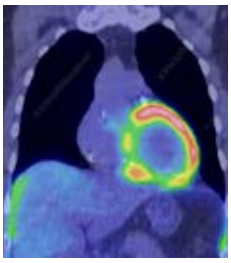
education

FROM THE JOURNALS Edited highlights of weekly research reviews on https://bit.ly/2PLtil8

A withdrawal warning



This open label pilot trial randomised patients with dilated cardiomyopathy who were now asymptomatic to phased treatment withdrawal versus continued treatment. Forty four per cent of patients who had treatment withdrawal relapsed, while no patients relapsed in the continued treatment group. These data suggest that the resolution of cardiac function impairment may not necessarily represent recovery from dilated cardiomyopathy. This type of research is highly commendable as it can provide the data needed to accurately inform patients of the risks of coming off medications if they wish to do so. The impact of this work could have been even greater if it had been double blinded.

Lancet doi:10.1016/S0140-6736(18)32484-X

Troponin for stable coronary artery disease

The study question for Hammadah and colleagues was whether high sensitivity troponin could be useful for excluding inducible myocardial ischaemia in patients with known coronary artery disease. The apparent rationale for the study was the overuse of stress testing. They found inducible ischaemia and cardiovascular events to be unlikely with a very low troponin result. These data are interesting, but I'm not sure that the right question was asked in the context of a mostly asymptomatic population of people with known coronary artery disease. I question whether finding ischaemia in these patients has a meaningful impact on their management. Perhaps the implication is that those with inducible ischaemia should get invasive angiograms and be considered for revascularisation, but this has no evidence of prognostic benefit, so why test asymptomatic people?

Ann Intern Med doi:10.7326/M18-0670

A hypothesis on inflammation and CVD

There is a hypothesis that inflammation begets atherosclerosis. The CIRT investigators tested methotrexate (for inhibition of inflammation) for secondary prevention of cardiovascular disease, but unfortunately there was no benefit. This was even when they expanded the primary endpoint to include hospitalisation for unstable angina that led to urgent revascularisation (the aim being to have more events and therefore needing to enrol fewer patients to show a difference). Before the change in primary endpoint had been fully implemented, the trial was stopped early for futility. The golden bullet for cardiovascular prevention is far from close.

N Engl J Med doi:10.1056/NEJMoa1809798

Alex Nowbar is a clinical research fellow at Imperial College London

Nitrate for heart failure

The INDIE-HFpEF trial randomised patients to three times a day inhaled sodium nitrite or placebo to see if it would improve exercise capacity in patients with heart failure with preserved ejection fraction. The double blind crossover trial design seems flawless. Despite promise from preliminary work before this trial, there was no statistically significant difference between groups. Heart failure with preserved ejection fraction remains an enigma.

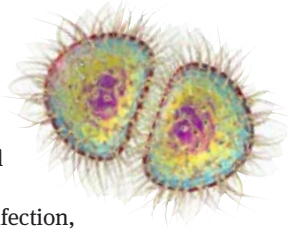
JAMA doi:10.1001/jama.2018.14852

A PIONEER-HF promise

The double blind PIONEER-HF trial randomised more than 800 patients with acute decompensated heart failure to sacubitril-valsartan or enalapril. In this trial, the medication was carefully initiated in inpatients and the primary endpoint was a change in N-terminal pro-B-type natriuretic peptide concentrations (NT-proBNP). There was a much greater reduction in the NT-proBNP concentration with sacubitril-valsartan compared with enalapril with a similar safety profile. I am surprised by this choice of non-clinical primary endpoint, but they did find fewer patients had hospitalisation for heart failure with sacubitril-valsartan.

N Engl J Med doi:10.1056/NEJMoa1812851

A textbook trial for new gonorrhoea antibiotic



This non-pharma funded US randomised controlled trial of zoliflodacin for urogenital gonorrhoea infection showed high microbiological cure rates. It wasn't as good as the control (ceftriaxone) for pharyngeal infection, especially when using a lower dose, but was otherwise promising (for rectal and urogenital disease) with no alarming safety signals. It was not blinded. Watch this space, I suppose.

N Engl J Med doi:10.1056/NEJMoa1706988

All roads lead to paglaflozins

This meta-analysis of three large randomised controlled trials confirms the benefit of sodium-glucose cotransporter-2 (SGLT2) inhibitors in reducing hospitalisations for heart failure in patients with type 2 diabetes. Interestingly, this benefit was seen in patients with and without a history of heart failure. For a moment, I'll consider something other than hearts though. Developed for use in those with type 2 diabetes, these drugs also reduced the risk of progression of renal disease. So, from this analysis at least, it would seem that for patients with type 2 diabetes, all roads lead to a SGLT2 inhibitor—especially if they have established cardiovascular disease.

Lancet doi:10.1016/S0140-6736(18)32590-X

Investigating sudden hearing loss in adults

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CPD READING
0.5 HOURS

A 55 year old woman presented with difficulty in hearing from the left ear. She first noticed this when she found it difficult to hear her husband over dinner. She also described a feeling of dizziness, where the room spins around, and ringing in the left ear. She was otherwise well. Clinical examination revealed a normal tympanic membrane.

Hearing loss affects 1 in 6 adults and has an enormous personal, social, and economic impact.[1] Patients may be frightened by the sudden loss of hearing, and tinnitus can cause anxiety. Prompt diagnosis and management may improve hearing recovery.[2]

In this article, we review the assessment of sudden hearing loss in adults and provide an overview on initial diagnostic tests. A lack of specialist diagnostic tests within the primary care setting makes the condition challenging to diagnose, and an awareness and high index of suspicion are required when non-specialists are faced with a patient with acute hearing loss.

Box 1 lists common causes of conductive and sensorineural hearing loss.

