


BMJ Open Utility of a smartphone application in assessing palmar circulation prior to radial artery harvesting for coronary artery bypass grafting: rationale and design of the randomised CAPITAL iRADIAL-CABG trial

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To cite: Goh CY, Parlow S, Di Santo P, *et al.* Utility of a smartphone application in assessing palmar circulation prior to radial artery harvesting for coronary artery bypass grafting: rationale and design of the randomised CAPITAL iRADIAL-CABG trial. *BMJ Open* 2022;**12**:e055580. doi:10.1136/bmjopen-2021-055580

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2021-055580>).

Received 10 August 2021
Accepted 09 March 2022



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ABSTRACT

Introduction There is emerging evidence supporting the use of the radial artery (RA) as a preferred secondary conduit for coronary artery bypass grafting (CABG) as it is associated with higher rates of graft patency at 5 years when compared with saphenous vein grafts (SVG). The modified Allen's test (MAT) is traditionally regarded as the standard of care in the assessment of ulnar artery (UA) patency prior to RA harvesting. Unfortunately, due to high false-positive rates, a substantial number of pre-CABG patients are found to have an abnormal MAT despite normal UA patency, resulting in inappropriate exclusion from RA harvesting. The SVG is generally used in its place when this occurs, resulting in potentially lower rates of long-term graft patency.

Methods and analysis The CAPITAL iRADIAL-CABG trial is currently enrolling participants 18 years of age or older undergoing CABG for whom the treating physician is considering the use of an RA conduit. Eligible patients will be randomised in a 1:1 fashion to MAT or smartphone-based photoplethysmography application assessment to assess collateral palmar circulation prior to RA harvesting. The primary outcome of the trial is the use of the RA as a conduit during CABG. The primary safety outcome is postoperative palmar ischaemia as determined by clinical assessment or requirement of vascular intervention. Secondary outcomes include vascular complications, early graft failure, need for rescue percutaneous coronary intervention during the index hospitalisation and a composite cardiovascular outcome of myocardial infarction, stroke and cardiovascular death prior to discharge from hospital. A total of 236 participants are planned to be recruited.

Ethics and dissemination The study was approved by the Ottawa Heart Science Network Research Ethics Board (approval number 20180865-01H). The study results will be disseminated via conference presentations and peer-reviewed publications.

Trial registration number NCT03810729.

Strengths and limitations of this study

- CAPITAL iRADIAL-CABG is the first randomised trial to use a smartphone application to evaluate collateral palmar circulation as part of pre-coronary artery bypass grafting (CABG) surgical assessment.
- If proven safe and efficacious, smartphone assessment might be considered as an evidence-based approach prior to radial artery (RA) harvesting in CABG.
- This could result in increased use of the RA which has been associated with improved patient outcomes.
- A potential limitation of the study is the comparison to the modified Allen's test, which despite being the clinical standard, is a test with poor diagnostic accuracy.

INTRODUCTION

Coronary artery bypass grafting (CABG) is a common form of coronary revascularisation used to treat obstructive epicardial coronary artery disease. Traditionally, CABG is performed using the left internal thoracic artery and additional conduits include the saphenous venous graft (SVG), radial artery (RA) and/or the right internal thoracic artery. Most commonly, SVGs are used; however, SVGs frequently develop progressive atherosclerosis, leading to 50% graft failure 10 years following the initial operation.¹

An increasing body of evidence has emerged supporting the use of the RA as a preferred secondary conduit as it is associated with higher graft patency rates at 5 years when compared with the SVG.²⁻⁴ Although

most randomised controlled trials assessing this have been individually underpowered to demonstrate a significant difference in outcomes,^{3 5 6} a recent large pooled meta-analysis demonstrated a significant reduction in adverse cardiac events, with a higher rate of graft patency at 5 years in RA conduits when compared with SVGs.⁷

Prior to harvesting the RA for bypass grafting, guidelines recommend an assessment of ulnar artery (UA) patency to ensure sufficient collateral circulation in the palmar arch.⁸ The gold standard diagnostic tool for determining UA patency and collateral competency is colour Doppler ultrasound imaging,⁹ however the preoperative utilisation of this modality remains labour and resource intensive and is seldom feasible in routine clinical practice. More commonly, a bedside assessment using the modified Allen's test (MAT) is regarded as the clinical standard. Due to low specificity with high false-positive rates,⁹ a substantial number of pre-CABG patients with normal UA patency are found to have an abnormal MAT, resulting in inappropriate exclusion from RA harvesting, which may impact longer-term outcomes.

A recent randomised controlled trial demonstrated that a point of care smartphone-based application which uses photoplethysmography was diagnostically superior to MAT in assessing UA patency prior to RA access for coronary angiography.¹⁰ In the proposed randomised trial, we hypothesise that the use of smartphone-based photoplethysmography application (SBPA) would result in increased RA use when compared with the clinical standard in patients undergoing CABG.

