A Feasibility Study Investigating the Relationship between Ankle Brachial Pressure Index and Colorectal Anastomotic Leak

A cohort study by The West Midlands Research Collaborative

Protocol v2.3
Background
Following large bowel surgery, the surgical complication with the greatest threat to life is from disruption of the colonic anastomosis; this is known as an anastomotic leak. Its occurrence varies from 3-25% in different patient groups. The key to healing of a colorectal anastomosis is the blood supply to the bowel during recovery. Identifying patients with a poor blood supply to the bowel prior to surgery would allow us to recognise a group of patients at high risk of an anastomotic leak. Better stratification of these patients would improve pre-operative patient counselling and enable surgeons to protect high-risk anastomoses with a temporary stoma, or in appropriate cases to advise against anastomosis altogether.

Aim
We intend to investigate whether the ankle-brachial pressure index (ABPI), a marker of both peripheral and central vascular disease, may serve as a simple non-invasive, reproducible test to identify those at highest risk of anastomotic failure. The primary aim of this feasibility study is to evaluate whether the ABPI test, used in this novel application, has sufficient specificity and sensitivity to warrant a large-scale trial exploring its efficacy in the prediction of anastomotic leak risk. The feasibility study will inform our power calculation for the main trial. We will also be able to explore recruitment rates, optimal patient pathways and the practicalities of ABPI measurement, which will all be highly beneficial for the possible full trial.

Primary Outcome
Obtain sufficient data to calculate a false positive rate and estimate a specificity of the ABPI as a marker for anastomotic leak. This will allow us to evaluate the feasibility of proceeding to a second phase study.

Secondary Outcome
- To inform the power calculation for a second phase study
- To evaluate whether the current data collection pathway is deliverable
- To evaluate ABPI inter-observer error
- To evaluate whether routinely performed pre-operative CT scans of the abdomen and pelvis can be used to assess the calcification of major pelvic blood vessels. This may identify patients at a higher leak risk. The findings will guide whether this warrants parallel investigation in the second phase study.

Design
A prospective double-blind cohort study, of 150 patients in 3 trusts within the West Midlands. Data collection will be performed pre-operatively and 6 weeks after surgery.
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1. Study Rationale

Disruption of colonic anastomoses is a potentially life threatening complication of large bowel surgery. Its occurrence varies from 3-25% in different patient groups. The key to healing of a colorectal anastomosis is the blood supply to the bowel during recovery. This study seeks to investigate ankle-brachial pressure index, a marker of both peripheral and central vascular disease, as a simple non-invasive, reproducible test to identify those at highest risk of anastomotic failure. Better stratification of these patients would enable surgeons to protect high risk anastomoses by a temporary stoma, or in appropriate cases to advise against anastomosis altogether.

A colorectal anastomosis is a commonly performed procedure, with over 50 000 colorectal anastomoses being performed each year in the UK alone. The majority of these are performed for colorectal cancer. A failed anastomosis will result in one of the most serious complications of gastrointestinal surgery; an anastomotic leak. Large international trials have identified clinically evident anastomotic leak occurs in 3% of all colonic anastomoses, but the rate is higher (7-10%)\(^1,2\) in patients undergoing rectal anastomosis and may be as frequent as 25% in high risk patients.\(^3,7\)

The consequences of an anastomotic leak are serious. There is a significant associated morbidity, prolonged hospital stay, and a mortality rate which exceeds 20% in several series.\(^8-14\) A recent high quality meta-analysis also suggests oncological outcomes are significantly worse in those patients that leak.\(^15\) To mitigate the sequelae of an anastomotic leak surgeons may choose to defunction the patient or to avoid an anastomosis altogether by forming an end stoma.

A defunctioning stoma decreases the severity of sepsis due to anastomotic leak, reduces the need for emergency reoperation and reduces mortality.\(^16-19\) However, a stoma is not without risk. Forming a defunctioning stoma is a difficult decision and one that patients and surgeons will naturally wish to avoid\(^20,21\) The morbidity associated with a stoma is also not insignificant\(^20,22\). Stomas reduce the quality of life for the patient and stoma closure requires a second operation at a later date, this requires an additional length of stay, further financial burden to the health service and a mortality rate which may exceed 2%.\(^17,23-25\) Currently most patients with low rectal anastomoses are routinely considered
for defunctioning, on the basis that this group has a leak rate of 10-12%, however no stratification systems exists to assess the risk of leak to an individual patient. Patients are currently largely stratified by their ability to withstand the consequences of a leak, rather than an estimate of their leak risk. Providing an objective test to stratify the patients by their leak risk would contribute substantially to this management decision.

A number of factors predispose to leak but an adequate blood supply is essential. Animal models strongly support this; temporarily occluding the blood supply to the bowel for 30 minutes prior to anastomosis led to anastomotic dehiscence within 3 days in 100% of the affected rats. One canine study demonstrated that impairing the blood supply to the sigmoid colon, by ligating the mesocolon 1cm from the bowel anastomosis, caused clinically evident leak, in 7 of 10 dogs. The importance of blood supply is also demonstrated in clinical studies elsewhere in the gastrointestinal tract; an inadequately perfused oesophagus causes anastomotic leak. In low rectal anastomoses there is a lower rate of leak with coloanal pouch anastomoses compared with colorectal pouch anastomoses. This difference correlated strongly with laser Doppler assessment of capillary blood flow.

