A cross-sectional study and a novel screening survey for radial artery assessment in surgical coronary revascularisation.

PROTOCOL

DATE 09/04/2024

CHIEF INVESTIGATOR – Vincenzo De Franco

List Investigators – Dr Naim Abdulmohdi
Dr Edward Purssell
Dr Dan Robbins

Investigation Sites: Royal Papworth Hospital; Royal Brompton Hospital

Principal Investigator: Vincenzo De Franco

Protocol Identification Number: P00258

Date of Protocol: 20th November 2023

Review Date: 9th April 2024

Protocol Version Number: 4.0

Trial Sponsor: Royal Papworth Hospital (R&D Study Registration Number: P03105)

Contents

TRIAL OVERVIEW

TRIAL OVERVIEW

1. Trial Overview

Primary Research Question

What factors influence the diagnostic accuracy of radial artery assessment in patients undergoing surgical coronary revascularisation?

Study Design

A multi-centre cross-sectional study to investigate the validity of radial artery assessment techniques in adults' people with ischaemic heart disease undergoing surgical coronary revascularisation with their radial artery being selected as an autologous graft conduit. Maximum expected duration of subject participation is 12 weeks.

Primary Outcome

Measure the sensitivity, specificity, negative and positive predictive values of the Modified Allen test (+/- pulse-oximetry), the Barbeau Test and ultrasonography examination.

Secondary Outcome(s)

- Measure the morphological and physiological quality of radial arteries through a validated structured questionnaire (Radial Artery Quality Evaluation Survey).

- Measure the patients' finger movements, cold tolerance sensitivity and tactile/touch perception through an ordinal symptoms scale (Follow-up Radial Artery Harvesting Scale).

Rationale

The study will explore the accuracy of radial artery (RA) assessment in people with ischaemic heart disease (IHD) undergoing coronary artery bypass grafting (CABG). IHD affects 2.3 million people in the United Kingdom and is responsible for over 65,000 deaths per year. CABG results in the most effective therapeutic strategy for multi-vessel IHD while the RA is one of the preferred graft conduits.
A comprehensive peri-operative RA assessment is essential to ensure disease-free RA segments are selected, precluding surgical complications such as hand ischaemia and graft failure. Whilst numerous screening tests are documented, their validity (diagnostic accuracy) is under debate. The literature is lacking evidence regarding the use of a standardised protocol for RA screening. The patients' experiences are seldom considered while surgical complications still occur. The expert opinion of professionals involved within the RA assessment and harvesting, generally the surgical care practitioners (SCP), is also not explored.
The intended research will provide an in-depth understanding of how assessment techniques inform RA harvesting in patients undergoing CABG, calibrating clinical decision and improving surgical practice. The research will uplift the SCP profession and address knowledge gaps, resulting in disciplinary and academic contributions.

Schedule of Events

Patients taking part in the study will receive an assessment of the arterial forearm circulation from their non-dominant upper extremity through the observations below.

- **Pre-operative observations**. Before surgery (in the ward environment after the patient is being admitted or whilst patient in the anaesthetic room) the forearm blood circulation is measured through the measures 1, 2, 3 and 4 to inform decision to surgically expose the RA.

1) Modified Allen Test (MAT). Instruct the patient to clench his/her wrist while the examiner occlude with three fingers the patient's ulnar and radial arteries; instruct the patient to unclench his/her wrist; release the ulnar artery. The MAT result is negative or positive considering in how long the palm flushes:

≤5 seconds negative MAT; good collateral hand circulation (suggesting harvestable radial artery)
>5 seconds positive MAT; poor collateral hand circulation (suggesting not-harvestable radial artery)

2) Pulse-oximetry guided MAT. A pulse-oximetry probe is positioned on the patient's index finger; both radial and ulnar arteries are occluded by the examiner (with three fingers) until flattening of pulse waveform is obtained. Pressure on the ulnar artery is released and the result of the assessment is calculated considering in how long the pulse waveform returns to baseline:
≤5 seconds negative result (suggesting harvestable radial artery)
>5 seconds positive result (suggesting not harvestable radial artery)