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EDUCATION INTO PRACTICE

- How would you evaluate a patient with sudden sensorineural hearing loss?
- What signs should prompt referral to ENT for further testing?
- How will you explain to your patient specialist investigations that may be required?

WHAT YOU NEED TO KNOW

- Pure tone audiometry is the gold standard investigation to diagnose the type and severity of hearing loss
- Offer referral for people with sudden sensorineural hearing loss, which is an acute otological emergency
- Magnetic resonance imaging is recommended to rule out acoustic neuroma as a cause for sudden sensorineural hearing loss

What tests should I do?

Take a history (box 2) and examine the patient to narrow the cause of the hearing loss and to assess the degree of urgency for investigation and treatment.

Non-specialists can perform otoscopy, tuning fork testing, and free field testing[3-6] to

- confirm that there is hearing loss
- differentiate conductive from sensorineural loss.

These test results will be helpful when making a referral to ear, nose, and throat (ENT) specialists, who can advise on further investigation and management.

• **Otoscopy**—examination of the tympanic membrane and external auditory canal to exclude certain causes of conductive hearing loss (box 1). An ENT specialist would remove any wax present from the ear to visualise the entire tympanic membrane and because this may be contributing to the hearing loss.[1]

• **Tuning fork testing (Rinne's and Weber's tests)** can help make a preliminary diagnosis of conductive or sensorineural hearing loss where audiometry facilities are not available.[3] Ideally, use a 512 Hz tuning fork. The sound emitted from vibration of higher frequency tuning forks (eg, 1024 Hz tuning forks) decays too quickly for routine testing. Lower frequencies (eg, 256 Hz) results in vibrotactile feedback (ie, the tone is "felt" as well as heard), leading to test bias, ie, the patient may feel the noise within the ear and therefore the clinician may be falsely reassured that hearing is normal (false positive).[3]

• **Free field hearing tests (whispered voice testing)** indicate the severity of hearing loss. They are not as reliable as pure tone audiometry,[3 4] but are immediately available to non-specialist clinicians. On a pure tone audiogram, patients with a hearing loss of >30 dB HL are typically unable to hear a whispered voice 60 cm from the test ear (sensitivity 95%, false-positive rate 10%').[5]

• **Neurotological and balance assessment** in patients with coexisting vertigo can help identify a vestibular pathology such as Ménière's disease, acoustic neuroma, perilymphatic fistula, and acute ischaemia of the labyrinth or brainstem.[6] This includes Romberg's testing, cerebellar assessment, full cranial nerve examination assessing for cranial nerve deficits (including assessment for nystagmus), and Unterberger's (stepping) testing. In the latter test, the patient is asked to march on the spot with their eyes closed and their arms outstretched. Rotation (>45°) to one side may indicate an ipsilateral vestibular lesion. Further details are described elsewhere.[6]

Box 1 | Common causes of adult onset hearing loss

Conductive hearing loss

Caused by any pathology in the external ear, tympanic membrane, middle ear air space, or ossicles, ie, structures that "conduct" sound waves to the cochlea:

- ear wax and foreign bodies
- otitis externa
- otitis media (acute or chronic; serous or suppurative) ‡
- tympanic membrane perforation
- cholesteatoma
- temporal bone trauma (resulting in haemotympanum or ossicular disruption) *
- otosclerosis (stapes fixation)

Sensorineural hearing loss

Caused by abnormalities of the cochlea, auditory nerve, or other structures that translate neural impulses to the brain:

- presbycusis (age related hearing loss)
- Ménière's disease
- acoustic neuroma (vestibular schwannoma) and other cerebellopontine angle lesions
- temporal bone trauma (resulting in otic capsule disruption) *
- late onset hereditary hearing loss
- noise induced hearing loss
- infections, eg, following meningitis, HIV, syphilis
- vascular causes (eg, apoplexy)
- autoimmune inner ear disease (eg, Cogan's syndrome)
- idiopathic sensorineural hearing loss *

‡ Refer adults of Chinese or southeast Asian family origin who have hearing loss and a middle ear effusion (especially unilateral) not associated with an upper respiratory tract infection on the 2 week pathway to ear, nose, and throat specialists as these symptoms may be associated with a nasopharyngeal carcinoma[1]

* Urgent referral to ENT/emergency department is indicated

Box 2 | History

Ask about

- The pattern of hearing loss:
  When did it start and how long did it last?
  - Did anything seem to trigger the hearing loss, such as exposure to loud noise?
  - Does the hearing loss affect only one ear, or both?
  - What was hearing like before, including in the opposite ear?
  - Has the hearing come and gone? Ménière's disease typically presents with unilateral, fluctuating hearing loss, often leading to permanent low frequency sensorineural hearing loss
- Associated symptoms:
  - otorrhoea (ear discharge)
  - otalgia (ear pain)
  - vertigo
  - tinnitus
  - aural fullness (sensation of pressure within the ear)
  - facial weakness and/or other neurological symptoms suggestive of central nervous system involvement.
- Treatment received to date (eg, courses of steroids)
  - Drug history: recent use of ototoxic medications such as aminoglycosides, furosemide, cisplatin, and quinine?
- Medical history such as previous sudden sensorineural hearing loss, head injury, cerebrovascular accidents, barotrauma, Ménière's disease, previous otological surgery
- Family history of hearing loss at a young age in first degree relatives, which may indicate a genetic cause such as otosclerosis

Box 3 | Red flags for referral

The hearing loss is

- sudden or rapidly progressive +/– vertigo (over a 72 hour period). This is an acute otological emergency*
- progressive, ie, worsening over time
- unilateral/asymmetric (with or without tinnitus)**
- bilateral and profound (›95 dB HL; box 4)
- associated with other symptoms, such as otorrhoea (which may indicate chronic ear disease) or facial nerve palsy
- associated with head trauma*
- in an immunocompromised patient with accompanying otalgia with otorrhoea*

* Urgent referral to ENT/emergency department is indicated

**Acoustic neuroma needs to be excluded

Box 4 | Degree/severity of hearing loss based on pure tone audiogram

Normal ‹20 dB HL
Mild: 20-40 dB HL
Moderate: 41-70 dB HL
Severe: 71-95 dB HL
Profound ›95 dB HL

What is the next investigation?