An inadequate blood supply to the colon and rectum also arises from compromised perioperative maintenance of blood pressure, giving rise to target organ ischemia. This is seen in epidural related hypotension leading to impaired splanchnic circulation causing bowel ischaemia and colonic mucosal ischaemia. In addition, animal models and clinical studies demonstrate a reduced splanchnic perfusion and increased colonic mucosa ischaemia following a myocardial infarction. Finally, the use of vasopressors, causing splanchnic vasoconstriction, are also associated with anastomotic leak.

Recently assessment of anastomotic perfusion has been attempted by laser doppler flowmetry, angiography and by measuring inferior mesenteric artery (IMA) stump pressures. Between 2003-2008, Kudszus et al performed a cohort study using intraoperative laser fluorescene angiography (LFA) in 332 patients with 306 matched controls. The device assessed on-table perfusion to the anastomosis; inadequate perfusion prompted refashioning of the anastomosis (13.9% of cases). Anastomotic leak occurred in 3.5% of the LFA group compared with 7.5% in the control arm (p<0.01). Despite assessing colonic perfusion effectively, these techniques are restricted from
widespread evaluation and hence clinical application by their invasive nature, expense, inter-user variability, technical difficulty and time requirements.

There is a clinical need for a non-invasive validated test, which is better suited to widespread clinical use and which can serve as a predictor of leak. The Ankle Brachial Pressure Index (ABPI) is a well established, simple, non-invasive, and reliable test, which essentially compares the blood pressure in the ankle with the blood pressure in the arm. An abnormal ABPI reflects calcified or atherosclerotic vessels and is routinely used in clinical practice for the assessment of peripheral arterial disease.47 The utility of the tool has also been successfully proven in other clinical fields with level 1a evidence demonstrating that an abnormal ABPI is associated with up to a four-fold increased risk of cardiac events, and similar findings in renovascular and cerebrovascular disease.48-52

Therefore the ABPI can be seen to reflect generalised arterial disease, and it is likely that an abnormal ABPI would also indicate arterial disease of the vessels supplying the colon. This in turn would lead to insufficient colonic perfusion and insufficient perfusion to the colorectal anastomosis increasing the likelihood of anastomotic leak. This is further supported by a recent publication that demonstrated that patients with calcified, hence atherosclerotic, aortoiliac vessels on CT scan, were significantly more likely to develop an anastomotic leak.53

Finally the risk factors for an abnormal ABPI such as smoking, ischaemic heart disease (IHD), diabetes mellitus (DM) correspond to other risk factors associated with leak.8,10,56-63 Cardiac symptoms are associated with up to 40% of anastomotic leaks54 and for elective rectal resections, smoking and IHD are associated with a 6 and 7 fold increased risk of leak.55

We believe an abnormal ABPI therefore brings together a number of the risk factors associated anastomotic leak to provide a global assessment of leak risk.

**Hypothesis**

We propose that the ABPI, a marker of both peripheral and central vascular disease, may serve as a non-invasive marker for the risk of anastomotic leak.

This feasibility study is intended to evaluate whether the ABPI may serve as a useful test
to warrant its use in the prediction of anastomotic leak. We intend to assess the specificity and the false positive rate of the test. This will guide whether or not we proceed to a second phase study to evaluate the sensitivity and positive predictive value of the test.

Glossary

*Defunctioning:* forming a stoma upstream of the anastomosis, diverting the faeces into a pouch mounted on the abdominal wall and away from the anastomosis. This is performed because if an anastomosis does leak there is less faecal contamination at the leak site and consequently the severity of peritonitis is reduced.

*Anastomotic leakage:* A clinical diagnosis will require symptoms related to leakage (gas, pus or faecal discharge from the drainage site, peritonitis or discharge of pus from the rectum). In the event of a clinically suspicious leak (fever or abdominal pain) the diagnosis can be established by operative or radiological diagnosis. When an anastomosis is defunctioned the presence or absence of a leak will be established by contrast radiology.

*Hypertension.* For the purpose of the data collection form (CRF A) this is defined as an established diagnosis of hypertension for which pharmacotherapy as been prescribed.

2. Outcomes

We intend to investigate whether the ankle-brachial pressure index (ABPI), a marker of both peripheral and central vascular disease, may serve as a simple non-invasive, reproducible test to identify those at highest risk of anastomotic failure.

This feasibility study is intended to evaluate whether the ABPI may serve as a useful test in predicting anastomotic leak. We intend to assess the specificity and the false positive rate of the test. This will guide whether or not we proceed to a second phase study to evaluate the sensitivity and positive predictive value of the test.

Primary objective:

Obtain sufficient data to calculate a false positive rate and estimate a specificity of the ABPI as a marker for anastomotic leak.

Secondary Objective:

a) To inform the power calculation for a second phase study
b) To evaluate whether the study patient pathway, from recruitment to data collection and analysis, is deliverable

c) Using a standardised technique for ABPI, to evaluate inter-observer error of the test

d) To evaluate whether routinely performed pre-operative CT scans of the abdomen and pelvis can be used to assess the calcification of major pelvic blood vessels. This may identify patients at a higher leak risk. The findings will guide whether this warrants parallel investigation in the second phase study.

3. Methods

Study design
Multicentre prospective double blinded cohort study

Study setting
Three NHS colorectal units within the West Midlands have agreed to participate (New Cross Hospital, Wolverhampton; University Hospital North Staffordshire, Stoke; Queen Elizabeth Hospital, Birmingham). We anticipate recruiting 50 patients from each site.

Inclusion Criteria
All surgical patients who are pre-operatively assessed for elective bowel resection and anastomosis (for any indication, at any colorectal site, using any anastomotic technique and using either a laparoscopic or an open approach).

