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PROTOCOL PAPER
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Safety and care of no fasting prior to catheterization laboratory procedures: a non-inferiority randomized control trial protocol (SCOFF trial)

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Aims Cardiac catheterization procedures are typically performed with local anaesthetic and proceduralist guided sedation. Various fasting regimens are routinely implemented prior to these procedures, noting the absence of prospective evidence, aiming to reduce aspiration risk. However, there are additional risks from fasting including patient discomfort, intravascular volume depletion, stimulus for neuro-cardiogenic syncope, glycaemic outcomes, and unnecessary fasting for delayed/cancelled procedures.

Methods and results This is an investigator-initiated, multicentre, randomized trial with a prospective, open-label, blinded endpoint (PROBE) assessment based in New South Wales, Australia. Patients will be randomized 1:1 to fasting (6 h solid food and 2 h clear liquids) or to no fasting requirements. The primary outcome will be a composite of hypotension, hyperglycaemia, hypoglycaemia, and aspiration pneumonia. Secondary outcomes will include patient satisfaction, contrast-induced nephropathy, new intensive care admission, new non-invasive or invasive ventilation requirement post procedure, and 30-day mortality and readmission.

Conclusions This is a pragmatic and clinically relevant randomised trial designed to compare fasting verse no fasting prior to cardiac catheterisation procedures. Routine fasting may not reduce peri-procedural adverse events in this setting.

Keywords Fasting • Preoperative care • Angiography • Cardiovascular surgical procedures • Patient satisfaction

Introduction

Cardiac catheterization procedures are typically performed with local anaesthetic and proceduralist guided sedation. Fasting (4–6 h for solid food and 2 h for clear liquids) is routinely recommended prior.[1] Fasting is implemented to reduce risk of aspiration, a rare but significant clinical event. A meta-analysis of randomized trials demonstrated that longer fasting (>4 h) is not associated with differences in gastric

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volumes and pH compared with shorter fasting (2–4 h)[2]; in fact, the analysis showed that shorter fasting periods seemed to have lower rates of aspiration with reduced thirst and hunger.

Evidence to support fasting for cardiac catheterization procedures is lacking.[3,4] An observational study showed that in practice, patients fast significantly longer than recommended.[5] In over 1000 patients, the average fasting period was 11.6 h with high rates of hunger (47%) and headache (11.7%), similar to the anecdotal experience at our institutions. Longer fasting periods may increase the likelihood of patient discomfort, post-procedure nephropathy, hypotension, and adverse glycaemic outcomes.

There are numerous potential benefits to removing fasting requirements including improved patient satisfaction, superior hydration status, and prevention of procedure delays and cancellations. CHOW NOW, published in abstract form, compared fasting and no-fasting before cardiac catheterization procedures.[6] This single-centre randomized trial suggested non-inferiority of no fasting with a primary composite endpoint of contrast-induced nephropathy, periprocedural hypotension, aspiration pneumonia, nausea and vomiting, hyperglycaemia, and hypoglycaemia. CHOW NOW accepted an absolute risk increase of 5.9% in the no-fasting arm as the upper limit of the non-inferiority margin. The aim of our study is to assess non-inferiority of no-fasting compared with fasting for cardiac catheterization (including coronary angiography and planned percutaneous coronary intervention) and cardiac device-related procedures.

Methods

Clinical trial design

This is a multicentre non-inferiority randomized trial with a prospective open-label, blinded endpoint design (PROBE). Inclusion and exclusion criteria are listed in *Table 1*. Coronary angiography, percutaneous coronary intervention, device implantation/replacement and lead revisions will be included. Structural cardiac interventions, calcium modification therapy, biventricular cardiac resynchronization therapy and electrophysiology procedures will be excluded. The composite primary endpoints and secondary outcomes are listed in *Table 2*. Thirty-day outcomes will be assessed via International Classification of Diseases 10th Revision diagnoses on discharge summaries. Patients will be randomized 1:1 via REDCAP to fasting (minimum of 6 h solid food and 2 h clear liquids) or to no-fasting requirement. Those in the no-fasting arm will be encouraged to have their regular meals but will not be mandated to do so. Time between solid food and clear liquid intake and procedure start will be collected. Procedure start will be defined as time of local anaesthesia administration. Single-sequence randomization will be performed with stratification by procedure type (coronary-based procedure vs. device implantation) and procedure site. Proceduralists will be permitted to know group allocation. Patient satisfaction will be assessed with the prospectively validated preoperative fasting questionnaire by Popovic *et al.* (*Table 3*).[11] Data collection will occur on

