Fasting Versus Non-fasting prior to elective Cardiac catheterisation

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1 Study Summary

Title	Fasting Versus Non-fasting prior to elective Cardiac catheterization
Short Title	Fasting or no fasting before cardiac catheterization
Version & Date	Version 1.7 12 October 2017
Principal Investigator	Dr Hesham Abdelaziz
Objectives	To show that there is no increased risk of peri-procedural complications between fasting and non-fasting patients as well as improved patient satisfaction when allowed to eat up to the point of elective coronary angiography/angioplasty compared to patients kept nil by mouth. We aim to
Methodology / Design	Prospective single centre, single blinded (investigator) randomized Study Consented patients will be randomised in 1:1 ratio to either standard hospital fasting policy or allowed to eat freely up to the point of transfer to the Catheter Laboratory.
Duration	12 months
Participating Centres	Blackpool Victoria Hospital
Primary End Point	Composite of nausea, vomiting, abdominal pain, emergency endotracheal intubation and aspiration,
Number of participants	400 patients
Main Inclusion /Exclusion Criteria	INCLUSION

	1. All patients >18 years undergoing elective coronary angiography or angioplasty procedures in the 2 months window. EXCLUSION 1. Patient choice 2. Other cardiac procedures such as EP studies, pacing, structural heart disease intervention 3. Emergency PPCI 4. Patients already admitted in the hospital with UA / NSTEMI 5. Patients unable to give informed consent
Statistical Methodology and Analysis	Our composite primary endpoint will be analysed using 95% confidence interval between the fasting and non-fasting group using the Fisher's exact test. Categorical secondary outcomes will be presented as number and percentages and compared between the two groups using the Chi-square test or Fisher's exact test. Secondary continuous outcomes will be presented as mean and standard deviation and compared using the independent samples t-test. P-values will be used to assess evidence of difference. P value <0.05 will be considered significant.

2 Introduction

This document is a research protocol and this study will be conducted in compliance with the protocol, The Research Governance Framework, International Conference on Harmonisation, Good Clinical Practice Guideline ICH/GCP, and all applicable Blackpool Teaching Hospitals NHS Foundation Trust Research Office requirements.

This study aims to demonstrate that pre procedural fasting for elective cardiac procedures is unnecessary and outdated practice. It is without doubt that induction of general anaesthesia depresses cough and swallow reflexes and therefore increases the risk of aspiration with airway manipulation. However, coronary angiography and angioplasty does not require general anaesthesia and is carried out purely under local anaesthetic. So why do we still need periods of fasting?

2.1 Background

Nil by mouth (NBM) has been the standard of care for cardiac catheterization since its inception, because of the associated vomiting that was common with the first generation of radio contrast materials that were almost toxic and use of general anaesthesia. Induction of anaesthesia depresses the cough and swallow reflex thus increasing the risk of aspiration, this is also true for deep sedation.

Today, the cardiac catheterization procedure is done under local anaesthesia with anxiolytic sedatives often used peri-procedurally to achieve minimal sedation whereby verbal contact is maintained. Both the royal college of anaesthetists and the royal college of emergency medicine state that fasting is not required for minimal or conscious sedation but does recommend fasting for general anaesthesia.[1,2] There is only 1% risk of needing emergency surgery for percutaneous coronary interventions (PCIs). The risk of developing pulmonary aspiration following emergency coronary artery bypass grafting (CABG) surgery or emergency direct current conversion (DC) in patients without pre-procedural fasting is in the order of 0.001%.[3]

There was no evidence that the volume or pH of participants' gastric contents differ significantly between fasting and non-fasting population as shown by Brady et al.[4] In addition, the overall

incidence of nausea and vomiting was reported to be 1% before elective cerebral angiography in a study carried out by Kwon et al[5] with no significant difference between fasting and non-fasting group.