Exclusion criteria
- Emergency colorectal cases
- Patients <18 years and those unable to consent independently
- Patients who have had a previous colonic or rectal resection

Assessor eligibility
The assessor will be trained to complete the electronic CRF forms and to perform a standardised ABPI. For the feasibility study the site principle investigator will be responsible for assessor training.
Primary endpoint
Anastomotic leak

Secondary Endpoint

• To assess if the abnormal ABPI may predict for:
  Mortality
  Peri-operative cardiac event
  Wound Infection
  Length of Stay
  HDU or ITU admission

• To assess the feasibility of performing a second phase study:
  The rate of patient recruitment
  The percentage of complete CRFs
  Identify the questions which are unclear or unsuccessfully answered

• Assess the relationship between the extent of aortoiliac calcification and anastomotic leak

Data collection
Recognised risk factors for anastomotic leak will be recorded (Form A) along with the ABPI (Form A). This data will be recorded pre-operatively within fourteen days of the bowel resection.
Intra-operative and post-operative data will be collected retrospectively on Form B. Form B is intended to identify those people that leak following surgery and will record the relevant events of first 6 post-operative weeks. Form B will also serve to identify patients who have been defunctioned. The defunctioned patients will be reviewed again at 6 months, CRF C will be completed at this stage.
This data will be recorded, pseudoanonymised, and stored electronically, on a secure database.

ABPI assessment technique
The optimise the reliability of the ankle brachial pressure index a standardised training session by the unit principle investigator will be delivered. A summary card will be provided (Figure 2), this is based on the best available evidence. The trials unit will
carefully monitor the ABPI values, to identify outlying assessors or outlying units. Sporadically the inter-user variability will be assessed; repeat ABPIs will be performed by the site principle investigator the pre-operative clinic. The following standardised materials will be used:

1. Huntleigh Handheld Doppler and D900 Vascular Probe (E28, D900), Huntleigh Healthcare, UK
2. Welch Allyn Durashock DS 66 Sphygmomanometer (SKU PART NUMBER: DS66-01-189), Welch Allyn, UK
3. Welch Allyn Flexiport Large Long Adult Cuff size 12L for Durashock Sphygs (SKU PART NUMBER: REUSE-12L-1TPE), Welch Allyn, UK
4. Welch Allyn Flexiport Small Adult Cuff size 10 for Durashock Sphygs (SKU PART NUMBER: REUSE-10-1TPE), Welch Allyn, UK

Calcification Assessment

The majority of patients undergoing an elective bowel resection routinely undergo a pre-operative CT scan. Using the methodology described in the Komen et al paper,\textsuperscript{53} two independent radiologists will review the CT Abdomen/Pelvis to evaluate the extent of the calcification of the aorta and iliac vessels. The calcium mass, volume and plaque number in the aorta and each common iliac, internal iliac and external iliac vessel will be assessed (CRF D).

Statistics

The required specificity for the test to be useful:

Currently we routinely defunction patients with a leak risk of 15%. Therefore if the test has a positive predictive value 20% so that one in five (or more) patients picked up really did have a leak then this would guide practice. The risk of leak is 5% for all colorectal anastomoses combined. Based on this the following table gives specificities required which yield a PPV of 20% - the value depends on the sensitivity of the test and the prevalence. Hence these figures are for prevalence’s of 1% through to 5%. Ensuring that the specificity is over 80%, if the prevalence of leak is less than 3% we would require a specificity of 88% or higher.
prevalence of leak (%) | sensitivity of test (%) | 100 | 95 | 90 | 85 | 80
---|---|---|---|---|---|---
5 | 79% | 80% | 81% | 82% | 83% |
4 | 83% | 84% | 85% | 86% | 87% |
3 | 88% | 88% | 89% | 89% | 90% |
2 | 92% | 92% | 93% | 93% | 93% |
1 | 96% | 96% | 96% | 97% | 97% |

The required sample size:

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*These figures are based on a 5% leak rate.

If the sensitivity of the test was truly 85%, the specificity was 85%, and the prevalence of leak really is 5%, we need to have the lower limit of the confidence interval to be above 82% to be sure it is useful, which could be achieved with a sample size of 500. We plan to recruit 150 patients, this will allow us to look at a consecutive series of over 100 patients that have not leaked. We will then review the results, and a decide if there is scope to proceed to 500. If the specificity and sensitivity are very high (95%) we may obtain an answer without extending the study beyond 150 patients, if the specificity is very low we will not proceed to a further study and the test will be ruled out as useless.

4. Trial Conduct

Data Safety Monitoring and Ethics Committee

This study is being supported by the University of Birmingham. Data will be stored securely on a computerised databases (ACCESS).

A steering committee developed the protocol and will provide academic leadership for the overall conduct of the trial. Data will be transferred and stored electronically in accordance with NIHR recommendations. In line with Good Clinical Practice guidelines, all essential documentation and data will be retained for at least 15 years.
Trial Management Protocol
One named principle investigator (PI) will be recruited at each study site. With the support of the ABPI training they shall provide training in pre-operative data collection and ABPI recording (Form A). They will also be responsible for post-operative data collection (Form B and C). The data collection process is outlined in Figure 1.

Maintaining the equipment
The devices used for ABPI measurement will need maintaining and sporadically testing and calibrating. This will be carried out according to manufacturing guidelines.

Adverse Events
The ABPI is a non-invasive test and we do not anticipate any adverse events. Patients will not be informed of their ABPI result as this may adversely effect the outcome of the study.