People with hearing loss frequently require referral to ENT or audiology for further investigation and management. Box 3 lists red flags for referral.

Urgent referral is required if the hearing loss is sudden (over a period of three days or less), traumatic in aetiology, or where patients are immunocompromised and have otalgia with otorrhoea.[1]

Routine blood testing is not recommended.[2]

Pure tone audiometry is the first line investigation to diagnose the type (ie, conductive, sensorineural, or mixed) and severity of the hearing loss (figure and box 2).[1] A hearing loss above 30 dB at three consecutive frequencies that occurs within a 3 day period suggests idiopathic sensorineural hearing loss if no other underlying condition is identified.

Magnetic resonance imaging (MRI) can help distinguish sensorineural hearing loss caused by an underlying tumour from the more common idiopathic variety. Unilateral symptoms (ie, unilateral sensorineural hearing loss and/or unilateral tinnitus) should alert the clinician that further investigation is required.[1] Between 2% and 10% of patients with sudden sensorineural hearing loss are found to have cerebellopontine angle space occupying lesions/neoplasms such as acoustic neuromas (also known as vestibular schwannomas), or meningiomas on MRI.[2]

Tympanometry evaluates the mobility of the tympanic membrane and assesses middle ear function. It is routinely carried out in all patients with hearing loss as it can assist in elucidating the cause for the hearing loss.

Computed tomography imaging may be helpful if the patient has a history of trauma to look for a temporal bone fracture, or in the presence of chronic ear disease (eg, cholesteatoma). Otherwise, computed tomography of the head/brain is not routinely recommended in evaluating hearing loss.

Further specialist audiological testing, eg, otoacoustic emissions, auditory brainstem response testing, speech audiometry, acoustic reflexes, and vestibular function testing, may be indicated in secondary care.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

Two patient reviewers, including a patient with adult onset hearing loss, provided feedback on this paper. They highlighted the psychological impact of hearing loss and the importance of good quality of care in terms of streamlining the process for quick referral and investigations. We have more clearly outlined the steps for assessment in primary care, and specialist referral for further tests and management. We also mention the impact of hearing loss on quality of life and the need to discuss with patients the options for hearing rehabilitation and social support.

How are these patients managed?

Further management is typically provided by the specialist dependent on the cause of hearing loss. A short course of oral corticosteroids may be offered to patients with idiopathic sudden sensorineural hearing loss, ideally within 14 days of onset of hearing loss.[2-8] Robust evidence is lacking on the effectiveness of steroids; however, some degree of spontaneous improvement in hearing has been observed in 32-65% of patients,[2] most likely within the first two weeks. Late recovery has been reported but is rare.[2] Discussing the limitations of treatment with the patient is important to set reasonable expectations of recovery. Intratympanic steroids may also be considered in secondary care, either alone or in combination with oral steroids.[9 10] Serial audiograms are used to monitor hearing thresholds.

Other treatments, such as antivirals, thrombolytics, vasodilators, vasoactive/rheological substances, and antioxidants are not recommended for idiopathic sudden sensorineural hearing loss.[2]

Patients who have incomplete hearing recovery will require rehabilitation with amplification and hearing assistive aids. The simplest option is a conventional behind-the-ear air conduction hearing aid. Other options are available depending on the type of hearing loss, its severity, and underlying aetiology, eg, contralateral routing of signal (CROS), bilateral CROS, bone anchored hearing aids, and middle ear and cochlear implants. Patients may find it helpful to contact organisations that offer social support to people with hearing impairment.

Outcome

Tuning fork testing and pure tone audiometry revealed a severe/profound sensorineural hearing loss in the left ear (fig 1). An MRI scan of the internal auditory meati was normal. The acute onset suggests idiopathic sudden sensorineural hearing loss. A one week course of oral steroids was prescribed and the patient was referred to the ENT emergency clinic for further management. She later received an intratympanic steroid injection. Her hearing recovered partially and a conventional behind-the-ear air conduction aid was advised. The patient was told she had a slightly increased risk of a further episode of sudden sensorineural hearing loss and was advised to seek early medical attention if her hearing deteriorated.[11]

Competing interests: We have read and understood the BMJ policy on declaration of interests and do not have any relevant financial conflicts of interest. JMF is a senior editor for the *Journal of Laryngology and Otology* (Cambridge University Press

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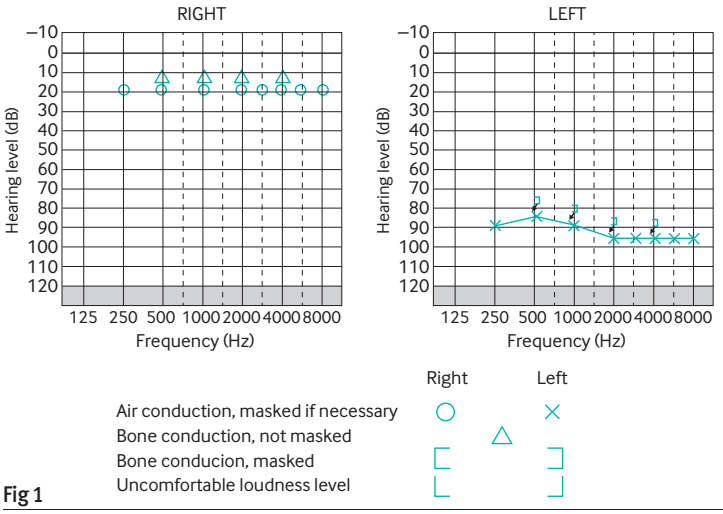