Hamid et al[6] recently conducted a retrospective analysis of registry data for 1916 percutaneous coronary intervention (PCI) patients over a 3 years period. None of the patients were kept nil by mouth (NBM) pre-procedure and no patients required immediate endotracheal intubation nor did any develop aspiration pneumonia intra or post procedurally. They concluded in their observational study that patients undergoing PCI do not need to be fasted prior to their procedures.

The American Society of Anaesthesia guidelines discuss this extensively and have concluded that there is no strong relation between fasting, gastric volume, or risk of aspiration. In any case, the patients at highest risk for nausea and vomiting are those who present with ST-elevation myocardial infarction (STEMI), who are not fasting anyway and the need for emergency intubation/CABG remains rare in these patients.

Prolonged unnecessary fasting can often leave patients dissatisfied and add to the discomfort and anxiety of waiting for a procedure. Patients may also choose to miss their usual medications on the morning of the procedure due to restrictions advised with oral intake, increasing the risk of complications such as poorly controlled hypertension and the associated peri-procedural complications.

There is also evidence that patients often choose to fast longer than advised by healthcare professionals. The reasons for this include: misunderstanding by the patient that a longer period of fasting may be more protective, apprehension and loss of appetite before an invasive procedure, or practical problems with timing of the procedure.

It is very important to address this fasting issue as many patients undergo prolonged periods of fasting prior to a procedure and whilst this is not usually a problem for young fit patients, many of the patients do not fall into this category. Many are elderly with multiple co morbidities and thus run the risk of hypoglycaemia and lethargy.

A further consideration has to be that of patient flow through the cardiac unit. If patients have to be NBM for a certain period prior to cardiac catheterisation then it reduces the ability to fill lists at short notice if patients need to be cancelled. If we can demonstrate that this period of NBM is not necessary then we open the door to maximizing the catheter lab as a resource thus reducing length of stay. This improves patient experience along with the associated financial benefits.

Finally, and probably most importantly we feel that the overall patient experience will be improved if patients are allowed to eat up to the point of procedure decreasing the number of hungry, disgruntled patients who complain to nurses.

In essence, there is little evidence available about the benefits of pre-procedural fasting and prospective randomized trials are lacking with no clear guidelines recommendations that advocate the benefit of fasting prior to cardiac catheterization. Therefore, we aim to investigate the safety of this approach by this study.

2.2 Study Objectives

- To show that allowing patients to eat freely up to the point of elective coronary angiography/angioplasty is not associated with any increased risk of nausea, vomiting, abdominal pain, emergency intubation or aspiration pneumonia compared to patients kept nil by mouth.
- To show improved patient satisfaction when allowed to eat up to the point of elective coronary angiography/angioplasty compared to patients kept nil by mouth.

We aim to provide evidence from a prospective study to help the development of guidelines that can be implemented nationally and internationally regarding pre procedural care of cardiac patients.

3 Study Design

3.1 General

This will be a prospective single centre, single blinded randomized study.

3.2 Study procedure

All patients to be admitted electively for coronary angiography or angioplasty will be given the opportunity to participate. An invitation letter together with patient information leaflet outlining the study will be sent along with the pre-procedure appointment letter to give the patient time to read and think about the study. Once at pre-procedure assessment clinic, the study will be explained further including potential risks and intended outcome and patients concerns will be addressed. Patient will be given the opportunity either to take part in the study or abstain and follow the standard procedure. If the patient agrees then they will sign the consent form and then be randomised in a 1:1 ratio to either the fasting or non-fasting group and be allocated a patient identification number. This will be done at the pre-procedure assessment clinic.

1**- Fasting group (current practice)**: Clear fluids up to the time of the procedure and no food for at least 2 hours before the procedure.

2-**Non Fasting Group**: Clear fluids and food up to the time of the procedure.

The pre procedure preparation will then be documented in the notes. Intention to treat analysis will be used to avoid the effects of crossover and dropout providing unbiased comparisons among the treatment groups.

The case report form (CRF) will be appended inside the front cover of the notes to be completed on the day of procedure by the operating physician and the remainder completed by the research team. Finally once the patient is ready for discharge they will be asked to complete an anonymous questionnaire relating to their experience and satisfaction.