5. Organisation

Each centre will designate individuals who would be chiefly responsible for local coordination of the clinical and administrative aspects of the study. The ABPI study Trial Office will provide as much assistance as they can to local co-ordinators and investigators in obtaining Trust approval in each centre and helping resolve any local problems that may be encountered.

Principal Investigator
Each Centre should nominate a Consultant Colorectal Surgeon to act as the local Principal Investigator and bear responsibility for the conduct of research at their centre. Close collaboration between all clinical teams is particularly important in order that patients for whom the ABPI Trial is an option can be identified sufficiently early for entry. The responsibilities of the local Principal Investigator will be to ensure that all medical and nursing staff involved in the care of potential patients are well informed about the trial and trained in trial procedures, including obtaining informed consent. The local PI should
liaise with the Trial Coordinator on logistic and administrative matters connected with the trial.

Central Coordination
The Trial Office at The University of Birmingham will coordinate the RM&G process and paperwork, ensuring that all appropriate conditions are met. The Trial Office will be actively involved in all site openings, and will provide the following trial materials:

- The Site File, containing all documentation required under the Medicines for Human Use (clinical Trials) Regulations 2004 to define the involvement of the centre in the trial.
- An Investigators folder containing printed materials, such as participant information sheets, and consent forms.
- An online data entry system, including individual log-in and passwords, guidance and data entry for CRF A, B and C will created for this study. These will be supplied to the three collaborating centre, after relevant authorisations have been obtained. Additional supplies of any printed material can be obtained on request. The Trial Office will maintain and monitor the database to ensure that it operates efficiently. The Trial Office will also ensure the day to day management of the trial, liaising with appropriate personnel in each trial site and providing administrative support for internal and external trial meetings (operations group, trial management group, data monitoring committee).

- The trial office will also be responsible for collection and checking of data (including managing any reports of serious adverse events), for reporting of serious and unexpected adverse events to the sponsor and regulatory authorities on behalf of the Chief Investigator and for analyses. The Trial Office will help resolve any local problems that may be encountered in trial participation and will ensure that local arrangements are made to avoid disruption to the trial when registrars move hospitals as part of their training. The Trial Office will also assist with the organisation of national meetings, training events and dissemination conferences.

Clinical Queries
During office hours, the clinical coordinators (see inside front cover for contact details) provide an on-call service for any clinical queries about the trial.
Funding and Cost Implications

We are currently applying for a research grant with the Bowel Disease Research Foundation (BDRF). In addition to the cost of running the trial, the grant will provide the funding for equipment required for the assessment of the ABPI in each unit.

Resources

We will require 3 of the following:

1. Huntleigh Handheld Doppler and D900 Vascular Probe (E28, D900), Huntleigh Healthcare, UK
2. Welch Allyn Durashock DS 66 Sphygmomanometer (SKU PART NUMBER: DS66-01-189), Welch Allyn, UK
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Publications

A meeting will be held after the end of the trial to allow discussion of the main results among the collaborators prior to publication. The success of the trial depends entirely on the wholehearted collaboration of a large number of doctors, nurses and researchers. For this reason, chief credit for the main results will be given not to the committees or central organisers but to all those who have collaborated in the trial. A writing committee will be convened to produce publications on behalf of the ABPI Study collaboration group. Centres will not be permitted to publish data obtained from participants in the trial that use trial outcome measures without discussion with the Chief Investigator and the TSC.

6. Research Governance

The conduct of the trial will be in accordance with the EU Directive on Clinical Trials (2001/20EC), the UK Medicines for Human Use (Clinical Trials) Regulations 2004 and the principles of the International Committee on Harmonisation of Good Clinical Practice Guidelines (E6) and any subsequent amendments.

Sponsor

National sponsorship will be provided by the University of Birmingham upon signing of the Clinical Study Site Agreement with each trial site.
Trials Unit
Data from this trial will be handled by the Academic Department of Surgery, University of Birmingham, which has substantial experience in, the design and conduct of cohort studies. The University of Birmingham recognises the responsibilities of a data management centre with respect to the ethical practice of research and the adequate protection of human subjects.

Confidentiality of Personal Data
The trial will collect personal data about participants, and medical records will be reviewed. Participants will be informed that their trial data and information will be securely stored at the academic department of surgery, and will be asked to consent to this. The University of Birmingham abides by the UK law Data Protection Act 1998. The data will be stored on a secure computer database, and all personal information obtained for the study will be held securely and treated as strictly confidential. Any data processed outside of the Birmingham University will be pseudoanonymised.

Indemnity
The ABPI study was developed by the West Midlands Research Collaborative. The University of Birmingham is the trial ‘sponsor.’ It should be noted, however, that negligent liability remains the responsibility of the hospital, whether or not a patient is part of a clinical trial, because of the duty of care that the hospital has for their patients.
7. References


18) Manifold, D Boyle N. Intraoperative Assessment of Colonic Perfusion Using Scanning Laser


8. Figures and Appendices

Figure 1  Flowchart illustrating study process
Figure 2  ABPI Technique, aide memoir.
Appendix A  Patient letter & information sheet
Appendix B  Patient consent sheet
Appendix C  GP letter
Appendix D  Pre-operative CRF (CRF A)
Appendix E  Post-operative CRF (CRF B)
Appendix F  CRF for defunctioned patients (CRF C)
Appendix G  Calcification scoring CRF (CRF D)

Figure 1. Flowchart Illustrating Study Process
Figure 2. ABPI Measurement

Standardised ABPI Measurement

Materials:

- Huntleigh Handheld Doppler and D900 Vascular Probe (E28, D900), Huntleigh Healthcare, UK
- Welch Allyn Durashock DS 66 Sphygmomanometer (SKU PART NUMBER: DS66-01-189), Welch Allyn, UK
- Welch Allyn Flexiport Large Long Adult Cuff size 12L for Durashock Sphygs (SKU PART NUMBER: REUSE-12L-1TPE), Welch Allyn, UK
- Welch Allyn Flexiport Small Adult Cuff size 10 for Durashock Sphygs (SKU PART NUMBER: REUSE-10-1TPE), Welch Allyn, UK

Method:

1. Patient supine for 5 minutes (then perform test with pt supine and the sphyg at chest level).
2. Appropriate cuff selection (aim for cuff width approx. 40% of limb circumference)
3. Measure systolic pressure at both brachial and record all values
   a. Identify pulse with Doppler probe
   b. Inflate cuff until signal disappears
   c. Inflate a further 20 mmHg
   d. Deflate slowly until signal reappears
4. Measure the systolic pressure in both feet, both DP and PT and record each value
   a. Ensure cuff is just above ANKLE (ie not mid calf)
   b. Identify pulse with Doppler probe (pt behind med maleolus, dp lateral to ext. hallucus longus tendon)
   c. Inflate cuff until signal disappears
   d. Inflate a further 20 mmHg
   e. Deflate slowly until signal reappears
5. Record each value in the notes on the CRF A.

References:
Dear

Recently you met the surgical team at the Hospital where you were offered an operation on your bowel. This operation is due to take place in the near future and as part of the planning for the operation you have been asked to attend a clinic to make sure you are as fit as possible for the operation.

As part of this assessment we routinely measure your blood pressure. In a study with the University of Birmingham we would like to ask your permission for the doctor or nurse who assesses you to take an extra five minutes to perform a more detailed assessment of your blood pressure by checking the blood pressure in your ankles at the same time as they measure the blood pressure in your arms. This is a pain free, simple test, which we already perform routinely in some clinics, and is known as the Ankle Brachial Pressure Index or ABPI for short.

We would like to know if measuring your ABPI would provide the surgical team with useful information, which may help to guide the type of operation that future patients with your condition have. A study like this has not been performed anywhere in the world, we do not as yet know if this is the case. We would be very grateful if you choose to spend the five minutes required to participate in the study. Whether or not you participate, this will not impact on your care but we believe this will help to guide the type of operation for patients with a similar problem to yours in the future.

We have attached an information sheet about the study, you may also want to ask the doctor or nurse who sees you in your preoperative assessment clinic about the study.

Best Wishes,

Dr Nick Battersby
On behalf of the ASLAN study team
Contact: aslan@wmresearch.org.uk
The ASLAN Study

Patient Information Sheet

Summary of invitation to take part in a feasibility study called ASLAN

- Your surgeon has recommended you undergo an operation on your abdomen (tummy) involving removing a section of the large bowel. In most cases we would expect to then join the bowel back together. In the vast majority of cases the new join heals well but your surgeon will have indicated to you that in a small number of cases there can be a problem with healing that leads to a leak from the join. The frequency of this happening varies from 2 out of 100 operations to 14 out of 100, depending on the type of operation performed. This can sometimes have serious side effects.

- This hospital is taking part in a feasibility study called the ASLAN study, which aims to find out whether a simple blood pressure test before your operation can predict the likelihood of patients developing a leak.

- If you choose to come into this trial, your Ankle-Brachial Pressure Index (ABPI) will be checked before your operation, normally at the time of your normal pre-operation assessment visit.

- This test takes about five minutes to perform and is painless. It is just like having a normal blood pressure test on your arm; we then also repeat the same blood pressure test on your lower legs.

- All patients are then closely observed to determine which ones have a normal recovery after the operation and which ones may develop problems. This observation involves no extra effort from you, and you are not required to fill any further forms in or return to the hospital at a later date.

- You do not have to take part in the ABPI study, and if you decide not to, no-one will think badly of you and this will not affect the quality of your care in any way.
What is the purpose of the ASLAN study?
As part of your treatment you will be undergoing an operation on your abdomen. During the operation your surgeons will remove a piece of bowel. In most cases we would expect to join the bowel back together. This new join is called an anastomosis.

In the vast majority of cases the new join heals well and there are no problems. Your surgeon will have indicated to you that in a small number of cases there can be a problem with healing that leads to a leak from the join. The frequency of this happening varies from 2 out of 100 operations to 14 out of 100, depending on the type of operation performed. This can sometimes have serious side effects.

Lots of research has been carried out to try and work out why some joins leak. Amongst other factors, a good blood supply to the area of the join has been shown to be very important.

At present, there is no way of predicting before an operation how good the blood supply to the area of a join may be. This is the aim of the ASLAN study.

We hope to show that a simple blood pressure test which can be performed before an operation helps to predict how good the blood supply to the bowel is, and therefore how likely a join in the bowel is to break down (leak). In the future, surgeons may then be able to use this information when planning operations.

At present, this is a feasibility study. What we mean by this is that we are currently carrying out the study in a small number of hospitals (three) to check that the study design works as planned and that enough surgeons and patients are happy to take part. If the study plan works and the results generated do suggest that this simple test may predict for a bowel leak then we would carry the study forwards on a much larger, national scale. This would involve many more patients at hospitals all around the country.

What is ABPI?
ABPI stands for Ankle Brachial Pressure Index.
In simple terms, it is a measurement of how good the blood pressure in your legs is compared to the blood pressure in your arms.
How is it measured?
ABPI can be measured very quickly and without discomfort.

