Clinical abstracts
A retrospective, comparative study between Plenvu and Moviprep as bowel preparation agents for colonoscopy

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Introduction

Optimal bowel preparation is crucial for a successful colonoscopy. Plenvu is a low volume (1 litre) polyethylene glycol (PEG) plus ascorbate-based bowel preparation which has demonstrated a superior cleansing and equal safety and tolerability profile compared with standard agents.\textsuperscript{1,2} The current bowel preparation agent in use at our trust is Moviprep which is a 2 litre PEG preparation consumed in two divided doses. The recommendation is that patients have at least a litre of water alongside this. This can pose a challenge, especially for patients who are unable to tolerate higher volumes of liquids. The aim of this study was to assess the cleansing efficacy of Plenvu compared with Moviprep.

Materials and methods

A retrospective data collection was carried out from our endoscopy database for patients who received bowel preparation from February 2020 to March 2020. Patients who had a colonoscopy during this period were randomly allocated to receive either Plenvu or Moviprep. We collected data from 126 patients who were equally divided between each arm of the study.

Data were obtained on age, gender, timing of the procedure and endoscopic evaluation of bowel preparation on a scale of inadequate to excellent

Results and discussion

There were no significant demographical disparities between both arms; the majority of our sample size fell within the 51–70 years age category (63% of the Plenvu group and 47% of the Moviprep group).

Plenvu provided superior cleansing efficacy with endoscopists rating the bowel preparation as excellent/good in 59% (n=37) of patients compared with 46% (n=29) in the Moviprep group.

In addition, Plenvu is marginally cheaper (36p) than Moviprep. At our trust, we perform an average of 3,000 colonoscopies per year. This translates to potential savings of £1,000 per annum.

Conclusion

This study supports the use of Plenvu as an efficacious bowel preparation agent. It remains the lowest volume bowel preparation agent on offer and, given its cost effectiveness, it is an attractive alternative to conventional agents.

References


Subacute dyspepsia: a curious presentation of an ominous pathology

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Introduction

Dyspepsia is a symptom for a wide range of medical conditions. It is common for practitioners to treat it symptomatically in the first instance. However, sometimes it can reflect ominous pathology that requires robust intervention. In this article, we present a case of a patient with dyspepsia.

Case presentation

A 45-year-old man presented to the hospital with subacute dyspepsia. He was seen by primary care team who administered proton pump inhibitors that failed to resolve the symptoms. The patient re-presented to the hospital as he started to have leg swelling and general feeling of tiredness.

Blood tests showed alarmingly elevated haemoglobin levels and conjugated hyperbiliurubinaemia. Also, the patient had hepatomegaly and bilateral pitting leg oedema. Thoraco-abdominal imaging elucidated a large malignant tumour emanating from the liver causing pressure on the intrahepatic ducts and a tumour thrombus invading the hepatic veins, inferior vena cava, and the right atrium, filling almost two-thirds of the right atrium and causing a picture of right heart failure (Fig 1).

Fig 1. Computed tomography of the thorax, abdomen and pelvis showing an 11 cm malignant mass in the caudate lobe of the liver, leading to intrahepatic biliary obstruction and inferior vena cava tumour thrombus precipitating a lower leg oedema.

Tumour markers were negative except for elevated lactate dehydrogenase, other causes of acute hepatitis were also negative (Table 1).

Table 1. Investigations showing basic blood tests, liver function tests and tumour markers
Given the extension of the tumour, it was deemed too risky to undergo biopsy and that a surgical option would be futile. Accordingly, a plan for palliative management was put for symptom control and early hospital discharge. The patient sadly died 1 month after presentation to the hospital.

**Discussion**

This patient presented with anatomical symptoms of his tumour, the feeling of distension, dyspepsia and jaundice. The symptoms weren’t thoroughly investigated on primary presentation due to it being a common complaint. Interestingly, the patient had high haemoglobin levels. It is known for sarcomas to cause the triad of polycythaemia, thrombocytopenia and intractable heart failure. This can be compared with this case as the tumour had likely emanated from vascular origin ie the inferior vena cava. Multiple studies have shown that primary hepatic leiomyosarcomas present insidiously, usually start in a vessel such as the portal vein and are associated with a tumour thrombus. It is of note that with this type of malignancy, the patient has normal levels of neoplastic markers such as alpha-fetoprotein, carcinoembryonic antigen and cancer antigen 19-9. Leiomyosarcoma is reportedly curable with surgical resection if the tumour has no extrahaepatic spread and the patient is fit for surgery. Unfortunately, in our patient’s case, the tumour had extrahaepatic spread and this option was not feasible.

