

Major Leg Wound Complications between the Proximal and Distal Segments of Saphenous Veins Harvested by No-Touch Technique in Coronary Artery Bypass Graft Surgery: study protocol for a single-center randomized within-subject controlled clinical trial

Meice Tian (✉ tianmeice@fuwaihospital.org)

Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Shengshou Hu

Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Xianqiang Wang

Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Sidong Li

Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Liqing Wang

Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Study Protocol

Keywords: Coronary artery bypass graft surgery, No-Touch saphenous vein harvesting technique, Leg wound complication, Vein graft occlusion

Posted Date: March 12th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-16885/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background : The No-Touch saphenous vein harvesting technique has been proved to reduce vein graft occlusion after coronary artery bypass graft surgery. However, the optimum segment of the saphenous vein for this technique is still undetermined. Previous studies implicated lower occlusion of proximal segments of saphenous veins compared to distal segments, but with concern of higher leg wound complications. No randomized trials have been carried out accordingly. This pilot study is a single-center randomized within-subject-controlled trial, comparing the leg wound complications of proximal segments of saphenous veins harvested by No-Touch versus distal segments.

Methods : The study is planning intending to enroll 100 coronary artery bypass graft surgery patients from our institution, with each patient requiring two vein grafts with or without cardiopulmonary bypass. Both proximal and distal segments of saphenous veins will be harvested by No-Touch technique from ipsilateral legs. The proximal vein segments will be randomized to the left or right coronary territory for bypassing. The primary endpoint is major leg wound complications at 6 days postoperatively. Secondary endpoints include major leg wound complications during 3-month follow-up and graft vessel occlusion at 3 months and 1 year. Clinical events include major adverse cardiac or cerebrovascular events and recurrence of angina

Discussion : This is the first study assessing the safety and effectiveness between different segments of No-Touch saphenous veins for coronary artery bypass graft surgery, and will help to establish preliminary evidence for decision making of precise vein graft conduit choice.

Trial registration : ClinicalTrials.gov: NCT04284956

Spirit Checklist

See Additional File 1 for the SPIRIT checklist

Administrative Information

Title	Major Leg Wound Complications between the Proximal and Distal Segments of Saphenous Veins Harvested by No-Touch Technique in Coronary Artery Bypass Graft Surgery: study protocol for a single-center randomized within-subject controlled clinical trial
Trial registration .	ClinicalTrials.gov: NCT04284956
Protocol version	Issue Date: 01 August 2019 First Version Author: Meice Tian
Funding	Supported by the Youth Fund of National Center for Cardiovascular Disease, China & Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China
Roles and responsibilities	Authors: Meice Tian, MD ¹ , Shengshou Hu, MD ¹ , Xianqiang Wang, MD ¹ , Sidong Li, PhD ² , Liqing Wang, MD ¹ Author Affiliations: 1 Department of Surgery, National Center for Cardiovascular Disease, China & Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China 2 Medical Research & Biometrics Center, National Center for Cardiovascular Disease, China & Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China MT: designer of the study and coordination and drafted the manuscript SH: participated in the design and co-ordination and helped to draft the manuscript XW: participated in the design and co-ordination and helped to draft the manuscript SL: participated in the design and statistical analysis helped to draft the manuscript LW: participated in the design and helped to draft the manuscript All authors read and approved the final manuscript.
Name and contact information for the trial sponsor	National Center for Cardiovascular Disease, China & Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China A 167, Beilishi Road, Xicheng District, Beijing, 100037, China Tel: +86-10-8839-8359
Role of sponsor	The sponsors did not participate in the design and will not participate in the implementation of the study, including the collection, management, analysis, interpretation of the data and the preparation of the manuscript

Introduction

Background and rationale {6a}

Saphenous vein grafts (SVG) are currently used in almost 80% of coronary artery bypass graft (CABG) surgery [1]. The Occlusion of SVG is part of the most crucial challenges in CABG; it increases the recurrence of angina substantially, and may require repeat revascularization [2-8] afterwards. Less than 50% of vein grafts remain patent in 10 years after surgeries [4, 9, 10]. The No-Touch saphenous vein harvesting technique, introduced by Dr. Souza in 1996, aimed to reduce vein graft occlusion after CABG,

by preserving the integrity of SVG preferably during the harvesting [11]. Short and long-term follow-up studies demonstrated less occlusion of SVG harvested by No-Touch technique compared with conventional approach [8, 12, 13]. Empirically, surgeons prefer to harvest veins from the distal end (shank) of the leg, which is reviewed easier to identify during harvesting. Previous studies implicated lower occlusion of proximal segments of saphenous veins compared to distal segments [8]. The proximal (thigh) segment of saphenous vein is usually located deeper, resulting in a larger skin flap after surgery. Hence, it brings to concern of leg wound complications of harvesting veins from the thigh [14]. However, no studies have been performed comparing the wound complications between these two sites of vein harvesting so far. Therefore, the optimum segment of No-Touch veins for bypassing is still undefined.

