Study Protocol and Statistical Analysis Plan

PREVENTION OF EDEMA AFTER CORONARY ARTERY BYPASS GRAFT BY CUSTOMIZED PRESSURE-GUIDED ELASTIC BANDAGES (PEACCE) 788/2566(IRB1)

- PROMPAK NITAYAVARDHANA, STAFF, MD, GRAD DIP CLIN SC (SURG), DIP THAI BRD THORAC SURG, FRCST, PRINCIPAL INVESTIGATOR
- RATCHARNON SRIFA, CARDIOTHORACIC RESIDENT, MD, SUB-INVESTIGATOR

Study Protocol and Statistical Analysis Plan

Sample size calculation

Sample size for comparing proportions of two independent groups	
Type I error (α)	0.5
Type II error (β)	0.2
proportion group 1(P1)	0.98
proportion group 1(P2)	0.8
N per group	47

$$n = \frac{\left[Z_{\alpha/2}\sqrt{2\bar{P}(1-\bar{P})} + Z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\right]^2}{(P_1-P_2)^2}$$

$$\bar{P} = \frac{P_1+P_2}{2}$$

Previous research reported a 98% incidence of leg edema at two weeks in patients who inconsistently wore compression stockings.(1) In this study, the use of high-pressure elastic bandages is hypothesized to reduce the incidence of edema by 20%. The study is designed with a Type I error rate of 0.05 and a Type II error rate of 0.2. The incidence of leg edema in patients who inconsistently wear compression stockings is 0.98, and the expected incidence with the use of high-pressure elastic bandages is 0.8. The sample size was calculated to be 47 participants per group, with an additional 10% dropout rate. Therefore, the study will require 53 participants per group.

Inclusion Criteria:

All patients undergoing elective coronary artery bypass graft (CABG) surgery with saphenous vein harvesting at Siriraj Hospital.

Patients aged 18 years or older who undergo CABG using saphenous vein grafts at Siriraj Hospital and voluntarily consent to participate in the study.

Exclusion Criteria:

Patients with an ankle-brachial pressure index (ABI) < 0.8.

Patients with severe leg edema (pitting edema grade 3+ or higher) or uncontrolled heart failure, pre- or post-CABG, despite the use of diuretics.

Patients with deep vein thrombosis (DVT) or chronic venous insufficiency (e.g., varicose veins with pain, CEAP 2s), or those with lymphatic disorders in the leg (lymphadenopathy).

Withdrawal or Termination Criteria:

Patients who develop postoperative complications from saphenous vein harvesting, such as wound dehiscence or infection, will be withdrawn from the study as they require appropriate treatment that may affect the primary outcomes.

Subject Allocation:

Participants will be divided into two groups:

1. Group receiving customized pressure-guided elastic bandages (CPG-EB) for 4 weeks after CABG surgery.
2. Group receiving standard post-CABG care.

The allocation will be done using simple randomization, ensuring equal numbers in each group.

Research Procedure:

1. **Recruitment**: Participants will be selected based on inclusion and exclusion criteria. All coronary artery bypass graft (CABG) candidates will undergo ankle-brachial index (ABI) measurements.
2. **Consent**: Eligible participants will receive detailed explanations of the study and sign informed consent documents.
3. **Baseline Measurements**: Leg circumference will be measured at key locations (mid-arch, above the ankle, calf, thigh) before the surgery to establish a baseline.
4. **Randomization**: Participants will be randomly assigned to one of the two treatment groups using sealed envelopes. Both participants and investigators will be blinded to group assignment.
5. **CPG-EB Group**: Participants in this group will be trained on using CPG-EB by clinical staff. The bandage will be applied starting at the foot, following specific instructions for achieving the correct pressure gradient.
6. **Surgery and Postoperative Care**: All patients will undergo saphenous vein harvesting using the conventional open technique. After surgery, an elastic bandage will be applied to control initial bleeding and swelling.
7. **Post-Surgery Wound Care**: After 24 hours, wounds will be dressed, and elastic bandages will be replaced with either CPG-EB or standard dressings, depending on group allocation. CPG-EB participants will be trained again on proper application before discharge.
8. **Follow-Up Assessments**: Leg circumference and edema severity (graded from 0 to +4) will be evaluated at 1-, 2-, and 6-weeks post-surgery. Wound healing and complications, including infections, will be recorded.
9. **Standard Care Group**: Participants will receive standard wound care instructions, without the use of CPG-EB.
10. **Outcome Measurements**: Edema will be assessed by examining the medial malleolus, tibia, and dorsum of the foot. Complications like wound non-union or infection will be recorded at regular intervals.