Your blood pressure is measured in each arm, using a cuff which is blown up and then released. The blood pressure is then checked in both lower legs using the same method. A result is then calculated. This is reported as a number between 0.1 and 1.7.

Why is it important?
ABPI has been used for many years by vascular specialists as a simple way of assessing for narrowing or ‘furring-up’ of the leg arteries of a patient. Research has shown it produces reliable results which match well with the state of the arteries at operation and a low ABPI can indicate problems with the circulation in the legs.

Recently, studies have shown that ABPI may also predict problems with the circulation of blood to the heart, brain and kidneys. The role of this test in the circulation to the gut has never been looked at before.

What should my ABPI be?
Research has shown that a ‘normal’ ABPI result should be between 0.9 and 1.4 for each leg.

What happens if my result is abnormal?
Unfortunately we cannot tell you result of the test until the study is complete. If you are having pains in the back of your legs when you are walking you should organise to see your GP.

Will taking part in this study alter my operation plans or treatment?
No. Taking part will not change your operation or treatment in any way.

Do I have to take part?
No. Taking part is purely optional and your treatment will not be affected in any way should you choose not to.

If I take part what would I have to do?
You will have your ABPI checked when you come for your pre-operative assessment. After that you continue with your operation and treatment as planned.

One of our investigators will then check up at a later date (by reading your notes and speaking to your surgeon) how the surgery went and how your recovery was.

Will my taking part be kept confidential?
If you decide to take part in the ABPI study, all information collected about you will be kept strictly confidential in the same way as all of your medical records.

Information about your operation and follow-up will be sent by your doctors to the ASLAN study office at the University of Birmingham, where it will be securely stored under the
provisions of the 1998 Data Protection Act. All information about you and your treatment will remain confidential.

With your permission, your relevant medical notes may be inspected by authorised individuals from the ASLAN study office. They also may be looked at by regulatory authorities to check that the study is being carried out correctly.

What will happen to the results of the study?
Once this preliminary study has finished the results will be carefully analysed. If the study has worked as we hope then it will be repeated at a number of centres across the country. Patients who come into the study will be able to see the results on the study website (see below) when they become available.

At the end of the study all data will be securely archived in line with regulations. Should you decide at any point to withdraw consent for your data to be used it will be confidentially destroyed.

What will happen if I don’t want to carry on with the study?
You can decide not to continue with study follow-up at any time but, if you do, we would still like your data to remain on file and be included in the final study analysis unless you specifically ask to be excluded.

What if something goes wrong? What if I have an anastomotic leak?
It is always possible to develop an anastomotic leak after an operation like yours and we cannot guarantee that you will not get one, regardless of whether or not you participate in the ASLAN feasibility Trial. If you do develop one, we will administer all standard surgical and medical care as necessary in the usual manner. It should be noted that this study is ‘observational’ in that we are only performing a simple extra test (the ABPI measurement) before your operation but actually changing any aspect of your operation or it’s after-care. As such your participation in this study would neither increase nor decrease the likelihood of you having a leak or other problem after surgery.
Whether or not you take part in the study, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms would be available to you. Taking part in the study would not affect your legal rights.

Who is organising the study?
The ABPI study was developed by the West Midlands Research Collaborative and is funded by the Bowel Diseases Research Foundation, a charity affiliated to the Association of Coloproctologists of Great Britain and Ireland.
Who has reviewed this study?
All research in the NHS is reviewed by an independent group of people called the Research Ethics Committee to ensure your safety, rights, wellbeing and dignity. This study has passed all of these reviews.

Where can I get further information?
If you have any further questions about your operation or this study please discuss them with your surgeon or local study investigator, as below:

<table>
<thead>
<tr>
<th>Name</th>
<th>.................................................................</th>
</tr>
</thead>
<tbody>
<tr>
<td>Position</td>
<td>.................................................................................</td>
</tr>
<tr>
<td>Contact number</td>
<td>.................................................................................</td>
</tr>
</tbody>
</table>
1. I confirm that I have read and understood the information sheet for the ASLAN feasibility study and have had the opportunity to ask questions.

2. I understand that my participation in this study is voluntary and that I may withdraw at any time without my medical and legal rights being affected.

3. I understand that my participation in this study will not alter in any way the treatment course planned for me.

4. I understand that a copy of my consent form and information relating to this study will be supplied to the study coordinators at the university of Birmingham.

5. I understand that sections of my medical notes and investigations may be looked at by responsible individuals from the ASLAN feasibility study office, or from regulatory authorities or from the NHS trust, where it is relevant to my taking part in this study. I give permission for these individuals to have access to my records.

6. I have agreed to take part in the above study and give permission for my GP to be informed of my participation.

Signature ...................................................... ......................................................
(participant) (investigator)

Print name ...................................................... ......................................................
(participant) (investigator)

Date ......................................................
Dear Dr ______________________________

Re:

Your patient consented to taking part in the above study to investigate the potential role of ankle brachial pressure index (ABPI) in the prediction of anastomotic leakage in Colorectal surgery.

As part of this study they have today had their Ankle Brachial Pressure Index measured as part of their routine pre-operative assessment, unfortunately we are blinded to these results and will not be able to provide them to you or your patients. The ABPI result obtained today will not affect your patient’s planned Colorectal surgery.

Yours sincerely,

On behalf of the ASLAN Committee
Appendix D

CRF A- Demographic Data and Preoperative Assessment

CONFIRMATION OF ELIGIBILITY TO STUDY – Is the patient undergoing an elective colorectal resection?