There is a proven link between hereditary retinoblastoma and development of sarcoma; our patient did not have family history of retinoblastoma but similar cases have been reported in the literature specifically for the development of liver sarcoma.

**Conclusion**

For patients with dyspepsia who do not readily respond to simple measures, further investigations such as abdominal ultrasound should be offered. High haematocrit, low platelets or acute heart failure should warrant further investigations. Future research is required to assess the link between childhood retinoblastoma and liver sarcoma to provide possible screening if such a link is proven.

**References**


Pericardial effusion and lung cancer: a retrospective analysis

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Introduction

Malignant pericardial involvement is present in 20% at post-mortems of cancer patients with up to 50% having a pericardial effusion (PErF). Common causes are lung and breast cancer. Survival of lung cancer and PErF is <5 months. Positive cytology and tamponade are adverse prognostic signs. We sought to retrospectively review lung cancer patients with pericardial effusions.

Methods

With Caldicott approval, in a search of computed tomography (CT) from January 2011 – August 2021 for ‘lung cancer’ AND ‘pericardial effusion’, 765 reports were found then reduced to 112. Basic demographics were collected. Continuous variables are presented as mean (range) and categorical variables as percentages where appropriate.

Results

Mean age was 70.6 years (44–91) and male:female was 56:56. Seven had no comorbidities, the others were all multi-morbid, with chronic obstructive pulmonary disease as the most common. Nineteen patients were clear of previous cancer. Many patients had lung cancers: 33 adenocarcinomas, 31 squamous cell, 13 small cell, 11 others (neuroendocrine, spindle cell or undifferentiated) and 25 had no pathology. PErFs were found on the first CT in 52 (time to death was mean 130 days (0–1,279) and median 70 days); the rest in scans showing disease progression (median time to progression 9 months; time to death was mean 160 days (0–1,138) and median 64 days; p=0.42). Twelve effusions were large (>20 mm). Eighteen echocardiographies were done, five drains were done for haemodynamic compromise (all at first presentation) and four fluid cytologies sent (all positive). Mean time to death in those five who required intervention was 15.1 day vs 148 days for whole cohort (p=0.037). There was no statistical difference for outcomes between cancer types.

Conclusions

PErF is associated with progressive disease and the need for intervention with mortality. Incidence is <3%. 
Diagnostic performance of machine learning-based magnetic resonance algorithm vs conventional magnetic resonance imaging for predicting the likelihood of brain tumours

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Introduction
Magnetic resonance imaging (MRI) forms an imperative part of the diagnostic and treatment protocol for both primary brain tumours and metastasis. Though conventional T1 weighted MRI forms the basis for diagnosis at present, it faces several limitations. Machine learning algorithms require less expertise and provide better diagnostic accuracy.

Objective
This systematic review and meta-analysis aimed to compare the diagnostic performance of conventional MRI with machine learning (ML) algorithms for brain tumours.

Materials and methods
A systematic review of PubMed, Google Scholar and Cochrane databases along with registries (World Health Organization International Clinical Trials Registry Platform and ClinicalTrials.gov) from 1980–2021 was done. Original articles in English evaluating conventional MRI or ML algorithms with/without usage of a reference standard were included. Data were extracted by two independent reviewers and meta-analysis was performed using a bivariate regression model.

Results
The study protocol was registered under PROSPERO (CRD42021289726). Twelve studies with 1,247 participants were included for systematic analysis and three studies for meta-analysis. ML algorithms had better aggregate sensitivity and specificity (80% and 83.14%, respectively) than conventional MRI (81.84% and 74.78%, respectively). The pooled sensitivity, specificity, diagnostic odds ratio (DOR) for the studies were 0.926 (95% confidence interval (CI) 0.840–0.926), 0.991 (95% CI 0.955–0.998) and 1,446.946 (312.634–6,692.646), respectively, with area under the curve (AUC) 0.904 under hierarchical summary receiver operating characteristic (Figs 1 and 2). On subgroup analysis, MRS (100% and 100%) and random forest model (100% and 100%) had highest sensitivity and specificity, respectively; dynamic susceptibility contrast MRI and deep neural network (DNN) had highest AUC (0.98 and 0.986, respectively).