A database will be composed on an encrypted flash drive and backed up on the catheter lab computer. Only the patient identification number will be included in this but will still be password protected.

All patients will be contacted by phone on day 30 or the nearest working day thereafter to ensure no chest infections.

3.3 Primary Study Endpoints

Primary endpoint is a composite of nausea, vomiting, abdominal pain, emergency intubation and aspiration

3.4 Secondary Study Endpoints

- Patient satisfaction
- Incidence of hypoglycaemia (blood sugar < 3.6 mmol/l) as assessed by finger prick test
- Incidence of hypotension (SBP<90 mmHg and /or DBP<60 mmHg)
- 30 day chest infection rate

3.5 End of study

Data collection will start November 2017 and we will continue until the 400 patients are enrolled or premature termination of the study due to safety issue. The last phone contact/ clinic visit will be done 30 days after the enrolment of the last patient.

4 Methods

4.1 Subject Selection and Withdrawal

Once enrolled in the study all patients will be identified by their study number alone and the arm of the study they are involved in. If the patient decides to withdraw from the study at any point after randomization, they will revert to the standard hospital procedure policy of fasting. However, they will still be included in the final analysis as intention to treat and any drop out or cross over will be documented.

4.1.1 Inclusion Criteria

- All patients >18 years undergoing elective coronary angiography or angioplasty procedures in the 2 months window.

4.1.2 Exclusion Criteria

- Patient choice
- Other cardiac procedures such as EP studies, pacing, structural heart disease intervention
- Emergency PPCI
- Patients already admitted in the hospital with UA / NSTEMI
- Patients unable to give informed consent (vulnerable group)

4.2 Subject Recruitment and Screening

All patients undergoing elective cardiac catheterisation procedures will be sent an invitation in the post including the patient information leaflet together with their pre-procedure assessment date. This will allow them to read about the study prior to the assessment to decide whether they would like to be included. Once at the pre-procedure assessment clinic, the study will be further discussed, any questions will be addressed and the consent form will be signed should they wish to be included.

4.3 Randomisation Process

Randomisation will take place in pre-procedure assessment clinic in a 1:1 ratio using sealed enveloped method. This information (whether fasting or not) will be relayed to the patient at the time of pre-procedure assessment and also stored on a spreadsheet with study number the only identifying factor. This will be password protected with individuals directly involved having access to this. This data will also be backed up on a password protected computer in the catheter laboratory.

4.4 Informed Consent

The patient will receive a detailed description of the study in the patient information sheet sent together with pre-procedure assessment letter by mail (around 1 week before the pre-procedure assessment clinic date). In the pre-procedure assessment clinic, the study will be explained further including potential risks and intended outcome, any patient's question will be addressed, with each

patient given the opportunity to abstain and follow standard procedure. If the patient agrees then they will sign the consent form and then be randomised in a 1:1 ratio to either the fasting or non-fasting group. This will be attached to the inside cover of the notes and checked on the time of presentation on the day of intended procedure.

4.5 Withdrawal of Subjects

If any patient chooses to withdraw from the study, they will revert to the standard hospital procedure. However, they will still be included in the final analysis as intention to treat and any drop out or cross over will be documented.

5 Prior and Concomitant Therapy

All previous medication and treatments should continue.

6 Clinical Procedure

As standard practice, operators will be allowed to use any techniques they commonly use throughout their practice (choice of access, balloon and stent type).

7 Statistical Plan

Given that the occurrence of pulmonary aspiration was so low in similar studies performed for cerebral angiography, we decided against using this as a single primary endpoint as thousands of patients would be required. We opted for a composite primary end point of nausea, vomiting, abdominal pain, emergency intubation and aspiration. These will be recorded both immediately intra/post procedure by the operation physician and again by the patient within 8 hours after the procedure. We will compare the two groups using 95% confidence intervals to ascertain the extent to which they overlap. Secondary end points will be overall patient satisfaction, the incidence of hypoglycaemia and hypotension, and 30 day chest infection rate which will be compared between the two groups.