METHODS AND ANALYSIS

Trial objectives and overview

The primary objective of this study is to evaluate the efficacy and safety of SBPA in the assessment of UA patency prior to RA harvesting in CABG. The trial began participant recruitment in May 2019.

Screening, eligibility and consent

Patients who are scheduled to undergo CABG surgery in our institution will be screened. Eligible patients who are greater or equal to 18 years of age for whom the treating physician is considering the use of an RA conduit will be recruited. Patients with haemodynamic instability, need for emergent CABG (such as non-resolving chest pain or ST-elevation myocardial infarction) or previous surgical removal of the RA or UA will be excluded. Patients must be able and willing to provide written informed consent prior to enrolment.

Study interventions

Participants will be randomised in a 1:1 ratio using a computer-generated random sequence to have UA patency assessed with either the MAT or SBPA. Participant allocation will be conducted using sealed envelopes, which will be opened by the investigator performing the assessment. This will be an open-label study, and

both investigators and outcome assessors will remain unblinded to the intervention arm throughout the study period.

Modified Allen's test

Each participant is requested to make a fist for 30s, with the investigator applying pressure over the RA and UA to occlude blood flow. The investigator will then instruct the participant to open the fist. At this point, the participant's hand shall appear pale. The UA is selectively released while the hand is monitored for palmar blush and the time to maximal palmar blush is recorded.

Smartphone-based photoplethysmography

The SBPA will be performed using the Instant Heart Rate application (V.5.282.39090; Azumio). This software was selected as it is commercially available free of charge on Apple and Android platforms and permits direct visualisation of the photoplethysmography tracing. It is also the most downloaded heart rate monitoring application worldwide. The software was originally developed for users to track their own heart rate without specialised equipment. It uses a proprietary algorithm by Azumio that was validated by comparing data collected via the application to electrocardiograms. The software uses the smartphone's camera to emit light through the participant's finger, resulting in colour and brightness changes. This information is then extracted by the camera lens and interpreted as changes in pulse, reflected both as a numerical value (ie, heart rate) and as a photoplethysmography tracing on the screen.

Photoplethysmography readings will be acquired by placing the smartphone camera lens over the pulp of the participant's index finger (a video demonstration of the application can be found at <https://www.cmaj.ca/content/190/13/E380/tab-figures-data>). This is conducted with the participant's hand in a supine position and resting on a firm surface. Readings before and immediately after isolated RA compression for 2min or less will be recorded. These readings will be divided into four categories as previously described by Barbeau *et al*¹¹—A, no damping of pulse tracing immediately after RA compression; B, damping of pulse tracing; C, loss of pulse tracing followed by recovery of pulse tracing within 2min; D, loss of pulse tracing without recovery within 2min. Readings categorised as A or B will be used to indicate UA patency, whereas those characterised as C or D indicate inadequate UA patency.

Each participant will receive an RA conduit during CABG if the assigned test demonstrates UA patency. If the test demonstrates inadequate UA patency, the participant will receive a different conduit for CABG at the discretion of the treating surgeon with no RA harvesting.

Outcomes

The primary outcome of this study will be the use of the RA as a conduit in CABG surgery. The primary safety outcome is postoperative palmar ischaemia as determined

by clinical assessment or requirement of vascular intervention. Secondary outcomes include vascular complications at the site of the RA harvest defined as minor bleeding (ie, haematoma not requiring intervention) or major bleeding (bleeding causing compartment syndrome or requiring ≥ 3 units of blood products, surgical intervention or need for anticoagulant reversal), early graft failure, need for rescue percutaneous coronary intervention during the index hospitalisation and a composite cardiovascular outcome of myocardial infarction, stroke and cardiovascular death prior to discharge from hospital. End-point definitions are available in online supplemental material.

Pre-specified variables such as age, sex, body mass index (BMI) and previous RA access for angiography will be used to determine predictors of poor diagnostic performance.

Data capture and statistical analysis

Data capture

The participant's medical record will be reviewed to obtain data regarding demographic information (eg, sex, age, height, weight, BMI, ethnicity), cardiac risk factors (eg, hypertension, diabetes, smoking status, family history of heart disease, hyperlipidaemia, previous myocardial infarction, previous cardiac intervention or surgery, previous strokes), previous use of the RA as access for coronary angiography or a medical procedure, past medical and surgical history, and current medications.

In addition, information regarding indication for CABG (ie, acute coronary syndrome or elective procedure), the native vessels that are being bypassed and the degree of native vessel occlusion as determined by preoperative invasive coronary or CT angiogram will be recorded. Outcomes from the time of randomisation until the time of discharge from hospital, including bypass conduits used, post-operative complications, further cardiac interventions, cardiovascular mortality, myocardial infarction, ischaemic stroke and bleeding will also be captured. At the time of discharge from hospital the study period will be complete, and there will be no follow-up planned after this point.