3) Barbeau Test. A pulse-oximetry probe is positioned on the thumb; the radial artery is then compressed by the examiner, and the pulse waveform is analysed for up to 120 seconds, providing four patterns of ulnar-palmar patency:

a. No damping of the pulse tracing immediately after compression (suggesting harvestable radial artery)

b. Damping of the pulse tracing (suggesting harvestable radial artery)

c. Loss of the pulse tracing, followed by recovery within 120 sec (suggesting harvestable radial artery)

d. Loss of the pulse tracing, without recovery within 120 sec (suggesting not harvestable radial artery).

4) Ultrasonography examination of the forearm arteries. The radial artery is surgically exposed (negative result) when the following apply:

a. ulnar artery inner diameter ≥2 mm

b. radial artery inner diameter ≥2 mm

c. absence of radial artery intraluminal calcifications and plaques.

- **Intra-operative observations**. The radial artery is surgically harvested when the following apply:
A) The radial artery morphological and physiological characteristics (diameter, calcifications, presence of pulsatile flow), quality of harvesting technique and surgical accessibility are considered satisfactory, good or optimal. Measures are taken through a structured questionnaire (Radial Artery Quality Evaluation Survey) currently being validated through a Delphi study.

B) Oxygen saturation reading (SpO_2) from the thumb through pulse-oximetry remains at 95% or above when an occlusive atraumatic clamp is applied on the mobilised RA.

- **Post-operative observations**. Patients' finger movements, cold tolerance sensitivity and tactile/touch perception is measured through an ordinal symptoms scale (Follow-up Radial Artery Harvesting Scale) at post-operative day 2-5 and at follow-up appointment (3-6 weeks after surgery). Bilateral comparison between hands and forearms will be undertaken. Tactile perception is assessed through Semmes–Weinstein monofilaments (single touch). Cold sensitivity is assessed through the use of ice-pack.
The Follow-up Radial Artery Harvesting Scale was developed from a verbal rating scale (VRS) questionnaire documented in the literature and considered an accurate rating method for pinpointing the intensity of cold sensation. The VRS questionnaire was re-adapted to appreciate people's post-operative experience with their finger movements, cold sensitivity and tactile/touch perception of their forearm and will be used in this cross-sectional study. A Patient and Public Involvement and Engagement (PPIE) was undertaken on the Follow-up Radial Artery Harvesting Scale, gaining feedback from 9 adult cardiac patients from a clinical institution from the Greater London region. The PPIE resulted in improving readability and clarity of the questions and answers included in the scale.

2. Patient Recruitment Criteria

Study Population

- Sixty-nine patients from two cardio-thoracic clinical institutions from the East of England and Greater London regions.
- Cardiovascular sample group.
- Recruitment period: April 2024 – February 2025.
- End of study: 31st March 2025.
  The end of study is the date of the completion of any follow-up monitoring and data collection described in the protocol.

Inclusion

- Diagnosis of ischaemic heart disease / coronary artery disease
- Age ≥ 18 years
- Male and Female participants
- Elective or urgent coronary artery bypass graft (CABG) surgery and radial artery (RA) harvesting, with the RA being selected as one of the autologous graft conduits for the coronary revascularisation.

Exclusion

- Paediatric patients
- Emergency CABG
- Patients lacking capacity to consent
- Patients with limited understanding of English language and non-English-speaking patients requiring use of interpreters

Recruitment

- The planned recruitment target rate is:
  - April – August 2024: *34 patients*
  - September 2024 – February 2025: *35 patients*

  The recruitment rate has been calculated based on evidence from retrospective data.
- *Recruitment review dates: June 2024, August 2024, November 2024, February 2024.*

Section 3. Sample Size and Data analysis

Sample Size

- A consecutive sampling method will be adopted for the recruitment of study participants. The minimum required number of participants to test and verify research hypotheses is sixty-nine patients (N=69). An adaptive trial design will be implemented: at quarterly assessment points the statistical power is assessed and the remaining sample size required is updated accordingly.