Fig 1

Pure tone audiogram typical of a sudden sensorineural hearing loss in the left ear. The masked bone conduction thresholds in the left ear (the '[' symbols) coincide with the masked air conduction thresholds (the 'X' symbols), indicating that this is a sensorineural hearing loss. Hearing thresholds in the left ear average 90-5 dB HL, placing this patient's sensorineural hearing loss in the left ear in the "severe" category

WHAT YOUR PATIENT IS THINKING

Holding out for an apology

A patient describes how her surgeon's gesture helped her to recover after she experienced complications

CPD READING

0.5 HOURS

WHAT YOU NEED TO KNOW

- Don't get obsessed with fault and blame—what is most important is for patients to know that you care, and that you are there to help them
- Remember that internal anger can cause vulnerable patients to spiral into depression; you have the ability to reduce that risk
- Sorry isn't only expressed in words—gently holding the hand of patients who are vulnerable, or sitting down at their bedside to give support can make all the difference

My emotional recovery from surgical complications was unbelievably difficult. The anger became haunting, and the physical pain made it impossible to forget the trauma. It was only when I was able to forgive my surgeon that the anger finally lifted—the forgiveness didn't occur in a self righteous way but by accepting that everyone makes mistakes and knowing that my surgeon was sorry for what had happened.

I'd had elective surgery, which went well, but afterwards I experienced complications. I was hit by intense pain, my surgeon came to see me, then went home. I felt that he had left me when I needed him most. He was called back a few hours later to carry out my emergency surgery.

The impression of complacency

During my recovery in hospital my surgeon didn't say that he was sorry, and I became angry. I didn't wonder "why me?" I understand that life is a lottery, but the lack of empathy made me think that my surgeon was complacent and indifferent about his patients, and that was why the complications had occurred. I was desperate for him to show that he was sorry.

A few months later, at an outpatient appointment, we discussed further surgery that I needed. The

ROSE LLOYD

I wished that when I was in hospital the surgeon had sat at my bedside and reassured me that he was there for me

meeting started well, with my surgeon talking about how he had evaluated my case with his colleagues and why he thought the complications had happened. Then he seemed to get defensive and it felt like the conversation became about him and his reputation. This wasn't helpful because I simply wanted him to reassure me that nothing was more important to him than my recovery, and that he would do whatever he could to help me.

I decided to continue with further surgery. If he was that worried about his reputation then he wouldn't allow anything to go wrong a second time.

A turning point

What I was looking for came in an unexpected form and at a time when I least expected it. I was on the recovery ward after my corrective surgery and my surgeon came to see me. I pretended to be asleep because I didn't want to talk to him. He held my hand and said that he hoped that I had a better recovery this time. The word sorry was never said, but the sentiment meant a great deal to me. It helped me realise that my surgeon did care about his patients—he just wasn't good at showing it. That moment was the turning point in my psychological recovery and the anger started to lift.

Understanding that surgeons are human too

Three years later, although my anger had lifted, I wanted closure. I decided to meet my surgeon to talk about how I wished that when I was in hospital he had sat at my bedside and reassured me that he was there for me, and to tell me that he was sorry for what I was going through. It was therapeutic but extremely difficult to talk about my feelings even after all that time. My surgeon listened patiently and reassured me that he was sorry. He described how doing my corrective surgery had been difficult for him because it brought back memories of the physical trauma he found during my emergency surgery; he recognised how much pain I'd been in. Those insights into his thinking are essential to me. They remind me that my surgeon is only human.

Talking about feelings isn't easy, for patients or for surgeons, but if it helps patients come to terms with what happened then it's worth it. Recovery from surgical complications is much more than just physical.

Anonymous

Competing interests: None declared

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EDUCATION INTO PRACTICE

- What circumstances influence whether you offer an apology, or how you approach it?
- If an operation has not gone well—for example, because of complications, how do you share this with the patient?
- When sharing bad news about an operation, or complication, to what extent do you, or could you, involve other members of the healthcare team?
- Is there anything else that you might think about or do differently having read this article?

These questions were developed by the editors and reviewed by the patient author

Is "watch-and-wait" after chemoradiotherapy safe in patients with rectal cancer?

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CPD READING
0.5 HOURS

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Colorectal cancer is the third commonest cancer worldwide.[1] About a third of these arise in the rectum. Approximately a third of rectal cancers are locally advanced and at high risk of recurrence. Long-course chemoradiotherapy followed by surgical resection is now standard treatment for these tumours in the UK,[2 3] Europe,[4] the US,[5] and Australia.[6] However, surgery is associated with major complications (up to 15%), perioperative mortality (up to 5%), and the need for a permanent stoma in up to a quarter of patients.[7]

Within the published literature, after chemoradiotherapy 10-25% of patients have no residual tumour on pathological examination after surgical resection.[7-10] Clinical examination before surgery in these patients has shown an equivalent favourable response, referred to as a clinical complete response. The criteria for defining a clinical complete response include absence of residual ulceration, stenosis, or mass within the rectum during digital rectal examination and endoscopic examination (figure).[9 10]

Nearly 15 years ago, a seminal study from a centre in São Paulo, Brazil reported that 71 patients with clinical complete response were managed without initial surgery. Instead they were managed by a non-surgical "watch-and-wait" approach and had equivalent survival compared with patients with complete response managed by major surgery.[11] Several centres have since replicated these results, but mainly in small case series.