All data will be collected in the outpatient clinic at scheduled follow-ups 1-, 2-, and 6-weeks post-surgery.

Study Duration:

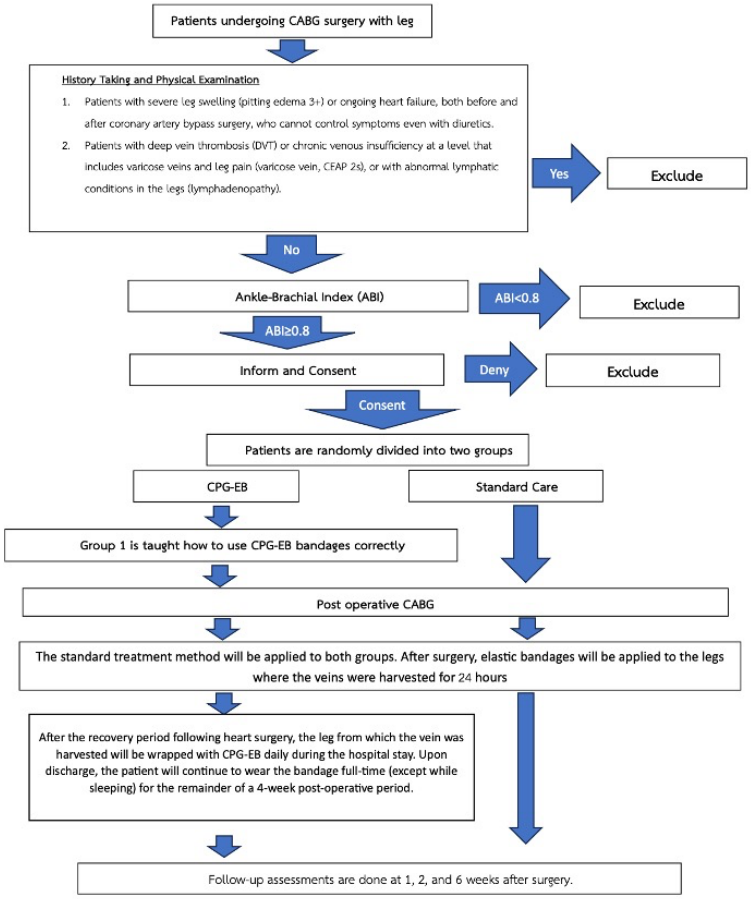
The total study duration spans from hospital admission for surgery until 6 weeks post-surgery. Outcome measurements will be conducted at 1, 2, and 6 weeks after surgery, with some participants discharged from the hospital during this period.

Data Collection:

All data recorded in case report forms (CRFs) must not include identifiable personal information, such as names, hospital numbers (HN), or any other identifying details. Participants will be assigned codes for data anonymization. The CRF will include the following information:

1. Date of study enrollment.
2. Demographic information: age, sex, weight, height, and BMI.
3. Comorbidities.
4. New York Heart Association (NYHA) classification.
5. Coronary artery disease characteristics: a. LVEF % b. Cardiac arrhythmia c. Valvular heart disease d. Aortic disease
6. Preoperative laboratory results: a. Hemoglobin (Hb) and hematocrit (Hct) b. Blood urea nitrogen (BUN), creatinine (Cr) c. Total protein d. Albumin
7. Circumferential measurements of both legs.
8. Pulse examination at the posterior tibial and dorsalis pedis arteries.
9. Ankle-brachial index (ABI) for both legs.
10. Leg edema severity, evaluated at the medial malleolus, tibia, and dorsum of the foot using the following scale:

- 0: No edema
- +1: Barely detectable
- +2: Slight indentation, 15 seconds rebound
- +3: Deeper indentation, 30 seconds rebound
- +4: > 30 seconds rebound



11. Postoperative complications: a. Surgical site infection (SSI) b. Delayed wound healing c. Tingling or numbness

Definitions of Postoperative Complications:

1. **Surgical Site Infection (SSI):** An infection occurring within 65 days post-surgery, with at least one of the following symptoms: a. Purulent drainage from the incision. b. Wound dehiscence or opening due to fever, localized pain, or a positive culture (if no culture or a negative result, both fever and localized pain are required). c. Evidence of infection through clinical examination or imaging (e.g., ultrasound or CT scan). d. Diagnosis of SSI by a physician.
2. **Delayed Wound Healing:** Defined as the wound not healing by 2 weeks post-surgery.