Explanation for the choice of comparators {6b}

Not applicable.

Objectives {7}

The purpose of this study is to assess, whether the safety of harvesting from proximal segment of saphenous veins by No-touch technique, is as the same as from distal segment, without increasing the incidents of leg wound complications after CABG surgery. Rates of graft occlusion between the two segments of veins for bypassing will also be compared during follow-ups.

Trial design {8}

This is a two-arm, single-center randomized within-subject-controlled trial. Patients will be randomized to bypass either the left or right coronary territory, by using their proximal segments of saphenous veins. Distal segment veins from the ipsilateral leg will be used to bypass the other coronary territory.

Methods: Participants, Interventions And Outcomes

Study setting {9}

The study will be undertaken in the Department of Surgery, Fuwai Hospital, Chinese Academy of Medical Sciences, with an amount of isolated CABG over 4000 cases annually. Data will be collected both in hospital ward and outpatient clinic during follow-ups. A web-based and paperless data submission system (<http://ccsr.cvs-china.com>) for the study has been set up.

Eligibility criteria {10}

Inclusion criteria

Patients aged 18 or older who undergo primary isolated open-chest CABG with two vein grafts, one to the left coronary territory and the other to the right, with or without cardiopulmonary bypass.

Exclusion criteria

- Concomitant cardiac or vascular surgeries (i.e. valve repair or replacement, Maze surgery)
- Redo CABG
- Emergent CABG (cardiogenic shock, inotropic pressure support, IABP)
- Severe vein varicosity as assessed after vein harvesting and before randomization
- Use of vascular stapler for anastomosis
- Endarterectomy of coronary artery during surgery
- Left ventricular repair due to ventricular aneurysm
- Concomitant life-threatening disease likely to limit life expectancy to less than two years
- Severe renal insufficiency (i.e. creatinine >200 µmol/L)
- Contraindications for dual antiplatelet therapy, such as active gastroduodenal ulcer
- Participant of other ongoing clinical trials

All surgical procedures will be expected to complete by qualified surgeons who have performed at least 100 CABGs. Vein harvesting will be done by qualified senior residents. We identify senior residents who have performed at least 100 cases of vein harvesting in CABG and give them standard training of No-Touch vein harvesting. When they perform at least 50 cases of No-Touch vein harvesting, they are evaluated by two independent training surgeons to be qualified for vein harvesting.

Interventions

Intervention description {11a}

Surgical Procedure

Anesthetic technique and method of myocardial protection are left to individual anesthesiologists and perfusionists to decide. All patients undergo either off-pump or on-pump CABG at the surgeons' discretion on the basis of anatomic and clinical findings.

For the No-Touch vein harvesting technique in our study, two longitudinal incisions are made on the thigh and the shank from unilateral lower limb (for harvesting of the proximal segment of saphenous vein, incision is started from about 3 or 4cms inferolateral to the pubic tubercle and then extended downward). As previously reported [11, 15], the adventitia and perivascular tissues are carefully kept intact to avoid damage. Then a margin of about 5 mm from both sides of the vein is created to include the fat pedicle using electrocautery, and all visible side branches are ligated with 4-0 silk or by metal clipping (branches are divided at the pedicle margin rather than the vein trunk). The saphenous vein is then separated from its bed using scissors and the electrocautery, together with the surrounding tissue. The vein is left in situ and covered with a saline-moistened gauze until systemic heparin is administered and graft anastomosis is ready. After removal, a small adaptor is inserted into the open distal end and secured with a ligature. The pedicled vein is stored in saline solution to which heparin (2500U) and papaverine (30mg) have been added. Since heparinized blood cannot be easily obtained during off-pump CABG, we use heparinized

saline with papaverine rather than heparinized blood to store vein grafts for patients undergoing either off-pump CABG or on-pump CABG. Forced distension or flushing using a syringe is strictly prohibited. Before each anastomosis, side branches of the vein are checked by the operator and re-clipped. After proximal anastomosis is completed, each graft is re-checked for leakage due to undiscovered branches or invalid clipping and re-clipped if necessary.

