018. Published 2017 Oct 29. doi:10.1510/mmcts.2017.018.
6. George w. snedecor. statistical methods, 4th edition, lowa, u.s.a.:oxford &ibh publishing co.;c1946, chapter-17, design and analysis of samplings,p-456-458.
7. Sakai Y, Miwa M, Oe K, et al. A novel system for transcutaneous application of carbon dioxide causing an "artificial Bohr effect" in the human body. *PLoS One*. 2011;6(9):e24137. doi:10.1371/journal.pone.0024137
8. Lee ME. (1997, March). Carbodissection of the internal thoracic artery pedicle [Letter to the editor]. The journal of thoracic and cardiovascular surgery. Retrieved fromhttps://www.annalsthoracicsurgery.org/article/S0003-4975(10)64671-1/pdf