In a "watch-and-wait" approach, patients may opt to forgo surgery, typically 8-12 weeks after the end of long-course chemoradiotherapy, and instead enter a surveillance programme of monitoring with regular digital and endoscopic examination supplemented with magnetic resonance imaging (box 1). There is uncertainty about the safety of watch-and-wait, with concerns that (in the absence of surgical resection) subclinical residual cancer cells may be undertreated and re-manifest later as inoperable local recurrence or as metastatic disease and compromise survival.[12]

WHAT YOU NEED TO KNOW

- After standard long-course chemoradiotherapy for locally advanced rectal cancer, up to a quarter of patients have no clinically apparent tumour—referred to as a clinical complete response
- Evidence from observational studies suggests these patients can be considered for a "watch-and-wait" approach with regular surveillance to avoid major surgery
- Up to a third of patients on a watch-and-wait programme develop tumour regrowth and require salvage surgery; the long term outcomes are uncertain

Box 1 | Example of a "watch-and-wait" approach to rectal cancer after clinical complete response to chemoradiotherapy

Years 1-2
- The most intensive monitoring period after chemoradiotherapy
- Patients will see a named organ preservation surveillance specialist every 3 months and undergo a digital rectal examination and flexible sigmoidoscopy. This should aim to incorporate narrow band imaging.
- Pelvic magnetic resonance imaging (MRI) will be carried out every 4-6 months
- Carcinoembryonic antigen (CEA) blood test every 4 months
- Computed tomography (CT) of thorax, abdomen, and pelvis performed every 6 months
- Colonoscopy carried out as per NICE surveillance guidelines

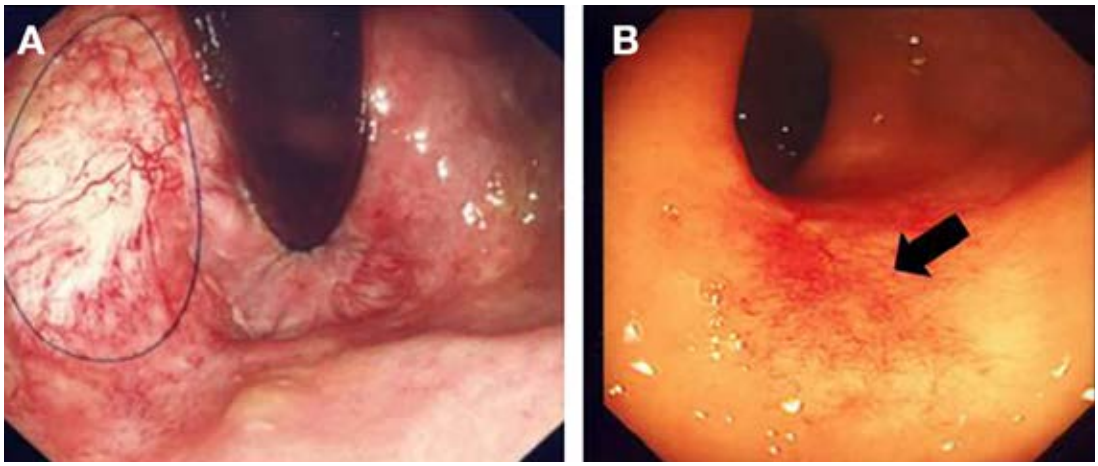
Years 3-5
- If clinical complete response is maintained, the frequency of flexible sigmoidoscopy and digital rectal examination will be reduced to every 6 months in year 3 and yearly thereafter up to 5 years
- CEA blood test every 6 months
- Patient's last MRI at 36 months, as relapse rate is very low after this
- One further CT of thorax, abdomen, and pelvis at 36 months

After 5 years
- Annual digital rectal examination, flexible sigmoidoscopy, and CEA blood test
- MRI or CT based on clinical suspicion

Suspicion or confirmation of tumour regrowth at any stage in surveillance programme
- Patient should be referred to colorectal surgeon immediately for full work-up for radical surgery

What is the evidence of uncertainty?

Our literature search identified three meta-analyses of observational data, two of study-level data[15 16] and one of individual participant data[17]; a matched-controlled study[18]; and an international registry, including published and unpublished data[19] (see table 1 on bmj.com). We found no published randomised controlled trial. Overall survival and disease-free survival are considered the metrics of oncological safety. The present evidence suggests that, after long-course chemoradiotherapy, patients on watch-and-wait have similar overall and disease-free survival compared with patients who undergo surgical resection. Around 30% of patients initially thought to have a complete response and opting for watch-and-wait experience tumour regrowth, most commonly in the first two years. Approximately 85% of patients with local regrowth are suitable for surgery and have no oncological disadvantage compared with patients who undergo immediate surgery. Most studies report on outcomes at two to three years, and longer term evidence is lacking. The International Watch and Wait Database (IWWD),[19] the largest series of patients with rectal cancer managed by watch-and-wait (880 patients), noted that five-year overall survival was 85% (95% confidence interval 80.9% to 87.7%) and five-year disease-specific survival was 94% (91% to 96%).



Endoscopic images of rectum after chemoradiotherapy for rectal cancer show (A) "white" scar (circled) and (B) telangiectasia changes (arrow). Both are accepted as "normal" and are compatible with a clinical complete response

Is ongoing research likely to provide relevant evidence?