Table 1 Inclusion and exclusion criteria

Inclusion criteria
• Aged over 18 years of age
• Referred for catheterization laboratory procedures
◦ Coronary angiography
◦ Percutaneous coronary intervention
◦ Device implantation or replacement (pacemakers and defibrillators)
◦ Device lead revision (pacemakers and defibrillators)
Exclusion criteria
• Inability to provide informed consent
• Pregnant or breastfeeding females
• Requirement for a general anaesthetic
• Emergent intervention (e.g. ST-elevation myocardial infarction for laboratory activation)
• Planned complex catheterization laboratory interventions
◦ Calcium modification therapy—Rotational atherectomy, shockwave lithotripsy
◦ Mechanical circulatory support—Impella or intra-aortic balloon pump
◦ Structural interventions—aortic and mitral valve interventions
◦ Electrophysiologic studies—diagnostic and/or ablation
◦ Biventricular pacing with cardiac resynchronization therapy

Table 2 Primary and secondary outcome components and definitions

Primary outcomes
• Aspiration pneumonia (diagnosis made on clinical and radiographic criteria)
◦ Syndrome of hypoxia/tachypnoea/tachycardia/fever with X-ray changes after an aspiration event[7]
• Periprocedural hypotension
◦ <90 mmHg systolic or low blood pressure requiring intervention (e.g. medications or fluid bolus)
• Hypoglycaemia—blood sugar level <3.9 mmol/L[8]
• Hyperglycaemia—blood sugar level >11 mmol/L[9]
Secondary outcomes
• Contrast-induced nephropathy
◦ 25% increase in serum creatinine from baseline or a 0.5 mg/dL (44 μmol/L) increase in absolute serum creatinine value 48–72 h after intravenous contrast administration[10]
• New intensive care unit admission required post procedure
• New non-invasive ventilation or intubation requirement post procedure
• 30-day readmission
• 30-day mortality
• Patient reported outcomes of satisfaction and comfort[11]
• Pre-procedure EQ-5D quality of life score

Table 3 Patient satisfaction questionnaire

Patient satisfaction questionnaire (5-point ordinal scale response)	
Pre-procedure questions[11]	Response options
(1) I am thirsty	(1) Strongly agree
(2) I am hungry	(2) Agree
(3) My voice is hoarse	(3) Neutral
(4) I am feeling anxious	(4) Disagree
(5) I feel weak	(5) Strongly disagree
(6) I am nauseous	