Leg incisions are closed with continuous suture for both two groups. Remaining coronary bypassing techniques are according to the clinical practice of the hospital and the preference of the operators. Before chest closure, mean flow values and pulsatile index are obtained with transit-time flow measurement (Medi-stim Butterfly flowmeter, Medi-stim AS, Oslo, Norway). If mean flow value is less than 10 ml/min, or pulsatile index is greater than 5.0, or any possible graft kinking or compression is detected, the anastomosis is redone.

An intraoperative paper questionnaire is answered by the operator after completion of the surgery, to evaluate the quality of each vein graft. Vein quality is classified as good, moderate, or poor, according to whether there is varicose or aneurysmal dilatation, inflammatory wall thickness, focally thinned wall, or too-small diameter.

Although ultrasonic mapping is reported to help prevent unnecessary incision and large skin flaps [8, 16], it is not commonly used in clinical practice in China. Based on our experiences, well-trained surgeons with sufficient qualifications can harvest the veins with No-Touch technique without ultrasonic mapping. Ultrasonic mapping is not adopted in this study.

Criteria for discontinuing or modifying allocated interventions {11b}

Not applicable.

Strategies to improve adherence to interventions {11c}

Not applicable.

Relevant concomitant care permitted or prohibited during the trial {11d}

Medication

All participants are prescribed dual antiplatelet therapy with aspirin 100mg plus clopidogrel 75mg daily from the first day post-CABG until 3 months post-operation. Prescription of other concomitant medications such as β -blockers, nitrates, statins, and antihypertensive agents, is determined by local surgeons according to ACC/AHA guidelines [17].

Outcomes {12}

Primary endpoint

Major leg wound complication at 6 days postoperatively.

Major leg wound complication is defined as a leg wound that has failed to respond to conservative treatment and required subsequent surgical interventions, such as debridement, re-suture, and delayed wound closure.

Secondary endpoint

1. Major leg wound complication during 3 months after the surgery.
2. Graft vessel occlusion at 3 months and 1 year after the CABG (determined by multislice computed tomography angiography (MSCTA)).

Graft occlusion is identified by MSCTA. Graft assessment is carried out according to the FitzGibbon criteria [18]. Each graft is graded as A (excellent), B (fair), or O (occluded). Contrast filling of the grafts, anastomoses, and coronary arteries beyond the graft are considered in each assessment. Grade A indicates that the graft is patent with $\leq 50\%$ stenosis. Grade B indicates that graft stenosis is $>50\%$ but not occluded. When a conduit does not fill with contrast at all, it is considered Grade O and included with string sign found in any segment (including proximal anastomotic site, distal anastomotic site, and main trunk). Both of these latter findings are considered together and referred to as occlusion in the analysis.

Clinical events

1. Major adverse cardiac or cerebrovascular events (MACCE, including cardiovascular death, non-fatal myocardial infarction (MI), stroke and target vessel revascularization) at 3 months and 1 year after the CABG.
2. Individual MACCE, including cardiovascular death, non-fatal MI, stroke and target vessel revascularization at 3 months and 1 year after surgery.
3. Recurrence of angina

All clinical events including myocardial infarction, stroke, target lesion revascularization, and death will undergo central adjudication by an independent clinical events committee (CEC) according to pre-specified criteria. Definition of clinical events used in adjudication is shown in Additional file 2

Participant Timeline {13}

Participant time line is shown in Fig. 1, and flowchart of the study is shown in Fig. 2

Sample size {14}

As a pilot trial, the primary consideration for the sample size is the ability to inform the feasibility of a full-scale study. We propose a sample size of 100 vein grafts in each group with a total of 100 patients.

Recruitment {15}

Not applicable.

Assignment Of Interventions: Allocation

Sequence generation {16a}

A web-based central randomization system incorporated in the registration system is used for allocation (<http://ccsr.cvs-china.com/>). The randomization code with fixed block size is generated by SAS.

Concealment mechanism {16b}

Not applicable.

Implementation {16c}

Enrollment of participants are performed by investigators. Each patient will be in an individual discussion with an investigator. The nature of the study and the procedure to be conducted will be explained in a way that is not difficult to comprehend. When an eligible patient signs informed consent, the investigator logs in to the randomization webpage, and obtains the random number along with the proximal group (left or right coronary territory), automatically distributed by the system after the basic patient information was confirmed. The statistician who is responsible for the randomization code and the staff that develops the Interactive Web-based Response (IWR) system, are independent of each other.