We searched clinicaltrials.gov to identify ongoing trials and found 16 registered proposals to the search "watch and wait" plus "rectal cancer." However, we found only one protocol designed to evaluate equivalence in oncological outcomes (three-year disease-free survival) for patients with locally advanced rectal cancer with clinical complete response after long-course chemoradiotherapy randomly assigned to upfront radical surgery or to watch-and-wait (NCT02052921).[22] This is a phase II trial from São Paulo, Brazil, which is due to close in 2019. This will be the first randomised trial, and in theory, it should directly address the current uncertainty. However, with a target of 150 patients, this trial seems underpowered, and, in the UK at least, its inclusion criteria will include some tumours at an earlier stage than would normally be considered for long-course chemoradiotherapy.[2] The remaining trial protocols include watch-and-wait as part of a component of managements, intended to achieve the goal of "organ preservation." Nonetheless, trial environments will be important to standardise entry criteria—notably in terms of T stage of tumour.

There is now a debate as to whether the required safety evidence should come from "hard-to-do" randomised trials or from "scaled-up" analyses of observational data, in order for the watch-and-wait approach to become standard care. We have previously argued that, ideally, a watch-and-wait policy after clinical complete response could be tested against surgery in a randomised controlled trial assessing both oncological and functional results.[18] Our clinical experience is that many patients who have a clinical complete response express a strong preference to avoid major surgery, even when explicitly informed about the experimental nature of the watch-and-wait approach.[18] This is echoed by other commentators[23 24] and our Patient and Public Involvement and Engagement (PPIE) team involved in preparing this article (see box on patient involvement). Thus, there is a need for more research on patient preferences.

Our clinical experience is that many patients who have a clinical complete response express a strong preference to avoid major surgery

WHAT PATIENTS NEED TO KNOW

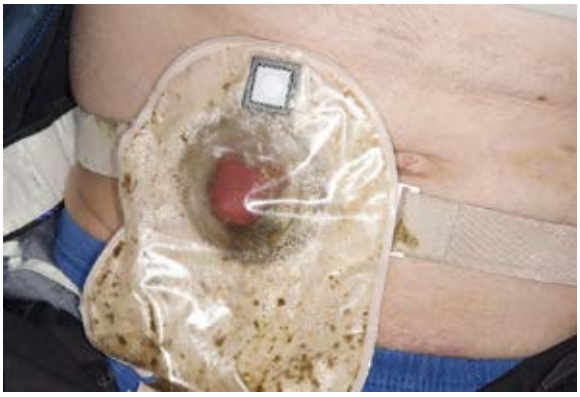
- Surgical removal of the tumour after chemoradiotherapy is the current standard treatment for rectal cancer and is regarded as the most reliable oncological treatment.
- Surgery is associated with side effects such as a temporary or permanent stoma bag, pelvic organ dysfunction, sexual dysfunction, bladder and bowel dysfunction, abdominal wall herniation, and a risk of death.
- 10-25% of rectal cancers can disappear completely after receiving neoadjuvant chemoradiotherapy, meaning that surgery can potentially be avoided in these cases.
- Clinical assessment of complete tumour disappearance ("clinical complete response") can be used to identify patients in whom the tumour is likely to have disappeared on pathological assessment and potentially select them for a non-operative "watch-and-wait" programme. In this case, surgery is reserved only for patients who experience tumour regrowth (see box 1).
- To date there is no randomised controlled trial comparing outcomes of watch-and-wait versus radical surgery for patients with clinical complete response, so we are uncertain whether "watch-and-wait" is safe.
- "Watch-and-wait" is not currently recognised as a treatment option for healthy patients otherwise suitable for surgery by many formal national guideline bodies.
- Around 30% of patients initially thought to have a complete response and opting for watch-and-wait will experience tumour regrowth that requires surgery.
- If tumour does regrow, about 85% of patients will be suitable for curative-intent salvage surgery, and they should be at no oncological disadvantage compared with patients who undergo immediate surgery.
- Discuss with your surgeon the options of "watch-and-wait" and surgery to determine the appropriate option for you after chemoradiotherapy for rectal cancer.
- If you choose "watch-and-wait" you will need frequent rectal examinations, endoscopic procedures, and scans to check that the tumour is not growing back (see box 1).
- A patient information sheet is available: http://www.complete-response.com

Box 2 | Practical guidance to clinicians in light of present evidence

- Before starting long-course chemoradiotherapy for rectal cancer, discuss with the patient that there is a 10-25% chance of no residual cancer after therapy. This should be included in the patient information sheet.
- At 8-12 weeks after long-course chemoradiotherapy, offer restaging to look for a clinical complete response. This constitutes a flexible sigmoidoscopy and digital rectal examination by a clinician experienced in the identification of a clinical complete response (typically a colorectal surgeon), and magnetic resonance imaging.
- If a clinical complete response is identified, the colorectal surgeon should discuss the options of resection surgery versus a watch-and-wait approach with the patient.
- Offer patients a counselling session with a stoma therapist before making a decision as to whether to undergo surgery if living without a stoma is their main reason for preferring watch-and-wait.
- If the patient chooses a watch-and-wait approach, offer monitoring in accordance with a pre-agreed surveillance protocol.
- Information on patient and tumour characteristics, treatment, and outcome should be collected and submitted to ongoing registries (such as IWWD) or research databases (such as OnCoRe).

EDUCATION INTO PRACTICE

- If you identified a patient with rectal cancer who required long-course chemoradiotherapy, how would you discuss the possibility of a clinical complete response and management options?
- Would you register patients receiving long-course chemoradiotherapy for rectal cancer in a national research database?



SPL

Nearly all patients undergoing rectal cancer surgery after chemoradiotherapy will require a temporary or permanent stoma

SPL

A watch-and-wait approach entails frequent monitoring to check that the tumour is not growing back

What should we do in the light of the uncertainty?