Fig 1. Forest plots for sensitivity and specificity.
Fig 2. Summary receiver operating characteristic curve for brain tumour diagnosis (combined conventional magnetic resonance imaging and machine learning algorithm).

Conclusion

Machine learning algorithms have superior diagnostic performance and faster diagnostic capability once trained than conventional imaging for brain tumours. They have immense potential to be the standard of care in the future.
Benefits of a falls service during the pandemic

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Introduction

The COVID-19 pandemic has caused disruption to various services across the healthcare system. The falls service, which was well supported in the pre-pandemic period, came under increasing pressure during the pandemic. Despite the challenges, we were able to run a modified service, which was vital in improving the care of people who are frail by decreasing falls and hospitalisations.

Aim

We aimed to evaluate the value of the falls service by reviewing the interventions carried out.

Methodology

We reviewed 52 patients who presented to the falls service in 2020. Both electronic and paper records were reviewed and interventions assessed.

Findings

We undertook interventions in all patients. Out of the 52 patients, 49 were alive at the end of the year. Most of our patient (44/52) were in the 70–89 years age group. A majority (44/52) were referred in from general practitioners. Most were living in private accommodation, with only six residing in care homes.

Almost all (45/52) had a medication intervention. These included the adjustment of Parkinson’s medications (n=3), stopping or decreasing the dose of beta blockers (n=8), calcium channel blockers (n=5), and antidepressants (n=6). Other medications stopped or reduced included statins, tramadol, diuretics and digoxin. Other interventions included altering the time of administrations for angiotensin-converting enzyme (ACE) inhibitors (n=6) and tamsulosin (n=2).

Fourteen patients were started on vitamin D, seven on protein supplements, three on folate supplements and two on iron supplements.

In six patients, new abnormalities in the spine (including spinal stenosis) were found and referrals made to the neurosurgical team. Three patients were newly diagnosed with Parkinson’s disease. Other new neurological conditions found in the falls service include normal pressure hydrocephalus, vertigo, stroke and meningioma.

Two patients were found with new atrial fibrillation and began on oral anticoagulation. Two were found to have bradycardia and were referred to cardiology for consideration of a pacemaker. Other new cardiac diagnosis included aortic stenosis, mitral stenosis and a patient with ventricular tachycardia.

Other diagnoses found for the first time included sleep apnoea and rheumatoid arthritis. Referrals were also made to the orthopaedic team for osteoarthritis in one patient and ankle injury in another, and to the ophthalmologist for cataract removal.

All patients were assessed for bone protection. Four were begun on an oral bisphosphonate, three on zoledronate and two on denosumab.
Multidisciplinary interventions included issuing of a new frame in four patients, foot splint in one patient, a referral to the orthotic department in one patient and a referral to podiatry in one patient.

Other new conditions picked up were cognitive impairment in four patients, iron deficiency in three and hypothyroidism in one patient.

**Discussion**

The falls service is a valuable resource in the assessment of a person who is frail. It offers a comprehensive assessment. Despite the challenges of the pandemic, we were able to deliver patient-centred multiprofessional care.
Prevalence of established vertebral fragility fractures in patients admitted with acute hip fracture

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Introduction
Osteoporotic hip fracture carries a significant mortality risk with 6.1% of patients dying within 30 days of fracture and one-third within 12 months.\textsuperscript{1,2} Fracture liaison services (FLS) identify fragility fractures and intervene with appropriate assessment and treatment for further prevention of fragility fractures.\textsuperscript{3,4} Only approximately 6% of vertebral fragility fractures are identified by FLS through routine case finding.\textsuperscript{5} However, many diagnostic imaging tests include the spine, which provides a valuable opportunity to identify patients at risk of fracture.