Assignment Of Interventions: Blinding

Who will be blinded {17a}

Due to the nature of this surgery-based study, the investigators, CABG operators and vein harvesting surgeons will not be blinded. Participants will be blinded about which coronary territory his or her proximal vein segment is bypassed to during post-operative assessment and follow-up visit. Radiologists in charge of graft occlusion determining will also be blinded to the randomized allocation of each vein graft.

Procedure for unblinding if needed {17b}

Not applicable.

Data Collection And Management

Plans for assessment and collection of outcomes {18a}

A summary of the follow-up is shown in Table 1

A postoperative questionnaire regarding leg wound condition is filled before patient discharge and during follow-up visit. Visual Analogue Scale [19] is used for evaluation of leg pain, and other wound healing

disturbances including surgical debridement or re-suture, hematoma, persistent exudation, numbness of the skin, and leg edema were recorded. The Questionnaire and definitions are presented in Additional file 3.

We collect relevant anatomical characteristics, e.g., sites of proximal and distal anastomosis, graft type and quality, proximal lesion stenosis rate, graft flow and pulsation index, application of sequential anastomosis. As to sequential anastomosis, one failure of distal anastomosis will be considered occlusion of the sequential graft. Coordinators and investigators are required to submit complete in-hospital data within 14 days of discharge. The study adheres to a rigorous standard for medical record transmission and data abstraction, similar to the previously published China Patient-Centered Evaluative Assessment of Cardiac Events (China PEACE)-Retrospective Acute Myocardial Infarction Study and the Percutaneous Coronary Intervention Study [20, 21].

Clinic visits are required. Study coordinators will telephone participants to recall the scheduled date of return to the hospital. The 100 randomized patients will undergo predefined clinical follow-ups at 3 months and 12 months post-procedure. Two designated attending surgeons will inspect patients' leg wound healing at 3-month visit. MSCTA is to be performed, and image discs will be assessed by a central Core Laboratory. The results of MSCTA are independently reviewed by 2 radiologists blinded to patients' randomized allocation. Discrepancies in occlusion judgement are reviewed by a third radiologist and resolved by consensus. At each follow-up visit, all current medications and events since the last visit are recorded and compared between the two groups. A full list of classifications of data content can be seen in Additional file 4.

Table 1
Follow-up schedule

	Pre-op	Intra-op	6th day Post-op	3-month clinic visit (+ 1 m)	12-month clinic visit (+ 3 m)
Baseline characteristics	√				
Clinical history	√				
Physical exam	√			√	√
Medications	√		√	√	√
Operation details		√			
Graft quality assessment		√			
Leg wound assessment			√	√	
MSCTA				√	√
Clinical events				√	√

Plans to promote participant retention and complete follow-up {18b}

1. The 3-month and 12-month follow-ups are routine practice of the hospital. The study does not prescribe extra costs of patients.

2. The investigators and study coordinators will keep in close touch with all the participants by establishing a Wechat group chat, which is the most popular mobile social software in China.

Data management {19}

A web-based and paperless data submission system (<http://ccsr.cvs-china.com>) for the study has been set up. For web-data transmission, a high-level secure socket layer is adopted. For in-hospital data collection, 12 modules have been set (preoperative saphenous vein screening, patient basic information, preoperative risk factors, cardiovascular presentation, tests and examinations, general information of operation, record of CABG, post-operative complications, preoperative medications, medication prescriptions at discharge, 3-month follow-up results and 12-month follow-up results) with over 300 items. Double-entry of data is required by designated study coordinators. All web-based records will be exported monthly for range checks of values by investigators.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

Not applicable. No biological specimens will be collected.

Statistical Methods

Statistical methods for primary and secondary outcomes {20a}

The trial data will be analyzed on an intention-to-treat basis of patients included in the groups assigned to randomization, irrespective of future management and events. Any intentional or unintentional deviation from the study protocol should be documented and explained in the data collecting system. Demographic, clinical variables, in-hospital death, postoperative complications, follow-up death, and MACCE will be summarized as means (SDs) for continuous and counts (percentages) for categorical variables. A generalized-estimate-equation model will be used to estimate treatment effects on the graft level wound complications and occlusion analysis, to account for the cluster effect of grafts from the same patient. A P value of less than 0.05 will be considered as statistically significant for all analyses.

Interim analyses {21b}

Interim analysis will be carried out when 50% of subjects finish their scheduled follow-up, according to the charter of the data safety monitoring board (DSMB).