It has not been established which patients might benefit from a watch-and-wait approach. Many patients prefer avoiding surgery. Others may become anxious during watch-and-wait follow-up and may prefer initial surgery as reassurance that their tumour has been removed. In the UK, recent changes in consent law, based on the Montgomery Ruling, stipulate that patients must be informed of any risk that "a reasonable person in the patient's position would be likely to attach significance to."[19] This rationale, we feel, should not just be limited to the UK as it embodies the concept of patient centred care. We therefore recommend that, to fulfil the mandate of informed consent, patients undertaking long-course chemoradiotherapy are informed that there is a 10-25% chance they will have no residual cancer after the therapy, and, in turn, may consider a watch-and-wait programme with potential avoidance of major surgery. As surgery for rectal cancer includes risks of complications and perioperative mortality, and many patients might require a stoma, most patients are likely to "attach significance to" this information. Recent guidelines (2017) from the UK Association of Coloproctology of Great Britain and Ireland (ACPGBI)[3] and Australian Cancer Council[6] include watch-and-wait as an option, with the caveat that patients must be informed that it remains a new management under evaluation. The European Society of Medical Oncology (ESMO)[4] 2018 guidelines state that watch-and-wait can be considered in "high risk" patients (without defining criteria) with clinical complete response after long-course chemoradiotherapy. Older guidelines, such as those from the US (2013),[5] recommend that resection is standard care, whereas the UK National Institute for Health and Care Excellence (NICE, 2012)[2] does not mention clinical complete response. While we await wider endorsement in clinical guidelines, we recommend a practical guidance for clinicians on how to incorporate watch-and-wait into their practice in box 2 and provide a template watch-and-wait surveillance schedule in box 1.

Competing interests: The BMJ judged that there were no relevant financial interests. The authors declare: AGR has received lecture honoraria from Merck Serona and Janssen-Cilag, and independent research funding and lecture honoraria from Novo Nordisk (regarding insulins and cancer risk) and Sanofi Pasteur MSD (regarding HPV vaccinations and anal cancer).

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Find the full version with references at http://dx.doi.org/10.1136/bmj.k4472

HOW PATIENTS WERE INVOLVED IN THIS ARTICLE

We discussed this topic with a sub-group of the NIHR Manchester Biomedical Research Centre (BRC) Patient and Public Cancer Research Advisory Group, facilitated by the Public Programmes Team and the OnCoRe research database coordinator, Mr Lee Malcomson.
The group emphasised that, for the great majority of patients with cancer, the primary outcome of importance is survival. They welcomed the innovation of a "watch-and-wait" approach for patients with rectal cancer as a potential way to avoid major surgery, but sought reassurance that it would not compromise their chances of survival. Patients emphasised the need to discuss this new treatment pathway carefully and with sensitivity.

SPOT DIAGNOSIS

An unusual cause of right iliac fossa pain

A 34 year old woman presented to the emergency department with a history of worsening right iliac fossa pain over several days. She described the pain as alternating dull and sharp, and had found simple analgesia (paracetamol, non-steroidal anti-inflammatory drugs) to be ineffective. She had no other associated signs or symptoms and no history other than insertion of an intrauterine contraceptive device (IUCD) several years ago.

A transvaginal ultrasound was unremarkable except that it showed a trace of free fluid in the pelvis, close to the uterus, and the IUCD was not visualised. The patient went on to have an unenhanced computed tomography scan for further assessment (figs 1, 2). What is the diagnosis?

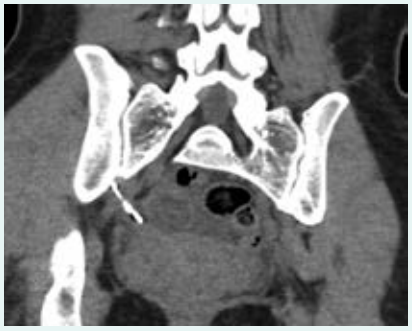

Fig 1| Coronal non-contrast computed tomography image through the pelvis

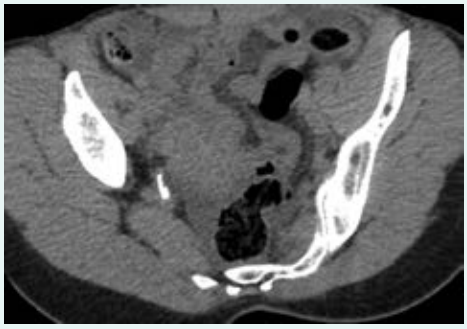

Fig 2| Axial non-contrast computed tomography image through the pelvis

Submitted by Omed Amin and David C Howlett

Patient consent obtained

Cite this as: *BMJ* 2018;363:k4153

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answers

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SPOT DIAGNOSIS **An unusual cause of right iliac fossa pain**

The diagnosis is IUCD migration.

The coronal computed tomography scan shows the IUCD lying in the right pelvis (fig 3, arrow A), separate from the uterus (fig 3, arrow B).

The axial computed tomography section through the pelvis shows the extra-uterine coil (fig 4, arrow A) and the uterus (fig 4, arrow B). Note some posterior pelvic free fluid (fig 4, arrow C).

Coil migration and uterine perforation is a well recognised risk of IUCD use, with an estimated incidence of 0.12 to 1.3 per 1000 patients.

Risk factors include lower level of experience in the fitter of the IUCD, the woman having a retroverted uterus, a small endometrial cavity, and a history of multiparity.

Women are usually diagnosed when the device strings are not visible on speculum examination or because of unexpected pregnancy. Those who have additional symptoms might complain of lower abdominal pain, irregular vaginal bleeding, and, more seriously, infection, features of bowel obstruction, damage to nearby abdominal organs, and fistulae. Such symptoms could occur soon after insertion of the IUCD, or possibly months later.

Transvaginal ultrasound, computed tomography, or abdominal radiograph can identify the IUCD and its location. Common locations include the omentum, pouch of Douglas, within the colon wall or myometrium, or freely within the abdomen.