### Patient Information

<table>
<thead>
<tr>
<th>Patient Name</th>
<th>ESTIMATED DATE OF OPERATION: ........../........../........... &lt;br&gt; dd mmm yyyy</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.O.B:</td>
<td>DATE OF THIS ASSESSMENT: ........../........../........... &lt;br&gt; dd mmm yyyy</td>
</tr>
<tr>
<td>Hospital</td>
<td></td>
</tr>
<tr>
<td>Number:</td>
<td></td>
</tr>
<tr>
<td>Consultant:</td>
<td></td>
</tr>
</tbody>
</table>

Person completing this electronic form: .................................................................
Person performing ABPI measurement (if different): ..............................................

### Patient Characteristics

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male □</th>
<th>Female □</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (or weight and height)</td>
<td>.......... kg/m²</td>
<td>............kg ............... cm</td>
</tr>
<tr>
<td>Diabetic?</td>
<td>NO □</td>
<td>YES □</td>
</tr>
<tr>
<td>Hypertensive ?</td>
<td>NO □</td>
<td>YES □</td>
</tr>
<tr>
<td>Previous MI or Angina?</td>
<td>NO □</td>
<td>YES □</td>
</tr>
<tr>
<td>Previous Stroke?</td>
<td>NO □</td>
<td>YES □</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Smoker?</th>
<th>Never smoked □</th>
<th>Ex-smoker □</th>
<th>Current smoker □</th>
</tr>
</thead>
<tbody>
<tr>
<td>(when stopped? ......)</td>
<td></td>
<td></td>
<td>(Pack years.........)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(20/day for a yr = 1 pack yr)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Non Drinker □</th>
<th>&lt;10 units/wk □</th>
<th>10-30 units/wk □</th>
<th>&gt;30 units/wk □</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 unit = 1 bottle of beer, 1 glass of wine or 1 measure of spirits.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Peripheral Vascular Disease?

| Current Claudication       | NO □   | YES □   |
| Rest pain                 | NO □   | YES □   |
| Previous Investigated     | NO □   | YES □   |
| Previous Surgery          | NO □   | YES □   |

Medications:

| Taking a Statin           | NO □   | YES □   |
| Taking an Antiplatelet    | NO □   | YES □   |
| Taking Antihypertensive   | NO □   | YES □   |
Appendix D

CRF A- Demographic Data and Preoperative Assessment (continued)

On Steroids or Immunosuppressed

NO ☐ YES ☐

within past 6 months?

Indication and duration .................................

Drug + dose ..............................

Pre-op Radiotherapy?  NO ☐ YES ☐

Previous Pelvic Radiotherapy  NO ☐ YES ☐

Blood Pressure Values

Right Brachial Pressure .................

Right Brachial Pressure .................

Right DP value .................

Left DP value .................

Right PT value .................

Left PT value .................

To the patient:

Was measuring the ABPI acceptable?  Yes ☐ NO ☐

Amount of discomfort?  0 1 2 3 4 5 6 7 8 9 10

BP record  blood test
### CRF B - Follow-up data (6 weeks)

#### Patient Information

<table>
<thead>
<tr>
<th>Patient Name</th>
<th>D.O.B</th>
<th>ACTUAL DATE OF OPERATION: ……/……/…… dd mmm yyyy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Number:</td>
<td></td>
<td>DATE OF THIS REVIEW: ……/……/…… dd mmm yyyy</td>
</tr>
</tbody>
</table>

Person completing this electronic form: ............................................................

#### Anaesthetic details and Operation Characteristics

<table>
<thead>
<tr>
<th>ASA</th>
<th>I (Normal healthy patient)</th>
<th>II (Patient with mild systemic disease)</th>
<th>III (Patient with severe systemic disease)</th>
<th>IV (Patient with severe systemic disease that is a constant threat to life)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidural?</td>
<td>NO □</td>
<td>YES □</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of operation</td>
<td>&lt;2hrs</td>
<td>2-4hrs</td>
<td>&gt;4hrs</td>
<td></td>
</tr>
<tr>
<td>Laparoscopic Operation?</td>
<td>NO □</td>
<td>YES □</td>
<td>Converted □</td>
<td></td>
</tr>
</tbody>
</table>

Anastomosis: Handsewn / Stapled.

Device Type..........................................................................................

Actual Operation performed*: ........................................................................

* as per operation note.

<table>
<thead>
<tr>
<th>Defunctioning stoma?</th>
<th>NO □</th>
<th>YES □</th>
<th>Type ..............................................</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proven malignancy?</td>
<td>NO □</td>
<td>YES □</td>
<td></td>
</tr>
</tbody>
</table>

Post-op critical care? ITU nights ..... HDU nights ..... |

Total Length of stay: ...... days

Post operative Death NO □ YES □ Date ……/……/……

If YES: details of cause of death..................................................................

ASA: American Society of Anesthesiologists
I Normal healthy patient.
II Patient with mild systemic disease.
III Patient with severe systemic disease.
IV Patient with severe systemic disease that is a constant threat to life.
V Moribund patient who is not expected to survive without the operation.
ANASTOMOTIC BREAKDOWN or CONFIRMED INTRA-ABDOMINAL OR PELVIC SEPSIS?

If YES:  Date Diagnosed ..................................

Mode of Diagnosis:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>USS</td>
<td>NO □</td>
</tr>
<tr>
<td>CT</td>
<td>NO □</td>
</tr>
<tr>
<td>REOPERATION</td>
<td>NO □</td>
</tr>
</tbody>
</table>

Re-admitted post operatively?