Methods for additional analyses (e.g. subgroup analyses) {20b}

Considering leg wound complications may be a function of baseline characteristics. We plan to compare the odds ratio of leg wound complications based upon different risk groups, such as male vs. female, BMI<30 vs. BMI≥30, diabetic vs. nondiabetic, smoking vs non-smoking, with vs. without peripheral artery disease. We also plan to conduct subgroup analysis by comparing odds ratios of graft occlusion and different vein graft qualities. An intraoperative questionnaire (see Additional file 3) for evaluation of the graft quality is required to be answered by the operators. Graft quality is stratified as good, moderate, or poor, according to the presence of side branch tears, inflammatory wall thickness, or signs of varicosity [22]. Subgroup analysis will be performed using generalized-estimate-equation models.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

We consider the missing data of the primary endpoint to be minimal. If any, missing data will be handled via worst observation carried forward (WOCF).

Plans to give access to the full protocol, participant level-data and statistical code {31c}

Not applicable.

Oversight And Monitoring

Composition of the coordinating centre and trial steering committee {5d}

The role of the trial steering committee (TSC) is to monitor and supervise the progress of the study. Members of TSC are listed in Table 3. The TSC will meet prior to the start of the trial and then once every two weeks.

Table 3
Trial Steering Committee membership

Name	Role	Title	Affiliation
Professor Shengshou Hu	Co-Principal Investigator Lead Surgeon Trial Advisor	President of Fuwai Hospital. Professor of cardiovascular surgery	Fuwai Hospital
Professor Xianqiang Wang	Co-Principal Investigator	Professor of cardiovascular surgery	Fuwai Hospital
Professor Liqing Wang	Surgeon	Professor of cardiovascular surgery	Fuwai Hospital
Yang Wang. PhD	Statistician Trial Advisor	Director of Statistics Medical Research & Biometrics Center	Fuwai Hospital
Dr Meice Tian	Principal Investigator	Surgeon of Fuwai Hospital. Professor of cardiovascular surgery	Fuwai Hospital
Dr Zhihui Hou	Radiologist	Deputy director of Department of Radiology	Fuwai Hospital

Composition of the data monitoring committee, its role and reporting structure {21a}

An independent data safety monitoring board (DSMB) is established before the start of recruitment. There is no pre-specified stopping rule for the primary efficacy endpoint, so there is no need to adjust the type I error rate. The DSMB members will suggest whether the study should be stopped due to unexpected risk of patients. If the safety signal is acceptable, the study will continue to the planned recruitment number and data analysis will be built on the entire population. Members of DSMB are listed in Table 4

Table 4
Data Safety Monitoring Board membership

Name	Role	Title	Affiliation
Professor Hansong Sun	Chairman	Professor of cardiovascular surgery	Fuwai Hospital
Professor Jing Li	Vice-chairman	Director of Clinical Trial Center	Fuwai Hospital
Professor Jian Zhang	Vice-chairman	Consultant Cardiologist	Fuwai Hospital
Professor Wei Li	Statistician	Director of Medical Research & Biometrics Center	Fuwai Hospital

Adverse event reporting and harms {22}

An independent clinical events committee (CEC) will review adverse events during the study and adjudicate them to ensure the events comply with the pre-specified definitions. All events will be independently adjudicated by two members of CES. Discrepancies in event judgement will be reviewed by a third committee member and resolved by consensus. CEC members will be blind to the knowledge of which arm of the trial the vein segments are in.

Frequency and plans for auditing trial conduct {23}

Not applicable.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

Not applicable.

Who will take informed consent? {26a}

Study investigators will take informed consent from patients after individual discussion about the nature of the procedure to be conducted.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

Not applicable.

Confidentiality {27}

Only study investigators, coordinators and network technicians have access to the patient information. Exported records will use encryption to avoid unauthorized reading.

Availability of data and materials {29}

Not applicable.

Provisions for post-trial care {30}

The investigators will touch with participants regularly through telephones, and continue to follow-up these patients at 5 years and 10 years postoperatively.

Dissemination plans {31a}

Not applicable.

Discussion

The optimum segment of saphenous vein graft in CABG about concerning the safety and efficacy by No-Touch technique is undetermined. Previous studies showed that the incidence of leg wound complications after CABG by open harvesting technique was from 3–25% [23]. According to our institutional database, major leg wound complications (defined by leg wound that had failed to respond to conservative treatment and required subsequent surgical interventions such as debridement and re-suture) after No-Touch vein harvesting was 6.2%, which was relatively low in literature findings. However, none of these results discriminated against wound complications between proximal and distal segments of the lower limb. Therefore, the choice of site for saphenous vein conduits harvesting was based on individual experience rather than evidence from researches.