Outcome Measurement and Data Analysis:

- **Primary Outcomes:**
    - **Incidence of leg edema:** Compared between the two groups using the Chi-square test.
    - **Edema severity:** Compared between groups using the Chi-square test.
    - **Leg circumferential differences:** Measured before and after surgery and compared between groups using the independent sample t-test or Mann-Whitney U test.
- **Secondary Outcomes:**

- **Infection rates:** Compared between groups using the Chi-square test.
- **Delayed wound healing rates:** Compared between groups using the Chi-square test.
- **Incidence of postoperative leg numbness:** Compared between groups using the Chi-square test.

Reference

1. Alizadeh-Ghavidel A, Ramezannejad P, Mirmesdagh Y, Sadeghpour-Tabaei A. Prevention of edema after coronary artery bypass graft surgery by compression stockings. Res Cardiovasc Med. 2014;3(2):e17463.

Participant Information Sheet/Consent Form

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For Parents/Legal Guardians

This document provides important information regarding the research study in which your child or ward is invited to participate. Please take your time to carefully read through this information, and feel free to ask any questions you may have before making a decision. You are encouraged to discuss this document with your family, close friends, or your child's/ward's physician to help with your decision. You may also take this document home for further review before deciding to participate.

Research Study Title: Prevention of Post-Coronary Artery Bypass Graft (CABG) Leg Swelling Using Pressure-Guided Compression Bandages

Principal Investigator:

Dr. Prompak Nitayavardhana, M.D.

Research Locations:

Cardiothoracic Surgery Outpatient Clinic

Wound Care Room 101, Syamindra Building

Pre- and Post-Operative Ward

Cardiothoracic Operating Room, Siriraj Hospital

Workplace and Contact Information for Principal Investigator:

Cardiothoracic Surgery Division, Syamindra Building, 12th Floor, Department of Surgery, Faculty of Medicine, Siriraj Hospital

Phone: 02-419-7998, 02-419-9003, +6685-914-1236, +6681-966-0944

Conflicts of Interest with Funding Sources:

☑ None

☐ Yes, specify: .....

Duration of the Study: 2 years

Background of the Study:

Coronary artery bypass graft (CABG) surgery is widely performed as a treatment for coronary artery disease. The saphenous vein in the leg is frequently used for grafting due to its size and length, making it ideal for multiple coronary bypasses. However, complications may arise from harvesting the saphenous vein, including swelling, infection, and delayed wound healing. These complications can cause pain or numbness in the leg, potentially reducing mobility and delaying recovery after surgery.

Compression therapy, which increases external pressure on the leg, has been shown to reduce swelling in patients with chronic venous insufficiency and lymphedema. By reducing blood pooling in the lower veins and improving lymphatic drainage, compression can help reduce swelling and support post-operative recovery.

In this study, we aim to evaluate whether the use of customized pressure-guided elastic bandages (CPG-EB) can help reduce the risk of leg swelling and other post-operative complications in patients who have undergone CABG surgery using the saphenous vein.

Study Objective:

This study seeks to determine whether compression therapy using customized pressure-guided elastic bandages (CPG-EB) can prevent post-surgical complications,

particularly leg swelling, in patients who have undergone CABG surgery using the saphenous vein.

Participants:

Patients invited to participate in this study must meet the following criteria:

1. Be 18 years of age or older.
2. Have coronary artery disease requiring CABG using the saphenous vein from the leg.

A total of approximately 106 participants will be enrolled in this study.

Study Procedures:

Currently, standard post-operative care for saphenous vein harvesting involves applying elastic bandages to the leg for 24 hours post-surgery to control bleeding. The bandages are then removed for wound care, and no further compression is typically applied.

However, some patients experience complications following saphenous vein harvesting, such as leg swelling, which is the most common, wound infections, delayed wound healing, and pain or numbness in the leg. These complications may reduce mobility and delay post-operative recovery.

In this study, patients scheduled for CABG will be screened to ensure they do not have pre-existing conditions such as heart failure or chronic leg swelling that would exclude them from the study. Eligible participants will have their Ankle-Brachial Pressure Index (ABI) measured to ensure there are no contraindications to high compression therapy, with a cutoff of ABI ≥0.8. If eligible, the patient will be asked to provide informed consent to participate in the study.