The World Health Organization advocates the removal of a migrated IUCD even in asymptomatic patients using one of several surgical approaches. Hysteroscopy may be a better option when the device is contained within the uterine serosa; otherwise laparoscopy is recommended as the first line approach. Occasionally, a conversion to laparotomy becomes necessary in cases complicated by substantial adhesion, bowel perforation, or where the device has become embedded within the omentum.

Learning point

In the absence of the IUCD threads on direct visualisation, ultrasound can help to locate a migrated IUCD.

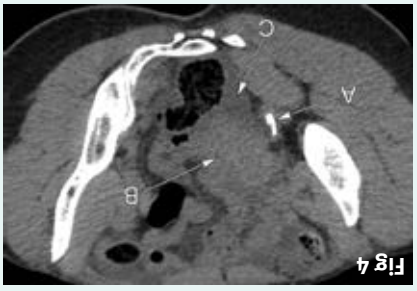


Fig 4

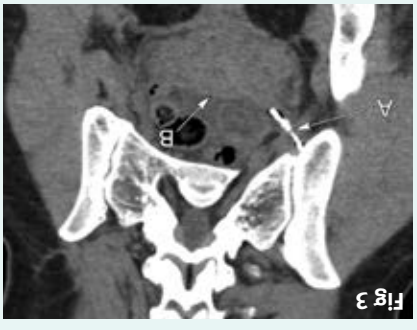


Fig 3

CPD READING

0.5 HOURS

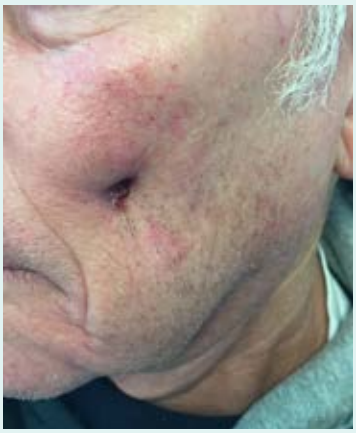
You can record CPD points for reading any article. We suggest half an hour to read and reflect on each.

LEARNING MODULE

Articles with a "learning module" logo have a linked BMJ Learning module at http://learning.bmj.com.

MINERVA

A dental sinus mimicking skin cancer



A 79 year old man was investigated for a six month history of an asymptomatic, slowly growing, indurated area on the cheek (right). Histology excluded malignancy.

Orthopantomography showed an odontogenic cutaneous sinus tract arising from a chronically infected tooth. The patient underwent tooth extraction and received oral antibiotics, and the lesion healed with residual scarring.

This case highlights the importance of intra-oral examination in patients with non-healing cutaneous lesions over the distribution of the dental roots.

Other intra-oral diseases to consider in the differential diagnoses of extra-oral pathology associated with the cheek include basal and squamous cell carcinoma, salivary gland neoplasm, and actinomycosis.

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Patient consent obtained.

Cite this as: *BMJ* 2018;363:k4461

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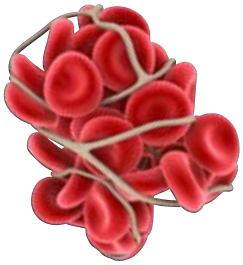
Preventing venous thromboembolism after arthroplasty



Venous thromboembolism is a well recognised risk after knee arthroplasty, but there's no consensus on the best prophylaxis. A large retrospective register based analysis from Michigan reports that patients given aspirin alone fared no worse than those given non-aspirin anticoagulants or a combination of the two, and a great deal better than those who received no prophylaxis (*JAMA Surg*). The problem here is that the various anticoagulants weren't allocated at random and the lack of difference between them might be due to confounding by indication.

Pancreatic cancer following acute pancreatitis

A nationwide survey of Swedish residents who had been diagnosed with an episode of acute pancreatitis reports that their risk of a subsequent diagnosis of pancreatic cancer is substantially raised over the next few years (*Am J Gastroenterol*). The increased risk diminishes over time and falls to baseline levels by 10 years. One interpretation is that, when pancreatic cancer presents as acute pancreatitis, the underlying tumour often goes undetected, either because in imaging procedures it's obscured by inflammation or because gallstones or alcohol abuse are assumed to be the cause.

Low air temperatures

In another study from Sweden, investigators linked 16 years' worth of meteorological data to a register of more than a quarter of a million patients admitted to coronary care units (*JAMA Cardiol*). They discovered that the incidence of myocardial infarction varied with the weather. Low air temperature, low barometric pressure, high winds, and shorter periods of sunshine all increased the likelihood of infarction. The strongest association was found for air temperature, and the highest incidence occurred on days when air temperatures were below freezing.

Childhood trauma

It's well known that traumatic experiences in childhood increase the likelihood of depression and other mental health problems in adult life. An investigation in *PLoS One* suggests that there can be a another side to these experiences as well (*PLoS One*). People who reported that they had experienced the death of a close family member, parental separation, sexual abuse, or violence before the age of 17 years showed increased levels of empathy, greater ability to see things from alternative perspectives, and had a better understanding of other people's emotional states.

Birth weight in California

Air temperatures also influence birth outcomes, according to a study from California that looked at rates of low birth weight in babies born at term. After adjusting for some of the many factors known to influence birth weight, including pre-pregnancy BMI, cigarette smoking, season of birth, baby's sex, mother's economic circumstances, and levels of air pollutants, it found that mothers who had been exposed to high air temperatures during pregnancy were more likely to give birth to low birth weight babies (*Am J Epidemiol*). Exposure to high temperature during the third trimester was most influential. Older mothers and mothers who were black or white seemed more vulnerable than younger or Hispanic mothers.

Cite this as: *BMJ* 2018;363:k4709