Methods
Nottingham University Hospitals NHS Trust has a well-established orthogeriatric service and we decided to use our local data on the National Hip Fracture Database (NHFD) to identify the imaging history of 245 consecutive patients admitted with acute hip fracture between December 2019 and July 2020 to find out how many of these patients had evidence of established vertebral compression fractures (VCFs) on cross-sectional imaging in the preceding 5 years before admission. Indications for the investigation were noted as unrelated to bone health (including malignancy), trauma or vertebral fracture. Data were obtained about history of known osteoporosis, prior osteoporosis treatment, cross-sectional imaging in the preceding 5 years before hip fracture, the number and type of vertebral fractures detected etc. Using our hospital IT systems, information was obtained from their electronic discharge summary following hip fracture as well as reports of their cross-sectional imaging (computed tomography / magnetic resonance imaging) and their indications in the preceding 5 years prior to hip fracture.

Results
The median age was 84 years; 165/245 (67%) were women; 49/245 (20%) had known osteoporosis; 19/49(39%) weren’t on any treatment; 20 patients were on antiresorptives (15 on oral bisphosphonate, three on intravenous bisphosphonate and two on denosumab); and 84/245 (34%) underwent cross sectional imaging in the preceding 5 years, out of which, 27 (32.1%) were found to have osteoporotic vertebral fractures with 14 (52%) having two or more VCFs. Of the 27 patients with VCFs, nine weren’t on any treatment while 13 patients were on calcium and vitamin D supplements alone. Interestingly, nine (33%) of these patients had evidence of symptomatic VCFs as per request for imaging carried out in the 5 years prior to hip fracture.

Conclusion
Eleven per cent of hip fracture patients in this study had evidence of prior vertebral fragility fracture and a missed opportunity for secondary fracture prevention. They represent a subset of patients with a greater risk of future fractures.\textsuperscript{6} The study did not scrutinise the imaging to verify report findings or identify vertebral fractures that were unreported or missed and, therefore, results and prevalence might be an underestimate. There is a need for radiology to alert all incidental VCFs to the fracture liaison service that would help in prompt assessment and management of their osteoporosis and reduction of their future fracture risk.
References

A not so ‘sweet’ cause of fevers, cough and chest pain

Authors: Shaza Elamin, Shahd Elamin, and Rick Plumb
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Introduction
During what seems like endless medical admissions, it is important to be vigilant and look out for any disease ‘mimickers’. We present an interesting and rare case of myocarditis and systemic inflammation secondary to Sweet’s syndrome.

Case presentation
Our patient was a 52-year-old woman who presented to the emergency department with a productive cough, shortness of breath and pyrexia. Accompanying this were new onset and multiple erythematous, pustular and painful lesions, predominately covering her upper and lower limbs. Preliminary investigations showed markedly elevated inflammatory markers with C-reactive protein (CRP) of 366 mg/L and erythrocyte sedimentation rate (ESR) of 127 mm/hour. She was admitted and treated with intravenous antibiotics for a presumed lower respiratory tract infection, with modest improvement in her inflammatory markers and clinically. Her admission was later complicated with new complaints of pleuritic chest pain, accompanied by elevated troponin levels and global concave ST elevation on electrocardiography, which was confirmed as acute diffuse myocarditis on cardiac magnetic resonance imaging.

A dermatology opinion was sought as the skin rash worsened. Sweet’s syndrome was clinically suspected and later confirmed on skin biopsy, showing the classical histopathological findings of heavy neutrophil presence within the dermis. She was commenced on high-dose oral corticosteroids and quickly began to show signs of improvement. After a few days, there was complete resolution of cardiac symptoms and temperature, and dramatic improvement to her skin rash and inflammatory markers. Corticosteroids were slowly weaned with no rebound symptoms. She was thoroughly investigated for potential triggers of Sweet’s syndrome including autoimmune, vasculitic and infective screen, as well as computed tomography of the chest, abdomen and pelvis, which were all unremarkable. Investigations did, however, reveal an elevated antistreptolysin O titre (ASOT) at 400 U/mL. She was, therefore, diagnosed with Sweet’s syndrome, triggered by a streptococcal respiratory tract infection. Following completion of the course of oral steroids, she made a complete recovery, and follow-up positron emission tomography – CT did not demonstrate any areas of inflammation.