Due to the fact that study investigators will need to communicate assigned test results to the treating surgeon, blinding of investigators will not be possible. Outcome assessors will also remain unblinded, as the primary outcome is dichotomous and not susceptible to subjective interpretation.

Statistical analysis

The formal statistical analysis plan will be finalised prior to unblinding of the study database. In brief, all continuous variables will be reported as mean (SD) for normally distributed variable or otherwise as median (IQR). Categorical variables will be described as number (percent). Comparisons between study arms will be performed using χ^2 or Fisher's exact tests, as appropriate. All calculations will be performed using SAS V.9.4 (SAS Institute).

Sample size calculation

Based on the diagnostic accuracy of each method observed in prior studies,^{9 10} it was estimated that the rate of exclusion from RA harvesting using MAT and SBPA to be 20% and 10%, respectively. With 80% power and an alpha of 0.05, it was initially calculated that 200 participants were needed in each arm. A prespecified blinded sample size re-estimation was performed after 75 patients were enrolled. There were 26 (35%) patients across both groups who did not have RA harvest and therefore the sample size was re-estimated to be 118 participants in each arm, using a minimal clinically important relative risk reduction of 40% and allowing for 1% cross-over between groups.

ETHICS AND DISSEMINATION

Ethics approval

The study protocol (20180865-01H, version 2) was approved by the Ottawa Heart Science Network Research Ethics Board (approval number 20180865-01H) and will be conducted in accordance with the Good Clinical Practice standards specified in the Declaration of Helsinki. Informed written consent will be obtained from all participants prior to enrolment. Participants' confidentiality will be strictly maintained in accordance with local and national regulations. The study results will be disseminated via conference presentations and peer-reviewed publications.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Withdrawal from study/early termination

Participants may voluntarily withdraw from the study at any time without penalty or prejudice. Participants may be terminated from the study if they fail to comply with study requirement, need additional treatment that would interfere with the study, or if their treating physicians feels it is in the best interest for them to withdraw.

Adverse event ascertainment

The main adverse event of the trial is post-operative palmar ischaemia. It is determined by clinical assessment, review of the medical chart or requirement of vascular intervention.

DISCUSSION

The CAPITAL iRADIAL CABG study is a novel, randomised study aimed to evaluate the efficacy and safety of SBPA in assessing UA patency prior to RA harvesting in CABG surgery. One recent proof-of-concept study by Di Santo *et al* which compared similar SBPA to MAT demonstrated the SBPA readings had a greater diagnostic accuracy and greater specificity during assessment of UA and RA patency prior to transradial coronary angiography.¹⁰



Given the higher specificity of SBPA, we hypothesise that the utilisation of this software will result in more RA harvesting in patients undergoing CABG.

We selected the MAT as our control intervention given that it is the standard-of-care method for assessing UA patency and we aim to compare SBPA to current real-world practice. Although Doppler ultrasonography has greater diagnostic accuracy, it is not commonly used in the preoperative setting as it is labour-intensive and not easily portable.

The integration of mobile digital and smartphone-based technology in the workplace and community has been far-reaching in the last decade, and has further extended its potential role in healthcare. For example, there are Food and Drug Administration-approved smartphone ECG sensors commercially available in North America, some of which include artificial intelligence-assisted calculations.¹² ‘Digital biomarkers’, developed using smartphone plethysmography and artificial intelligence can now detect diabetes among our population.¹³ The wide-spread availability of smartphone applications, and the free availability of this application, means the current technology could immediately be implemented with near zero cost and increase utilisation for patients undergoing CABG.

Barriers to utilisation of mobile health technology among healthcare providers include concerns regarding cost, ease of use, diagnostic accuracy and difficulty in maintaining patient confidentiality.¹⁴ For instance, a recent validation study highlighted inaccuracies in assessment of blood pressure by an application sold to 148 000 users, with which approximately 80% of hypertensive individuals will be falsely reassured that their blood pressure is in the normal range.¹⁵ Although these cases may warrant concern, numerous resources and endeavours are being invested to integrate diagnostics into smartphones for a wide range of conditions (ie, ResearchStack for Android, ResearchKit for Apple).¹⁶

The primary outcome of our study is the utilisation of the RA as a conduit in CABG surgery. In the past decade, numerous studies have demonstrated that the RA conduit has a significantly higher 5-year graft patency rate compared with SVG.^{2–4} Based on a study done by Deb *et al*, among 269 participants who underwent late coronary angiography after index non-emergent CABG in 9 Canadian centres, RA conduits had a lower frequency of functional graft occlusion and complete graft occlusion when compared with SVG.³ A recent patient-level meta-analysis demonstrated a number-needed to treat of 16 with the use of RA conduits instead of SVGs to prevent one death, MI or revascularisation.^{7 17} Given the negligible cost, this cost–benefit ratio of implementing a more diagnostically accurate screening tool is extremely favourable. Moreover, the primary safety outcome is post-operative palmar ischaemia, which is expected to be non-significant due to its rare incidence as previously shown.¹⁸