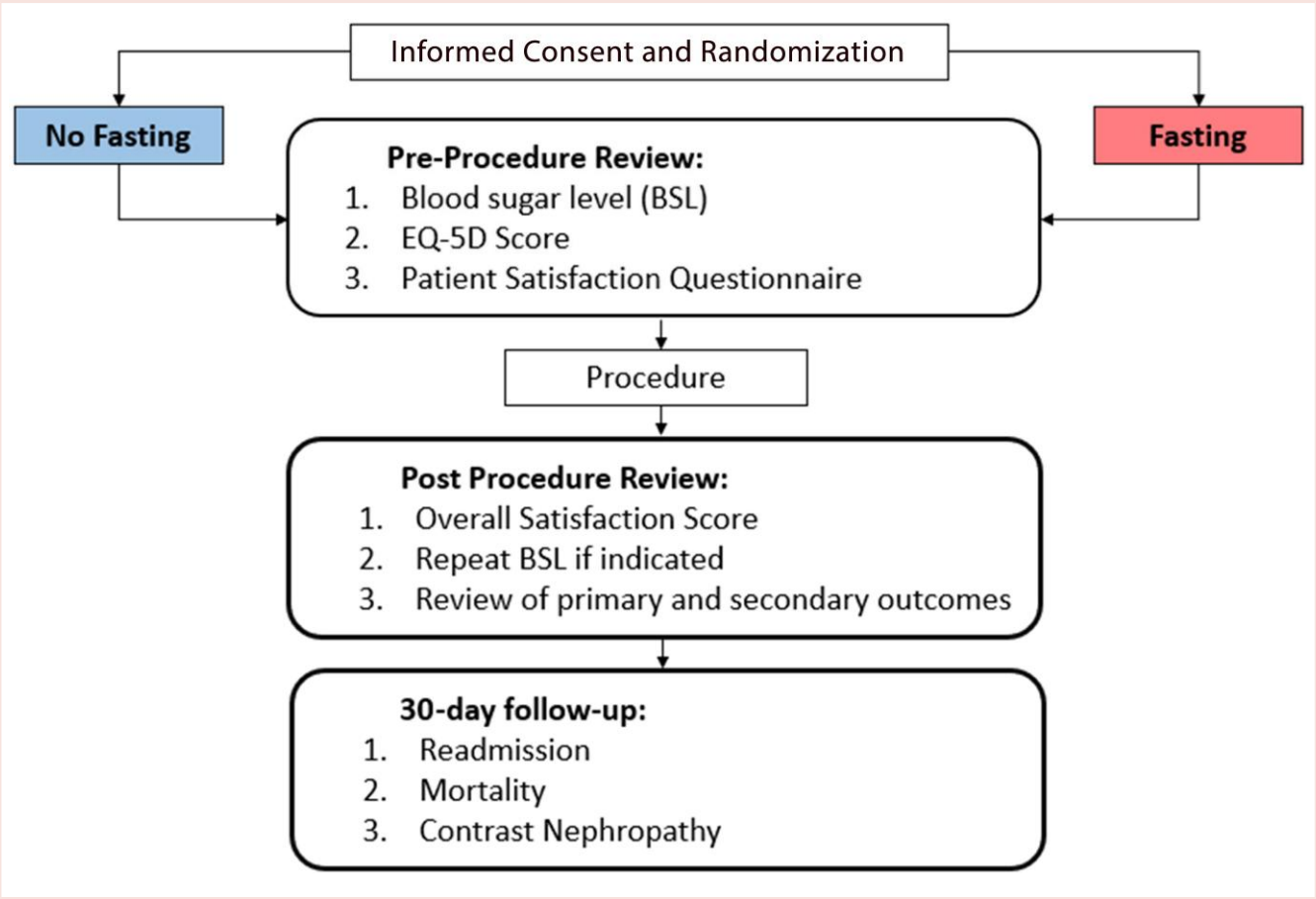

Figure 1 Clinical trial flow diagram.

REDCAP, a secure and internationally recognized database. The clinical trial flow diagram can be found in *Figure 1*.

Periprocedural instructions and care

Sodium-glucose transport protein 2 (SGLT2) inhibitors and metformin will be withheld for 24 h before and after the procedure for all patients, regardless of fasting status. If on insulin therapy, those who are not required to fast will be instructed to have their normal insulin dose based on food intake. Intravenous fluid hydration for angiography will be dictated by the proceduralist; however, the POSEIDON protocol will be suggested for those with glomerular filtration rates below 45 mL/min/m^2 without evidence of fluid overload.[12] Sedation will be at the discretion of the physician and normally includes fentanyl ± midazolam titrated to effect. Sedation type and doses will be recorded.

Ethics and trial registration

Ethics approval is confirmed via the Hunter New England Research Ethics Committee. Ethics reference number: 2021/PID02660. The trial has been registered on the Australia New Zealand Clinical Trials Registry (ACTRN12622001455752). Recruitment is ongoing across six sites in New South Wales, Australia: John Hunter Hospital, Calvary Mater Hospital, The Maitland Hospital, Belmont District Hospital, Gosford Hospital and Tamworth Rural Referral Hospital.

Sample size calculation

Based on the data from CHOW NOW, our stipulated composite primary outcome occurred in 5.9% of the fasting arm compared with 5.1% in the non-fasting arm. We assume that the 95% probability distribution in the primary outcome is between 3 and 12%, the number of participants with outcomes in each group follows a binomial distribution, and the proportion of patients experiencing outcomes follows a beta distribution. Through simulations, we estimate 300 patients per arm are required to declare non-inferiority on 80% of simulations (power) and incorrectly declare non-inferiority when the true difference is 3% larger in the non-fasting group (i.e. upper limit of the non-inferiority margin is an increase of 3% in the composite endpoint compared with fasting group) on 5% of simulations (a Type 1 error rate of 5%). We aim to recruit 600 patients in the coronary intervention arm and 100 patients in the device arm, making a total sample size of 700.