7.1 Sample Size Determination

With 200 participants in each group, if none of the participants has an event then the upper limit of the 95% confidence interval for event rate would be 1.5%. Hence if both groups, fasting and non-fasting, have no events recorded then it is highly unlikely that the event rate in the two groups would differ by more than 1.5%. Provided that a difference of 1.5% in event rate is deemed not clinically meaningfully different; then 200 participants in each group would demonstrate that not fasting has a similar event rate to fasting.

7.2 Statistical Methods

Our composite primary endpoint will be analysed using 95% confidence interval between the fasting and non-fasting group and the event rate will be compared using the Fisher's exact test. Categorical secondary outcomes will be presented as number and percentages and compared between the two groups using the Chi-square test or Fisher's exact test. Secondary continuous outcomes will be presented as mean and standard deviation and compared using the independent samples t-test. P-values will be used to assess evidence of difference. Any P value < 0.05 will be considered significant.

7.3 Interim Analyses

Final Analysis will take place once all data is collected. However, if sequentially the first 10 patients in the non-fasting group show signs of an event rate in excess of that shown in the fasting group as demonstrated by non-overlapping confidence intervals then stopping rules will be applied. For this pilot study, this will be monitored by the Chief Investigator.

7.4 Subject Population(s) for Analysis

All participants will be used in analysis. Intention to treat analysis will be used to avoid the effects of crossover and dropout providing unbiased comparisons among the treatment groups.

8 Safety and Adverse Events

Any complications will be treated in the usual way irrespective of study arm included in.

The Chief Investigator will be continuously monitoring the data and if sequentially the first 4 (15%) patients in the non-fasting group show signs of an event rate in excess of that shown in the fasting group, as demonstrated by non-overlapping confidence intervals then stopping rules will be applied.

8.1 Recording of Adverse Events

All adverse events occurring during the study period will be recorded. The clinical course of each event will be followed until resolution, stabilisation, or until it has been determined that the study treatment or participation is not the cause. Serious adverse events that are still ongoing at the end of the study period will be followed up to determine the final outcome. The cardiac anaesthetic team has been made aware of the study in case a non-fasting patient need to be taken for emergency surgery.

8.2 Expected non-serious Adverse Events

The following are expected non-serious events and will be recorded on the Case Report Form and reported to the CI as necessary. They do not need to be reported to the sponsor.

These include:

- Nausea and vomiting.
- Abdominal pain
- Procedure-related transient bradycardia (HR<60 bpm).
- Procedure-related transient hypotension (SBP<90 mmHg).
- Puncture site related hematoma/ecchymosis.

8.3 Serious Adverse Events (SAEs)

All SAEs will be recorded on the Case Report Form and reported to the CI within 7 days. The CI will be responsible for the prompt notification of findings that could adversely affect the health of patients or impact on the conduct of the trial. Only unexpected SAEs or fatal events will be

reported to the Sponsor immediately (maximum within 15 days). The sponsor will report events to the REC as necessary (usually only events that are both related to the intervention and unexpected).

The following information will be collected for each serious adverse event:

- Whether the event is considered expected or unexpected
- Full details in medical terms and case description
- Event duration (start and end dates, if applicable)
- Action taken
- Outcome
- Causality in the opinion of the investigator

8.4 Expected Serious Adverse Events

- Emergent CABG.
- Stroke/TIA.
- Coronary perforation and cardiac tamponade.
- Peri-procedural MI related to acute vessel closure (troponin > 300 ng/L).
- Allergic reactions to the dye or medications used during the procedure.
- Major vascular complications as acute thrombosis, distal embolization, dissection, major bleeding (>2 gm% drop in hemoglobin, requiring blood transfusion, retroperitoneal bleeding or resulting in shock).pseudo-aneurysm, or arterio-venous fistula.
- Infection
- Cardiac arrest requiring resuscitation involving ventricular defibrillation/DC shock

8.5 Unexpected and fatal Serious Adverse Events

- Emergency endotracheal intubation.
- Pulmonary aspiration.
- All other serious adverse events that are not listed under" expected SAEs".
- Events that results into death.