Discussion
Sweet’s syndrome, also known as acute febrile neutrophilic dermatosis, is an uncommon skin condition that consists of pyrexia and acute onset, painful and inflamed skin lesions. It is also often accompanied by other systemic features, where it is best regarded as a systemic inflammatory response. This response may be secondary to various triggers that include respiratory tract infections, autoimmune and inflammatory conditions, haematological malignancies, and drugs to name a few. In some cases, however, it may be idiopathic. Treatment with systemic steroids helps improve the symptoms quickly, but an underlying cause needs to be considered and treated.1,2

Conclusion
From this rare cause of myocarditis and systemic upset, we propose that Sweet’s syndrome should be considered in the differential of any patient presenting acutely with pyrexia and painful skin rash not responding to standard treatments, particularly if there is systemic involvement. Following a
multidisciplinary team approach, this patient was diagnosed and treated promptly resulting in complete resolution in her cutaneous, respiratory and cardiac symptoms.

References

Pulmonary vein thrombosis: clot in the wrong vessel

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Introduction

Computed tomography pulmonary angiography (CTPA) has become a quick and readily accessible test. As a result, clinicians frequently come across incidental findings such as a rare case of pulmonary vein thrombosis (PVT) as presented here.

Case presentation

A 66-year-old man with known squamous-cell lung cancer presented with worsening breathlessness. He had been diagnosed in 2016, for which he underwent a right middle and lower lobectomy. In 2020, he had recurrence of lung cancer with CT showing an extensive right hilar mass invading the mediastinum. He received palliative radiotherapy and subsequently was started on immunotherapy. Two weeks after undergoing radiotherapy, he presented with worsening breathlessness and a cough productive of greenish sputum. His exercise tolerance had reduced from 100 yards to just a few steps. Apart from his oxygen saturation being 94% on room air, his physical examination was unremarkable. His blood tests showed raised inflammatory markers. He was started on oral doxycycline for a possible respiratory infection. A CTPA was performed that was negative for a pulmonary embolism but showed a PVT (Fig 1). Anticoagulation was initiated after reaching a shared decision.

Fig 1. Computed tomography pulmonary angiography showing a thrombus in the right pulmonary vein, hilar soft tissue mass extending into the mediastinum.

Discussion

PVT can occur after surgical procedures involving manipulation of the pulmonary vessels, for example, lung transplant and lobectomy.\(^1\) Thrombosis in post-lung transplant patients can mimic acute graft dysfunction and incidence is as high as 15%.\(^2\) Rarely, radiofrequency ablation for atrial fibrillation can cause a clot. Non iatrogenic causes include malignancy, atrial fibrillation, left atrial thrombus, mediastinitis, sickle cell crises and trauma. Recently COVID-19 infection has also been associated with it.\(^3\) PVT can be completely asymptomatic and only picked up incidentally on imaging. However, if it is large enough to obstruct the pulmonary flow, it can lead to acute symptoms and even haemodynamic instability. Pulmonary oedema or an infarct can lead to symptoms like dyspnoea, haemoptysis or cough. Superadded bacterial infections can occur especially in the postoperative state. Long-term complications include heart failure and pulmonary
Systemic embolisation to almost all major sites including the brain, kidneys and limbs have been reported. CTPA is the cornerstone investigation, which helps to diagnose the thrombus and also rules out certain aetiologies. Echocardiography is used to ascertain presence of left atrial thrombus and differentiate a true thrombus from tumour invasion. Treatment is to start anticoagulation in order to prevent embolism. Case reports in post-surgical patients have shown a role for antibiotics in that scenario. In acutely unstable patients with haemodynamic compromise and a large obstructive clot, thrombolysis can be considered. Another alternative in these circumstances, especially in post-surgical patients, would be thrombectomy, however, availability to this service is limited.

**Conclusion**

PVT is an entity that we are likely to see more of due to an increase in frequency of radiological investigations. However, having an awareness of PVT as a cause of such complications may help to reduce the delay in diagnosis and treatment. It is essential that the risk of systemic embolisation be addressed with anticoagulation where appropriate.

**References**

Hyperglycaemia and inpatient mortality and morbidity

Authors: Yvette Farrugia, Jessica Mangion, Marie Claire Fava, Christine Vella and Mark Gruppetta

Introduction

Hyperglycaemia is frequent among hospital patients and is related to increased complications, poorer outcomes and increased mortality. We examined the relationship between hyperglycaemia on admission with morbidity and mortality. By reviewing hospital admissions during different seasons, we studied seasonal variation in the relationship of hyperglycaemia to mortality in view of the known seasonal variation in blood glucose levels.