Implication

To our knowledge, the CAPITAL iRADIAL CABG study is the first trial which uses smartphone-based photoplethysmography in evaluating UA patency as part of a pre-CABG surgical assessment. If proven safe and efficacious in this study, SBPA may be considered an evidence-based approach in assessing UA patency prior to RA harvesting.

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Funding This work was supported by the Innovation Fund of the Alternative Funding Plan for the Academic Health Sciences Centres of Ontario. Grant number UOH-20–009.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES

- 1 Goldman S, Zadina K, Moritz T, *et al*. Long-term patency of saphenous vein and left internal mammary artery grafts after coronary artery bypass surgery: results from a department of Veterans Affairs Cooperative study. *J Am Coll Cardiol* 2004;44:2149–56.
- 2 Possati G, Gaudino M, Prati F, *et al*. Long-term results of the radial artery used for myocardial revascularization. *Circulation* 2003;108:1350–4.

- 3 Deb S, Cohen EA, Singh SK, *et al*. Radial artery and saphenous vein patency more than 5 years after coronary artery bypass surgery: results from RAPS (radial artery patency study). *J Am Coll Cardiol* 2012;60:28–35.
- 4 Collins P, Webb CM, Chong CF. Radial artery versus saphenous vein patency trial I. radial artery versus saphenous vein patency randomized trial: five-year angiographic follow-up. *Circulation* 2008;117:2859–64.
- 5 Buxton BF, Raman JS, Ruengsakulrach P, *et al*. Radial artery patency and clinical outcomes: five-year interim results of a randomized trial. *J Thorac Cardiovasc Surg* 2003;125:1363–70.
- 6 Petrovic I, Nezic D, Peric M, *et al*. Radial artery vs saphenous vein graft used as the second conduit for surgical myocardial revascularization: long-term clinical follow-up. *J Cardiothorac Surg* 2015;10:127.
- 7 Gaudino M, Benedetto U, Fremez S, *et al*. Radial-Artery or saphenous-vein grafts in coronary-artery bypass surgery. *N Engl J Med* 2018;378:2069–77.
- 8 Aldea GS, Bakaeen FG, Pal J, *et al*. The Society of thoracic surgeons clinical practice guidelines on arterial conduits for coronary artery bypass grafting. *Ann Thorac Surg* 2016;101:801–9.
- 9 Jarvis MA, Jarvis CL, Jones PR, *et al*. Reliability of Allen's test in selection of patients for radial artery harvest. *Ann Thorac Surg* 2000;70:1362–5.
- 10 Di Santo P, Harnett DT, Simard T, *et al*. Photoplethysmography using a smartphone application for assessment of ulnar artery patency: a randomized clinical trial. *CMAJ* 2018;190:E380–8.
- 11 Barbeau GR, Arsenault F, Dugas L, *et al*. Evaluation of the ulnopalmar arterial arches with pulse oximetry and plethysmography: comparison with the Allen's test in 1010 patients. *Am Heart J* 2004;147:489–93.
- 12 Raja JM, Elsagr C, Roman S, *et al*. Apple watch, Wearables, and heart rhythm: where do we stand? *Ann Transl Med* 2019;7:417.
- 13 Avram R, Olgin JE, Kuhar P, *et al*. A digital biomarker of diabetes from smartphone-based vascular signals. *Nat Med* 2020;26:1576–82.
- 14 Gagnon M-P, Ngangue P, Payne-Gagnon J, *et al*. m-Health adoption by healthcare professionals: a systematic review. *J Am Med Inform Assoc* 2016;23:212–20.
- 15 Plante TB, Urrea B, MacFarlane ZT, *et al*. Validation of the instant blood pressure smartphone APP. *JAMA Intern Med* 2016;176:700–2.
- 16 Zens M, Grotejohann B, Tassoni A, *et al*. Development of a modular research platform to create medical observational studies for mobile devices. *JMIR Res Protoc* 2017;6:e99.
- 17 Gaudino M, Benedetto U, Fremez S, *et al*. Association of radial artery graft vs saphenous vein graft with long-term cardiovascular outcomes among patients undergoing coronary artery bypass grafting: a systematic review and meta-analysis. *JAMA* 2020;324:179–87.
- 18 Meharwal ZS, Trehan N. Functional status of the hand after radial artery harvesting: results in 3,977 cases. *Ann Thorac Surg* 2001;72:1557–61.