The No-Touch saphenous vein harvesting technique has been proved to reduce vein graft occlusion after CABG [8, 12, 13, 24]. However, no studies were conducted to discriminate effects on different segments of veins harvested by this novel technique. This is the first study comparing the incidence of leg wound complications as well as SVG occlusion between proximal and distal segments of saphenous veins harvested by No-Touch technique.

Graft occlusion will be assessed as secondary endpoints in our study. Differing from previous studies, CT angiography will be used in our trial for occlusion assessment instead of coronary angiography. The decision of using of CTA during follow-ups was made in light of patient compliance, as interventional coronary angiography is much more traumatic and costly, and too many cases of refusal or loss of contact from the patients will greatly bias the result.

One limitation of this study is the small sample size. As a pilot trial, the primary consideration for the sample size is the ability to notify the feasibility of a full-scale study. The comparison of a total of 200 vein grafts will help to establish preliminary evidence for the raised questions. Another limitation is that ultrasound mapping is not adopted, which is reported to be helpful in preventing unnecessary incision and large skin flaps [8, 16]. However, it is not commonly used in clinical practice in China and according to our experience, well-trained surgeons with sufficient qualifications can harvest veins with the No-Touch technique without this instrument.

This pilot study will serve to establish preliminary evidence for the decision making of precise vein graft conduit choice. Inherently, this surgical-based clinical trial is confronted with a number of challenges, that investigators must consider when designing the trial protocol. Although the follow-up of 1-year is not very long, we may consider follow-up studies with extended follow-ups of up to 10 years. Larger scale clinical trials are being warranted in the future.

Trial Status

Enrollment of patients is planned to start from March 1st, 2020. Completion of recruitment is expected by late June, 2020 with results of the primary endpoint becoming available in August, 2020.

Abbreviations

CABG

coronary artery bypass graft

SVG

saphenous vein graft

MSCTA

multi-slice computed tomography angiography

MI

myocardial infarction

CES

clinical events committee

IWR

Interactive Web-based Response

TSC

trial steering committee

DSMB

data safety monitoring board

Declarations

Ethics approval and consent to participate {24}

The study was approved by the Ethic Committee of Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (Approval NO. 2020-1324). Approval by Ethics Committee can be found in Additional File 5.

Consent for publication {32}

Not applicable. No personal data included in the paper.

Availability of data and materials {29}

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding {4}

This study is supported by the Youth Fund of National Center for Cardiovascular Disease, China & Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College. The sponsors did not

participate in the design and will not participate in the implementation of the study, including the collection, management, analysis, interpretation of the data and the preparation of the manuscript. Funding documentation can be found in Additional File 6.

Authors' contributions {31b}

MT: designer of the study and coordination and drafted the manuscript

SH: participated in the design and co-ordination and helped to draft the manuscript

XW: participated in the design and co-ordination and helped to draft the manuscript

SL: participated in the design and statistical analysis helped to draft the manuscript

LW: participated in the design and helped to draft the manuscript

All authors read and approved the final manuscript.

Acknowledgements

The authors thank Dr. Yiyao Shi for editing the manuscript.

Authors' information (optional)

Not applicable.

References

1. Klima U, Elsebay AA, Gantri MR, Bangardt J, Miller G, Emery RW. Computerized tomographic angiography in patients having eSVS Mesh(R) supported coronary saphenous vein grafts: intermediate term results. *J Cardiothorac Surg.* 2014;9(1):138-43.
2. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal mammary artery graft on 10-year survival and other cardiac events. *N Engl J Med.* 1986;314(1):1-6.
3. Cameron A, Davis KB, Green G, Schaff HV. Coronary bypass surgery with internal-thoracic-artery grafts—effects on survival over a 15-year period. *N Engl J Med.* 1996;334(4):216-9.
4. Fitzgibbon GM, Kafka HB, Leach HA, et al. Coronary bypass graft fate and patient outcome: angiographic follow-up of 5,065 grafts related to survival in reoperation in 1,388 patients during 25 years. *J Am Coll Cardiol.* 1996;28:616-26.
5. Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA Guidelines for CABG surgery: executive summary and recommendations. *Circulation.* 1999;100:1464-80.
6. Patrick W. Serruys, Marie-Claude Morice, A. Pieter Kappetein, et al. Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease. *N Engl J Med.* 2009;360(10):961-72.