Statistical analysis

Endpoints will be assessed by a blinded clinical events committee of three physicians: an electrophysiologist, interventional cardiologist, and cardiac anaesthetist. Continuous variables will be reported as means ± standard deviation or as medians and interquartile ranges, if appropriate. Categorical variables will be stated as absolute and relative frequencies and compared using the χ^2 test. The coronary angiography and device-related procedures will be analysed within a single cohort. The posterior distribution for the between-group difference in the proportion of patients experiencing the composite outcome will be estimated within a Bayesian framework. The posterior probability that the difference in proportion is no more than the non-inferiority margin of 3% will be estimated from this posterior distribution. The non-fasting treatment will be declared non-inferior to the fasting treatment, if this probability exceeds 95%. A 95% credible interval for the difference will be presented for the primary outcome and estimated for the dichotomous secondary outcomes. Ninety-five per cent posterior intervals for the difference in means will be presented for the continuous

outcomes estimated using the No-UTURN sampler and a combination of non-informative and informative prior distributions. Participants with any missing data will have values drawn from their assumed distributions within the Bayesian model. The analysis will have the intention to treat multiple imputation the primary method of dealing with missing outcome data, imputing missing variables using the chained regression equations method. Pre-specified *post hoc* analyses will include coronary vs. device-related procedures, diagnostic vs. interventional coronary artery procedures, inpatient vs. outpatient procedures, sedation provision, body mass index, and age.

Discussion

There is no prospective randomized data supporting fasting prior to cardiac catheterization laboratory procedures. While there are theoretical benefits to fasting, there are also risks. The CHOW NOW study was of great interest to the cardiology community but has not yet been published in a peer-reviewed journal.[1,6] We suggest that finding non-inferiority of no fasting would be practice changing. This is based on the preceding evidence from CHOW NOW, retrospective reviews, and the clinical experience of interventional cardiologists: aspiration is extremely rare during emergent procedural intervention. Indeed, those undergoing emergency interventions would probably have greater risk of aspiration than those having non-emergent procedures. Given aspiration events are so rare, a clinical trial powered purely to look for differences in aspiration rates would require unfeasibly large patient numbers. We have powered the analysis to accept a 3% absolute risk increase in the primary composite outcome (around a 50% relative risk increase) within the no-fasting arm. The authors suggest that this risk increase in the composite primary endpoint of hypotension, hyperglycaemia, hypoglycaemia, and aspiration in the no-fasting group would be clinically acceptable, provided aspiration rates were not significantly higher in the intervention arm.

Removing fasting requirements may benefit hospital and healthcare systems. Reducing delays in procedures will allow for improved cardiac catheterization laboratory efficiency by improving patient flow, decreasing length of stay and healthcare expenditure.

The inclusion of device-related procedures is novel to this study. At our centres, device interventions are performed in a similar manner to coronary angiography, with local anaesthetic and proceduralist guided sedation. As with coronary procedures, there is a paucity of data to support the role of fasting prior to device implantation. There is no reason to expect that outcomes would be different based on procedure type; rather, the risk of aspiration would more likely be influenced by individual patient characteristics.

In the spirit of integrity and openness, de-identified patient-level data will be available to researchers who provide sound analysis proposals. Our pre-specified primary outcomes match outcomes assessed by the CHOW NOW investigators. There may be a role for combining individual patient-level data from CHOW NOW and other fasting trials to improve precision in the results.

Conclusion

After completion, this will be the largest randomized trial in the pre-procedural fasting space. Routine fasting prior to cardiac laboratory procedures may not reduce the risk of periprocedural outcomes. We are performing a clinically relevant, pragmatic, randomized multicentre trial to assess this question in a prospective fashion. The authors argue that if the non-inferiority of no-fasting is confirmed, it would be a practice-changing finding. This may also have implications for fasting requirements for other non-cardiac procedures that utilize conscious sedation.

Lead author biography

David Ferreira is a Cardiology Trainee and PhD candidate at the Cardiovascular Department, John Hunter Hospital, Newcastle, Australia. He obtained his medical degree from the University of New England and completed his Physician's Training at Liverpool Hospital in Sydney. His research focused on randomized trials of low-cost interventions to improve patient care.

Data availability

De-identified patient level data will be available to researchers who provide sound analysis proposals.

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Conflict of interest: None declared.

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