Participants will be randomly assigned to one of two groups:

1. The standard post-CABG care group.
2. The CPG-EB group, patients will be treated with customized pressure-guided elastic bandages (CPG-EB) for 4 weeks post operatively.

Both groups will have elastic bandages applied to control bleeding for the first 24 hours post-surgery. Afterward, the bandages will be removed in the standard care group, while the CPG-EB group will continue using the pressure-guided bandages for the remainder of a 4-week post-operative period. Patients in the CPG-EB group will be instructed on how to properly apply the bandages at the Outpatient Clinic, Room 101, Siammin Building. They will be taught to wear the bandages daily (except while sleeping) after discharge and be provided with instructions on how to monitor for potential complications and how to address them.

Both groups will return for follow-up visits at 1-, 2-, and 6-weeks post-surgery to assess wound healing, leg swelling, and any complications

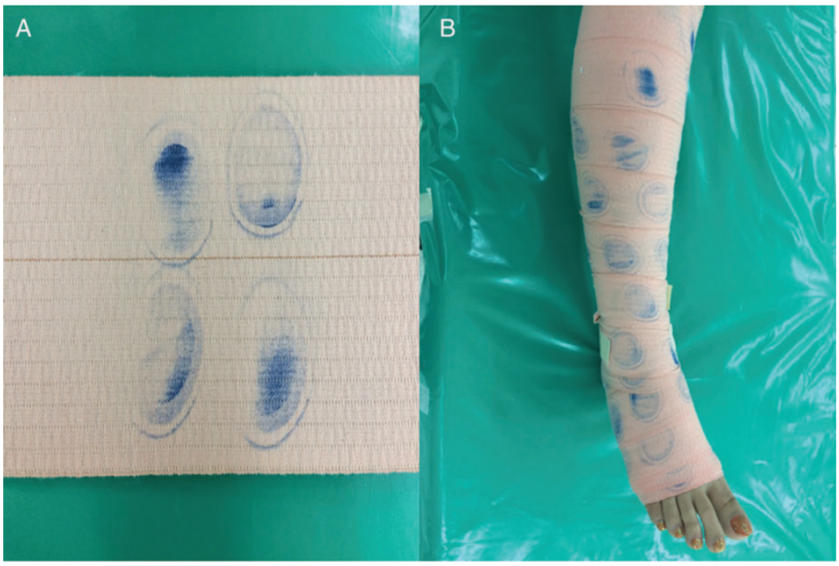

Figure 1: Example of Customized Pressure-Guided Elastic Bandages (CPG-EB)
Source: Sermsathanasawadi N, Chatjaturapat C, Pianchareonsin R, et al. Use of customised pressure-guided elastic bandages to improve efficacy of compression bandaging for venous ulcers. Int Wound J. 2017;14:636-640.