Material and methods

We retrospectively examined the records of 1,132 hospital admissions. Hyperglycaemia was defined as an admission random glucose level of above 11.0 mmol/L. For statistical analyses, we used the Mann–Whitney U test, complemented by Spearman’s rank correlation and chi-squared tests with a significance level of p=0.05.

Results and discussion

Hyperglycaemia was present in 14.1% of patients admitted to the hospital, of whom, 3.9% had no previously documented history of diabetes. Patients with new-onset hyperglycaemia on admission, had a significantly higher mortality rate than previously diagnosed diabetes (43.3% vs 17.9%; p=0.006). Logistic regression showed that plasma glucose on admission was independently associated with increased 1-year mortality (odds ratio 1.035; p=0.034). Table 1 shows the continuous variables significantly related with mortality at 1 year, while Table 2 shows the relationship of diabetes history and of plasma glucose on admission related with mortality and re-hospitalisation at 1 year.

Table 1. Continuous variables significantly related with mortality at 1 year (analysed using Mann–Whitney U test)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mortality, yes, median (IQR)</th>
<th>Mortality, no, median (IQR)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age on admission, years</td>
<td>80.0 (71.0–86.0)</td>
<td>69.0 (49.0–80.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length of stay in hospital, days</td>
<td>6.0 (3.0–13.0)</td>
<td>3.0 (2.0–6.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Plasma glucose on admission, mmol/L</td>
<td>7.0 (5.8–9.8)</td>
<td>6.4 (5.5–8.43)</td>
<td>0.005</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>94.0 (70–142.8)</td>
<td>81.0 (65–105.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum urea, mmol/L</td>
<td>9.2 (6.7–14.9)</td>
<td>6.5 (4.8–9.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estimated GFR, mL/min/1.73m²</td>
<td>60.0 (36.0–88.5)</td>
<td>80.0 (56.5–103.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum Sodium , mmol/L</td>
<td>138.0 (135.0–140.0)</td>
<td>139.0 (136.0–141.0)</td>
<td>0.005</td>
</tr>
<tr>
<td>Serum Chloride , mmol/L</td>
<td>98.0 (94.2–101.6)</td>
<td>100.2 (97.1–102.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum osmolality, mOsm/kg</td>
<td>302.2 (294.6–314.0)</td>
<td>300.8 (295.0–307.0)</td>
<td>0.020</td>
</tr>
</tbody>
</table>

GFR = glomerular filtration rate; IQR = interquartile range.

Table 2. Diabetes history and blood glucose on admission related with mortality and re-hospitalisation at 1 year

<table>
<thead>
<tr>
<th>Plasma glucose on admission</th>
<th>Mortality, n (%)</th>
<th>p-value</th>
<th>Re-hospitalised, n (%)</th>
<th>p-value</th>
</tr>
</thead>
</table>


Patient with known diabetes

| <11 mmol/L | 36 (22.8) | 0.006 | 90 (57.0) | 0.003 |
| >11 mmol/L | 14 (17.9) | 0.006 | 44 (56.4) | 0.003 |

Patient not known to have diabetes

| <11 mmol/L | 90 (18.1) | 0.006 | 217 (43.6) | 0.003 |
| >11 mmol/L | 13 (43.3) | 0.006 | 10 (33.3) | 0.003 |

Hyperglycaemia at admission was also an independent predictor of increased length of stay (p≤0.001). A longer inpatient course was associated with an increased 90-day and 1-year mortality (p<0.001 for both). After adjusting for confounding variables, admission plasma glucose and length of stay remained significant predictors of 1-year mortality outcome (p=0.034 and p=0.003, respectively). In April 2019, a higher 90-day and 1-year mortality rate were noted (p=0.001 and p=0.015, respectively), together with a higher proportion of patients admitted with new-onset hyperglycaemia (p=0.012). In January 2019, more previously known patients with diabetes were admitted with hyperglycaemia (p=0.012). Younger patients were more likely to be admitted in the summer. When comparing mortality at 90 days and 1 year, April 2019 had a higher mortality rate than expected (p=0.001 and p=0.015, respectively). Interestingly, this was not observed in April 2020.

**Conclusion**

Our results indicate that plasma glucose is an important prognostic marker and may indicate a more severe illness. We recommend that these patients are highlighted with a greater level of care. A glycosylated haemoglobin level taken at admission in cases of new-onset hyperglycaemia can aid differentiation between stress hyperglycaemia and undiagnosed diabetes.