7. Michael E. Farkouh, Michael Domanski, Lynn A. Sleeper, et al. Strategies for Multivessel Revascularization in Patients with Diabetes. *N Engl J Med.* 2012;367(25):2375-84.
8. Samano N, Geijer H, Liden M, Fremes S, Bodin L, Souza D. The no-touch saphenous vein for coronary artery bypass grafting maintains a patency, after 16 years, comparable to the left internal thoracic artery: A randomized trial. *J Thorac Cardiovasc Surg.* 2015;150(4):880-8.
9. Campeau L, Enjalbert M, Lesperance J, et al. The relation of risk factors to the development of atherosclerosis in saphenous vein bypass grafts and the progression of disease in the native circulation: a study 10 years after aortocoronary bypass surgery. *N Engl J Med.* 1984;311:1329-32.
10. Bourassa MG. Fate of venous grafts: the past, the present and the future. *J Am Coll Cardiol.* 1991;5:1081-3.
11. Souza D. A new no-touch preparation technique. Technical notes. *Scand J Thorac Cardiovasc Surg.* 1996;30(1):41-4.
12. Domingos S. R. Souza, Michael R. Dashwood, Janice C. S. Tsui, et al. Improved Patency in Vein Grafts Harvested With Surrounding Tissue: Results of a Randomized Study Using Three Harvesting Techniques. *Ann Thorac Surg.* 2003;73(1189-95).
13. Domingos S. R. Souza, Benny Johansson, Leif Bojö, et al. Harvesting the saphenous vein with surrounding tissue for CABG provides long-term graft patency comparable to the left internal thoracic artery: Results of a randomized longitudinal trial. *The Journal of Thoracic and Cardiovascular Surgery.* 2006;132(2):373-8.
14. Umberto Benedetto, Gianni D Angelini. Saphenous Vein Graft Harvesting and Patency: Still an Unanswered Question. *The Journal of Thoracic and Cardiovascular Surgery.* 2016;152(5):1462-3.
15. Papakonstantinou NA, Baikoussis NG, Goudevenos J, Papadopoulos G, Apostolakis E. Novel no touch technique of saphenous vein harvesting: Is great graft patency rate provided? *Ann Card Anaesth.* 2016;19(3):481-8.
16. Souza D, Samano N. Long-term patency versus leg wound healing in coronary artery bypass surgery: Surgical aspects of the no-touch harvesting technique. *J Thorac Cardiovasc Surg.* 2016;151(1):276.
17. Glenn N. Levine, Eric R. Bates, John A. Bittl, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery. *Circulation.* 2016;134(10):e123-e55.

18. FitzGibbon GM, Burton JR, Leach AJ. Coronary bypass graft fate: angiographic grading of 1400 consecutive grafts early after operation and of 1132 after one year. *Circulation*. 1978;57(6):1070-74.
19. Nicolas Bourdel, Joa~o Alves, Gisele Pickering, Irina Ramilo, Horace Roman, Michel Canis. Systematic review of endometriosis pain assessment: how to choose a scale? *Human Reproduction Update*. 2014;21:No.1 pp. 136–52.
20. Dharmarajan K, Li J, Li X, Lin Z, Krumholz HM, Jiang L. The China Patient-Centered Evaluative Assessment of Cardiac Events (China PEACE) Retrospective Study of Acute Myocardial Infarction: Study Design. *Circ Cardiovasc Qual Outcomes*. 2013;6(6):732-40.
21. Li J, Dharmarajan K, Li X, Lin Z, Normand SL, Krumholz HM, et al. Protocol for the China PEACE (Patient-centered Evaluative Assessment of Cardiac Events) retrospective study of coronary catheterisation and percutaneous coronary intervention. *BMJ open*. 2014;4(3):e004595.
22. Inderbitzin DT, Bremerich J, Matt P, Grapow MT, Eckstein FS, Reuthebuch O. One-year patency control and risk analysis of eSVS®-mesh-supported coronary saphenous vein grafts *J Cardiothorac Surg*. 2015;10:108.
23. Wing Kuk Tim Au, Shiu Wah Chiu, Man Ping Sun, et al. Improved Leg Wound Healing With Endoscopic Saphenous Vein Harvest in Coronary Artery Bypass Graft Surgery: A Prospective Randomized Study in Asian Population. *J Card Surg*. 2008;23(6):633-7.
24. Franz-Josef Neumann, Miguel Sousa-Uva, Anders Ahlsson, et al. 2018 ESC/EACTS Guidelines on Myocardial Revascularization. *Eur Heart J*. 2019;40(2):87-165.