Statistical Analysis

- Sample size calculation was undertaken using G*Power software (version 3.1) using Chi-squared Test (x^2) and adopting optimal effect size (w=0.4) and power (0.8).

4. Consent Process and Visit Schedule

Visit 1

- Potential participants will firstly be approached by clinicians within the healthcare team who is directly involved in delivering care and treatment to the patients. Clinicians will refer potential participants to the main investigator who will approach them for consenting purposes to take part in this study.

Follow-Up Visits

- Each patient will be assigned a study number; the study numbers will be allocated sequentially starting at 001.
- Visits should be scheduled and performed according to table 1.
- Trial specific procedures *versus* routine procedures are detailed in table 2 *if appropriate to the study*. The trial specific procedures will be performed after written informed consent has been obtained. The procedures that can be performed prior to consent being obtained are detailed in table 3 *(if appropriate)*.

Table 1 Visit Schedule

Visit Number	**Visit n**	**Visit n+1**	**Visit n+2**
Time interval of Visit	week 0-3	week 0-3	week 4-12
Consent	**X**		
Pre-operative observation (Modified Allen Test +/- pulse-oximetry)		**X**	
Pre-operative observation (Barbeau Test)		**X**	
Pre-operative observation (Ultrasonography examination of forearm arteries)		**X**	
Intra-operative observation (oxygen saturation reading)		**X**	
Use of Questionnaire (Radial Artery Quality Evaluation Survey)		**X**	
Post-operative observation (Follow-up Radial Artery Harvesting Scale)			**X**

Table 2 Trial Specific Procedures *versus* Routine Procedures

Routine Investigations	**Study Specific Procedures**
Modified Allen Test +/- pulse-oximetry	Seeking Consent
Barbeau Test	Use of Questionnaire (Radial Artery Quality Evaluation Survey) currently under validation
Ultrasonography examination of forearm arteries	Use of Follow-up Radial Artery Harvesting Scale
Intra-operative oxygen saturation reading	

Informed Consent Procedure

- Patients will receive written and verbal information about the trial.
- Written informed consent will be obtained by a member of the trial team after a suitable time has elapsed during which the patient has had time to read the information sheet, consider the trial and ask any questions (Consent form). The Investigator must explain to each patient the nature

of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits involved and any discomfort it may entail (*Ref. International Conference of Harmonisation of Good Clinical Practice (ICH/GCP)5 4.8.7*

- The ultimate responsibility for obtaining written informed consent lies with the Investigator but this responsibility may be delegated to a suitably trained, and experienced person.
- Prior to the patient's participation in the study, the written informed consent form must be signed and personally dated by the patient and by the clinician who conducted the informed consent discussion (*Ref. ICH/GCP 4.8.8*). Each box at the end of each statement on the consent form must be signed by the patient.
- Each subject must be informed that participation in the study is voluntary and that he/she may withdraw from the study at any time and that withdrawal of consent will not affect his/her subsequent medical treatment (*Ref. ICH/GCP 4.8.10*).
- A copy of the informed consent document will be given to the patient (*Ref. ICH/GCP 4.8.11*). One copy will be filed in the patient's hospital case notes and a copy filed in the Trial Management File by the Clinical Research Nurses.
- The Clinical Research Nurse will ensure that the patient does not have any trial specific procedures prior to giving informed consent.
- If a patient withdraws their consent a line will be drawn diagonally through the consent form and labelled 'consent withdrawn' and signed and dated by a member of staff (please refer to Section 8 re labelling of case notes).

5. Follow-up Visits and Travel Expenses

Follow up Visits

The follow up visits will be in accordance with the visit schedule in table 1. The patients will be seen by the Researcher or Clinicians directly involved in the primary care for the patients for conducting the above presented observations. Clinicians directly involved in the patient care include Surgical Care Practitioners, Cardiothoracic Specialist Registrars and Advanced Nurse/Clinical Practitioners.

