From FOBT to FIT: Making it work for patients and populations

National Conference: Royal College of Physicians 26th February 2019
Program Organiser Dr Robert Logan King's College Hospital.

Background

The 2015 updated NICE Suspected Cancer Referral Guidelines NG12 included the advice that patients with low risk of Colorectal Cancer (CRC) have a faecal occult blood test (FOBT). However, because of the limitations of that test, many regions did not offer this test.
In 2018 NICE Technical Guidance Document DG30 concluded that Faecal Immunocehemical testing (FIT) should be used to define the threshold for ruling out CRC.

Notes &Feedback

This conference was organised to bring together those working across the UK to share information on research and opinion on the use of FIT in the diagnostic pathway for CRC. To date there remains lack of consensus or clarity of how to implement or commission use of FIT.

Note that all the Pioneer Sites which presented at the conference focused on high risk patients who complied with the NG12 suspected cancer guidelines, that is TWW referrals. The SW Alliance FIT Pilot work was not included in the conference.

In the South West the work which is being done on FIT is on the cohort of low risk patients who would otherwise not have been investigated. Given the unique nature of the SW pilot there will be national attention and scrutiny of the findings. The final outcomes of the pilot will not likely be shared prior to peer review publication.

Take Home Points

- FIT is not the answer to the issue around lack of endoscopy resource. Long-term this must be addressed.
- Focusing on screening is where improvements in outcomes for CRC and increase in stage I & II diagnoses will be achieved.
- Despite negative predicative values >99% cancers will be missed in the high-risk patient cohort.
- FIT should be viewed as a risk assessment test, not a diagnostic test.
- FIT is a quantitative test that is influenced by gender, lifestyle, co-morbidities, ethnicity and family history. This is likely to lead to it being used in a more targeted way in the future
- Beta Thalassaemia major causes false negative results.
- FIT with anaemia and polycythaemia increases the risk of CRC markedly, this is an opportunity forfurther risk stratification, and machine learning.

Laboratory Implications for testing FIT.

- There are four different assay test systems available, and they give different results, so the a 10ug reading on one machine does not equate to a 10ug reading on another.
- Samples in stool pots should not be used because of degradation of the specimen.
- There is discussion on the various types of sample "pickers" however they all have a buffer solution which helps preserve the specimens.

- Laboratories are to be asked to report on their Limit of Detection LOD. This is distinct from the accuracy which is usually 95%. The Limit of Quantification LOQ is the lowest level that can be reliably measured.
- A nationally agreed standard is being developed.
- 10ug threshold is used by most labs, but some report on a FIT as low as 2ug.
- For screening which is aimed at asymptomatic populations a level of 120ug has been set by NICE.
- Note that this level is five times higher than in equivalent affluent countries, which have much better CRC outcomes.

Cancer Alliance Data Evaluation Service CADEAS

This is an NHSE evaluation providing analysis to support policy development, to support and spread the intervention and add value to Alliances. It is developing a tool to anticipate the impact of FITon endoscopy services and develop a road map for the NHS on the roll out of FIT.
There are six Pioneer groups across the UK where the use of FITin high risk (TWW Compliant) patients.

6Key Clinical Questions

- Is FIT effective in ruling out CRC in high risk patients.
- How frequent is CRC missed?
- What are the cut off levels of FIT for various groups?
- What is the impact on endoscopy?
- What is the acceptability to GPs and patients?
- What are the barriers to implementation?

Initial Findings

- Sensitivity 84-97%
- Anaemia may give false negative results
- There are demographic issues
- Colonoscopy can be avoided in 70% of patients
- Could the low risk group increase the endoscopy demand?
- There is impact on other services such as CT abdo and flexi sig.
- The barriers include confusion on various risk groups & FIT levels. Clarity is needed.

Pioneer Groups

There is work being done on FIT in various Poineer Sites across UK including Nottingham, Leicester, Croydon and York. They all focus on high risk patients, however each have different protocols, inclusion and exclusion criteria, used different assay machine, as well as different methods of collecting the stool samples.

Clinical Opinions & Project Reports

Mr Michael Macheseny from Barts

- the UK outcomes for CRC still lag behind other wealthy nations
- And compares poorly in the rate of colonoscopy or provision of CT scans.
- He was of the opinion that TWW referrals would not impact CRC survival
- He felt that improving screening uptake is where an impact could be made.
- The UK is an outlier in the use of FIT in symptomatic patients.
- Emergency presentation of CRC has not declined
- Removal of adenomas is the way of reducing the incidence of CRC

Dr James Turvill York District Hospital

- Is of the firm belief the FIT is a risk assessment tool, NOT a diagnostic test
- Even at FIT level 2ug, with a negative predictive Value (NPV) of 99.7% cancers will be missed especially Estrada's-colonic cancers such as pancreatic or Gynae.
- Management of high risk patients with negative FIT is a huge concern.
- Depending on where the level of FIT is set, the impact on endoscopy will vary in commissioning terms, but the number of scope needed to be done to find each cancer will vary, and cancers will still be missed.

Dr Alan Banerjea Nottingham University

- Since the introduction of FIT they have seen a steady increase in referrals.
- There were now more TWW than routine referrals
- They made a decision to do more CTC than colonoscopies
- More than 55% of cancers were stage I or II
- Audit of symptoms: Anaemia increased the risk of CRC 3x; FIT + anaemia increased risk 10%; platelets >400 also increased the risk of CRC
- All stage I cancers had FIT <150ug
- They concluded that FIT was better than symptoms at identifying risk; referrals will not be reduced; some cancers will be missed; but the right patients will be scoped.

Prof Stephan Halloran University of Surrey

- FIT is a new test, but we have been using it like the old FOBT, and applying old rules to it.
- Are we trying to improve survival of CRC or manage the endoscopy waits & resources?
- It is a quantitative test, so it can be risk stratified or individualised.
- Gender difference, men have a 40% greater risk than women
- Life style, co-morbidities, ethnicity and family history all have an impact on FIT
- Personalised population screening?? Is this the way forward?.

Summary

There are number of research projects currently underway across the UK, in Secondary Care which focus mainly on with patients at high-risk of CRC and which are awaiting full reporting.
The six key questions posed by the CADEAS group are yet to be answered definitively.
For commissioners the use of FIT in high risk symptomatic patients will result if fewer colonoscopies, but this will be at the risk of missed cancers so that safety netting and follow up of FIT negative patients in both low and high-risk symptomatic patients is a key piece of information required.
The Pilot within South Wet Cancer Alliances is unique in that it is limited to a specific group of patients in Primary Care with low risk symptoms of CRC and it is yet to be seen the impact on the rate of referral for colonoscopy