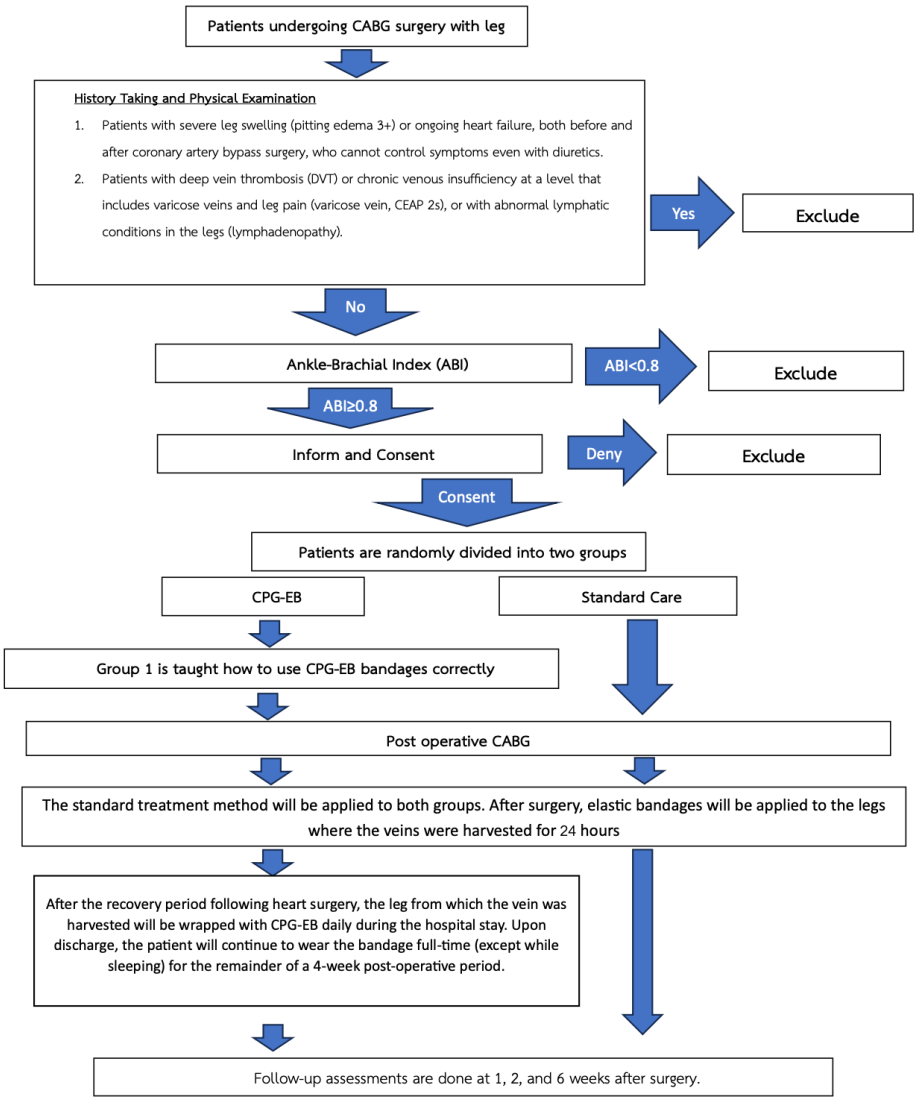

Figure 1: Patient Protocol During Research Participation

Potential Risks

Participants in both the standard post-surgical care group and the group treated with the customized pressure-guided elastic bandages (CPG-EB) may experience common post-operative complications such as leg swelling, delayed wound healing, and wound infection. These are typical risks for patients undergoing cardiac bypass surgery. However, patients in the CPG-EB group may feel discomfort or experience numbness if the bandages are applied too tightly or incorrectly. To mitigate this, a nurse will teach participants how to apply the bandages properly. If numbness occurs, participants are advised to loosen the bandage and review the correct application technique.

Alternatives to Participation

Even if patients do not participate in this study, they will still receive the standard care for post-surgical wound management following saphenous vein harvesting in coronary artery bypass grafting (CABG), which includes elastic bandage application for 24 hours post-surgery to control bleeding.

Contact for Questions and Adverse Reactions

For any questions related to the research or if adverse reactions occur, participants can contact:

Dr. Ratcharnon Srifa at +66819660944 or the Surgery OPD, Syamindra Building, Room 101.

Dr. Prompak Nitayavardhana at +66859141236, or the Surgery OPD, Syamindra Building, Room 101.

Medical Care for Research-Related Injuries

Participants will receive standard medical care for any injuries or illnesses caused by the research, with expenses covered by the Faculty of Medicine, Siriraj Hospital.

Expected Benefits of the Research

1. Professional Benefit: The study may provide insight into the efficacy of customized pressure-guided elastic bandages (CPG-EB) in preventing complications after CABG surgery.
2. Social Benefit: Potential reduction in healthcare costs related to post-operative complications of saphenous vein harvesting.
3. Participant Benefit: There are no direct benefits to participants in this study.

Compensation

Participants will receive 200 THB as compensation for their involvement in the research. There are no additional costs for participants**.**

Confidentiality and Data Use

Personal information will be kept confidential and not disclosed individually. However, the overall results may be shared in public reports or through clinical trial websites (http://www.ClinicalTrials.gov and http://www.ClinicalTrials.in.th). Certain regulatory bodies, such as the funding organization or ethical review board, may access individual data to ensure compliance.

Voluntary Participation

Participants have the right to withdraw from the study at any time without prior notice, and doing so will not affect their medical care.

For further understanding of research participation, participants can visit the Siriraj Human Research Ethics Committee website at http://www.si.mahidol.ac.th/sirb. Complaints can also be directed to the Ethics Committee via this website or by contacting the Siriraj Human Research Ethics Office at ChalermPhrakiat Building, 2nd Floor, or by calling 0 2419 2667-72, 06 3903 4255.

Participant's Signature: _____

Name: _____

Date: _____

Researcher's Signature: _____

Name: _____

Date: _____