8.6 Period for recording Serious Adverse Events

Data on serious adverse events will be collected from the time of procedure for the 1 month follow-up period.

9 Data Handling and Record Keeping

9.1 Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Data Protection Act and The Research Governance Framework for Health and Social Care.

- Subjects will be identified by Study number alone.
- All health professionals involved in the study and patient care will have access to this information if required.
- All patient data will be password protected in the computer in the cath lab
- If a patient needs to be identified for a clinical or safety reason, CI will be consulted.

The Chief Investigator (CI) is the custodian of the data.

9.2 Case Report Forms

The study case report form (CRF) is the primary data collection instrument.

- All data requested on the CRF/DCF will be recorded.
- All missing data will be explained. If a space on the CRF/DCF is left blank because the procedure was not done or the question was not asked, "N/D" will be written.
- If the item is not applicable to the individual case, "N/A" will be written.
- All entries should be printed legibly in black ink.
- To correct any data entry error, a single straight line will be drawn through the incorrect entry and enter the correct data above it. All such changes will be initialled and dated.

9.3 Records Retention

All records will be archived for 5 years in line with the Trust R&D Policy.

10 Study Monitoring, Auditing, and Inspecting

The investigator will permit study-related monitoring, audits and inspections by the Ethics Committee, the Sponsor and the Research Governance Manager.

Participation as an investigator in this study implies adherence to the principles and responsibilities of the Research Governance Framework, ICH/GCP and Directive 2000/20/EC

11 Ethical Considerations

The patient will receive a detailed description of the study in the patient information sheet send together with pre-procedure assessment letter by mail (around 1 week before the pre-procedure assessment clinic date) to give him/her time to think about the study. Then, at the pre-procedure assessment clinic, they will have the opportunity to ask questions with one of the research team and to answer any queries. Any patient will have the right to abstain from taking part into the study or to withdraw after taking part without affecting the standard of care they are receiving.

The Chief Investigator will ensure that the risk of the study does not outweigh the benefit at any point during the study time, and if so, the study will be prematurely terminated.
The benefit /risk of taking part into the study will be adequately explained to the patients. There will be no direct benefit to the patient from taking part in this study. However, the information gained from the study will help improve the quality of service offered to the patients, increase their satisfaction, may aid in changing the current practice and avoiding unnecessary delay to the patients. The potential risk will be made clear which is the occurrence of nausea and vomiting at an expected rate of 1-2% and no expected emergency endotracheal intubation or aspiration pneumonia cases.
Once patient is enrolled in the study, all his personal information will be anonymized with the only identifier the study number. All patient data will be password protected on the computer in the cath lab. All health professionals involved in the study and patient care will have access to this

information if required. Only the CI will have access to identify the patient personal data for the purpose of safety.
To ensure un-biased result, an adequate randomization process with intention to treat analysis will be undertaken. Analysis will be done by the Sub-Investigator who is blinded to group allocation.

11.1 Patient information Sheets

A patient information sheet with a detailed description of the study including the objectives, any risk to the patient and what is required from the patient to do if he/she accept to participate as well as safety issues and contact number for the research team. This will be distributed before pre-procedure assessment clinic date.

12 Funding

This pilot is supported by Blackpool Teaching Hospitals NHS Foundation Trust and no additional funding is required for the first 50 Patients in this Pilot study

13 Sponsorship

Blackpool Teaching Hospitals Foundation Trust is acting as sponsor for this pilot study.

No specific or additional training is required for the research staff in order to take part in the study.

14 Publication Plan

Once this Pilot study has finished, we aim to submit the result as an abstract in one of the cardiology journals and present it as a poster/ oral presentation in a national/international cardiology conference. In addition, there is a plan to carry out a large single/multicentre study to prove the result of this pilot study with the aim of large international publication.

15 References

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