Figures

TIMEPOINT**	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			Close-out
	1 day pre-operative	0	6 days after surgery	3 months after surgery	12 months after surgery	01 September 2021
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
<i>Proximal Group</i>			←—————→			
<i>Distal Group</i>			←—————→			
ASSESSMENTS:						
<i>Basic information, risk factors, presentation of CAD diseases, laboratory tests before and after surgery, angiographic findings, general information of surgery, in-hospital outcomes, pre-operative medications</i>	X	X				
<i>Leg wound condition 6 days after surgery</i>			X			X
<i>Leg wound condition 3 months after surgery 3-month and 12-month graft occlusion Clinical events</i>			X	X	X	X

Figure 1

Participant timeline of the study

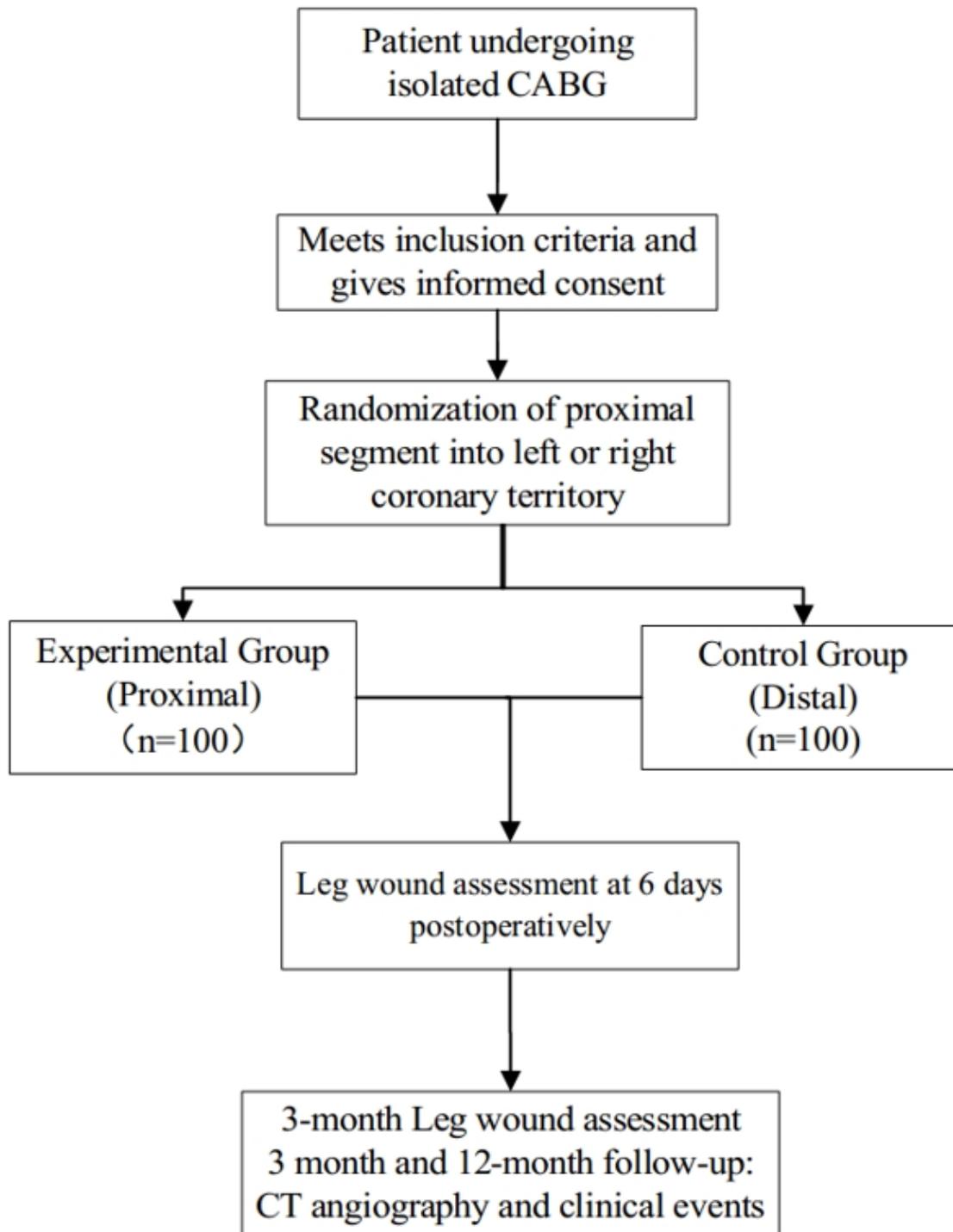


Figure 2

Flowchart of the study

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Additionalfile4.pdf](#)
- [Additionalfile2.pdf](#)
- [Additionalfile1.pdf](#)
- [Additionalfile3.pdf](#)