Travel Expenses

Participants are not required to travel to take part in the study as data will be collected during their hospital stay and during their pre- and/or post-operative follow up appointments to the clinical institutions.

6. Data Collection

Data Collection Form Completion

- The Investigator will ensure the accuracy, completeness, legibility and timeliness of the data recorded in the data collection forms (DCFs) and in all required reports to the Sponsor, R&D and REC.

Source Documentation

- The investigator must maintain source documents (patient's hospital case notes) for each patient in the study, consisting of all demographic and medical information, including laboratory data, and radiology results. A copy of the consent form and patient information sheet will also be filed in the patient's case notes. All information in the DCFs, apart from the questionnaires, must be traceable to and consistent with the source documents in the patient's hospital case notes (Ref. ICH/GCP 4.9.2).

Errors and Corrections

- Any change or correction to the DCF will be dated, initialled, and explained (if necessary) and should not obscure the original entry.

Storage of Documents

- DCFs will be kept in a locked filing cabinet or a locked room.

Retention of Documents

- All study documentation will be stored for 15 years after the last patient has completed their last visit.

Monitoring and Audit

- Upon request of the monitor, auditor, Sponsor, R&D, REC, MHRA or other regulatory authority, the Investigator will make available for direct access all requested study-related records.

The project data will be monitored by the Research Officer monthly. The first two patients from each participant site will be monitored in full. Thereafter fifty percent of the data will be monitored every month during the recruitment phase. After recruitment is complete ten percent of the data will be monitored.

7. Adverse and Serious Adverse Events

The definition of an adverse event is: 'Any untoward medical occurrence in a patient which does not necessarily have a causal relationship with this treatment'. This includes 'any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the study drug'. This may include, for example, a cold or an accident.

The definition of a serious adverse event is one that fulfils at least one of the following criteria:

- Is fatal- results in death
- Is life threatening
- Requires inpatient hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability/incapacity

OR

- Is a congenital anomaly/birth defect

Recording and Reporting

- No adverse and serious adverse events are predicted to occur for participants enrolling into this study.
- The chance of participants being identified from dissemination represents a risk of taking part in a research study. Every attempt will be made to avoid the identification of participants. Identity will be redacted from both participant information sheets and consent forms and no participants' details released to safeguard confidentiality.
- A general introduction to the research study (referral) will be made by someone else (NHS staff, acting as gatekeeper) to avoid pressuring participants best to participate.
- Agreement to participate in the study does not affect participant's legal rights.
- All research staff in contact with patients are responsible for noting adverse events that are reported by the patient and making them known to the Principal Investigator.
- At each visit or study assessment, adverse events that have occurred since the previous visit should be elicited from the patient. The event will be detailed in the patient's notes, as source document verification, including the start date (if known) and the end date.
- The action taken regarding the study procedure should be documented.
- Document any treatment/medication given for the event, including the dates the treatment/medication was commenced and the date it was stopped/changed, if applicable (an example of an AE form is in section 10 of the site file section). Documenting of adverse events is the responsibility of the Principal Investigator, Co-Investigator and Clinical Research Nurse/Assistant.
- Events, which are ongoing at the final study visit, should be followed up as clinically indicated.
- All serious adverse events (SAEs) will be documented as above using the appropriate reporting documentation in section 10 of the site file documents.
- All Unexpected SAEs should be reported to the hospital R&D department and may be require analysis through the hospital incident reporting system.
- Expected SAEs need to be reported to the Main REC in the annual REC report; the REC who performed the locality assessment does not need to be informed.
- Store all completed SAE forms with the patient's study documentation.

8. Amendments

Substantial amendments will be submitted to the Research Ethics Committee for review and approval.

Amendment Log

Revision	Section reviewed
1.	
2.	
3.	