<table>
<thead>
<tr>
<th></th>
<th>YES □</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO □</td>
<td>YES □</td>
</tr>
</tbody>
</table>

If YES:  Date…/…/….  Length of stay (days)………  Diagnosis..........................

Other post-operative complication?

<table>
<thead>
<tr>
<th></th>
<th>YES □</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>NO □</td>
</tr>
<tr>
<td>Pnuemonia</td>
<td>NO □</td>
</tr>
<tr>
<td>Wound infection</td>
<td>NO □</td>
</tr>
<tr>
<td>Other</td>
<td>NO □</td>
</tr>
</tbody>
</table>

Troponin Value…… Troponin I □ or T□

Details ………………………..
# CRF C - FOR PATIENTS WITH DEFUNTIONING ILEOSTOMY / TRANSVERSE COLOSTOMY

## Patient Information

<table>
<thead>
<tr>
<th>Patient Name</th>
<th>DATE OF PRIMARY OPERATION: ……/……/…… dd mmm yyyy</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.O.B</td>
<td></td>
</tr>
<tr>
<td>Hospital Number:</td>
<td>THIS FORM COMPLETED: ……/……/…… dd mmm yyyy</td>
</tr>
</tbody>
</table>

Person completing this (electronic) form: .................................................................

## Operation Characteristics

<table>
<thead>
<tr>
<th>Stoma type?</th>
<th>Loop ileostomy / transverse colostomy / other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-------------------------------------------</td>
</tr>
</tbody>
</table>

Has the stoma been reversed yet?  
No ☐ Yes ☐ (please go to section 2)

If no, why not:  
- just not scheduled yet ☐  
- pt too unwell ☐  
- pt doesn’t want it ☐  
- other ☐

Is there a possibility it may be closed in the future?  
No ☐ Yes ☐

---

### Section 2

Was the anastomosis assessed radiologically prior to reversal?  
No ☐ Yes ☐

If Yes, method of assessment  
- Contrast Enema ☐  
- CT Abdo/Pelvis ☐  
- Other……………………………

Evidence of anastomotic failure radiologically?  
No ☐ Yes ☐

- Contrast leak ☐  
- Pelvic collection ☐

Other. eg. Palpable defect in anastomosis………………………………………
Section 3

Date of reversal ....../..../....... (dd/mm/yyyy)

Length of stay after stoma reversal .......... days

Method of closure of bowel (if known) Sutured □ Stapled □

Method of skin closure (if known) Purse-string □ subcuticular continuous absorbable □
Skin clips □ Interrupted non-absorbable □
Left open □

Other:
____________________________________________________________________________
____________________________________________________________________________
____________________________________________________________________________

Any complications after closure (details)
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
## CRF D - Radiological Data

### Patient Information

<table>
<thead>
<tr>
<th>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Name</td>
<td>………………………………………...</td>
</tr>
<tr>
<td>Hospital ID number</td>
<td>………………………………………...</td>
</tr>
<tr>
<td>Date of Birth</td>
<td>……/…../…….</td>
</tr>
<tr>
<td>Person completing this form</td>
<td>………………………………………...</td>
</tr>
<tr>
<td>Scan Date</td>
<td>……/……/…….</td>
</tr>
</tbody>
</table>

### Technical Details

<table>
<thead>
<tr>
<th>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDCT scanner</td>
<td>4 / 8 / 16 / 64 / 128 / 256 / other</td>
</tr>
<tr>
<td>Slice Thickness</td>
<td>2mm / 5mm / other</td>
</tr>
<tr>
<td>IV Contrast</td>
<td>No ☐ Portal Venous Phase ☑ Arterial Phase ☑</td>
</tr>
<tr>
<td>Calcification Software</td>
<td>Siemens / other</td>
</tr>
<tr>
<td>Scoring Threshold</td>
<td>500 hounsfield / other</td>
</tr>
</tbody>
</table>

### Radiological Details

<table>
<thead>
<tr>
<th>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMA Patent</td>
<td>Yes / No / Uncertain</td>
</tr>
<tr>
<td>Aorta</td>
<td>Plaque Number…………… Calcium Volume…………… Calcium Mass…………… Calcium Score……………</td>
</tr>
<tr>
<td>Right CI</td>
<td>Plaque Number…………… Calcium Volume…………… Calcium Mass…………… Calcium Score……………</td>
</tr>
<tr>
<td>Right II</td>
<td>Plaque Number…………… Calcium Volume…………… Calcium Mass…………… Calcium Score……………</td>
</tr>
<tr>
<td>Right EI</td>
<td>Plaque Number…………… Calcium Volume…………… Calcium Mass…………… Calcium Score……………</td>
</tr>
<tr>
<td>Left CI</td>
<td>Plaque Number…………… Calcium Volume…………… Calcium Mass…………… Calcium Score……………</td>
</tr>
<tr>
<td>Left II</td>
<td>Plaque Number…………… Calcium Volume…………… Calcium Mass…………… Calcium Score……………</td>
</tr>
<tr>
<td>Left EI</td>
<td>Plaque Number…………… Calcium Volume…………… Calcium Mass…………… Calcium Score……………</td>
</tr>
</tbody>
</table>

### Maximum Aorta diameter (UK Screening Trial defn):

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 3cm</td>
</tr>
<tr>
<td>Small</td>
<td>3 - 4.4</td>
</tr>
<tr>
<td>Medium</td>
<td>4.5 - 5.4</td>
</tr>
<tr>
<td>Large</td>
<td>5.5 &gt;</td>
</tr>
</tbody>
</table>