**References**

Systematic review of endoscopic ultrasound-guided biliary drainage versus percutaneous transhepatic biliary drainage

Authors: Eyad Gadour and Zeinab Hassan

University Hospitals of Morecambe Bay NHS Foundation Trust, Kendal, UK; Stockport NHS Foundation Trust, Stockport, UK

Introduction

Endoscopic ultrasound-guided biliary drainage (EUS-BD) is a novel technique that allows biliary drainage by echoendoscopy and fluoroscopy using a stent from the biliary tree to the gastrointestinal tract. Percutaneous transhepatic cholangiography biliary drainage (PTBD) is a diagnostic and therapeutic procedure that involves inserting a needle into the biliary tree, followed by the immediate insertion of a catheter. This study examined the technical aspects and outcomes of these different approaches to biliary drainage.

Materials and methods

We compared the technical aspects and outcomes of two different approaches to biliary drainage: EUS-BD and PTBD. Different databases (including PubMed, Embase, ClinicalTrials.gov, the Cochrane library, Scopus and Google Scholar) were searched according to the PRISMA guidelines to obtain studies comparing PTBD and EUS-BD.

Results

Among the six studies that fulfilled the inclusion criteria, PTBD patients underwent significantly more reinterventions (4.9 vs 1.3), experienced more post-procedure pain (4.1 vs 1.9) and experienced more late adverse events (53.8% vs 6.6%) than EUS-BD patients (Table 1).1-6 The EUS-BD group had a higher success rate of biliary drainage (92% vs 46%; p>0.05) and a lower rate of adverse events (20% vs 46%; p=0.05) than PTBD group. There was a significant reduction in total bilirubin in both groups (from 16.4 μmol/L to 3.3 μmol/L for EUS-BD and 17.2 μmol/L to 3.8 μmol/L for PTBD; p=0.002) at the 7-day follow-up. There were no significant differences observed for complication rates between PTBD and EUS-BD (3.3 vs 3.8, respectively). PTBD was associated with a higher adverse event rate than EUS-BD in all procedures, including reinterventions (80.4% vs 15.7%, respectively) and a higher index procedure (39.2% vs 18.2%, respectively).

Table 1. Rates of clinical and technical success in the included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Technical success</th>
<th>Clinical success</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>EGBD, event/total cases, n</td>
<td>PTBD, event/total cases, n</td>
</tr>
<tr>
<td>Artifon et al1</td>
<td>13/13</td>
<td>12/12</td>
</tr>
<tr>
<td>Bapaye et al2</td>
<td>23/25</td>
<td>26/26</td>
</tr>
<tr>
<td>Khashab et al3</td>
<td>19/22</td>
<td>51/51</td>
</tr>
<tr>
<td>Giovannini et al4</td>
<td>19/20</td>
<td>17/17</td>
</tr>
<tr>
<td>Jung et al5</td>
<td>32/34</td>
<td>31/32</td>
</tr>
<tr>
<td>Sharaiha et al6</td>
<td>43/47</td>
<td>12/13</td>
</tr>
</tbody>
</table>

EGBD = endoscopic ultrasound-guided choledochoduodenostomy; PTBD = percutaneous transhepatic biliary drainage.
Conclusion
The findings of this systematic review revealed that EUS-BD is linked with a higher rate of effective biliary drainage and a more manageable procedure-related adverse event profile than PTBD. EUS-BD could become a first-line biliary drainage treatment instead of endoscopic retrograde cholangiopancreatography if the outcomes of clinical studies are positive and technologies are simplified. Prospective, randomised controlled studies are required to clarify these issues.

References
Giant cell arteritis with normal inflammatory markers

Authors: Mohammad Bilal Habib and Afifa Riaz

Leicester Royal Infirmary, Leicester, UK

Introduction
Giant cell arteritis (GCA) is a granulomatous medium to large vessel vasculitis. It typically occurs in older people and is associated with polymyalgia rheumatica (PMR). The condition usually manifests with involvement of the extracranial branches of the carotid artery. This results in the classical symptoms of a headache, temporal tenderness, jaw claudication and associated constitutional symptoms (such as fever, lethargy and malaise). The most serious manifestation is permeant visual loss that occurs due to optic nerve ischaemia.

In the UK, the incidence of GCA is approximately 2.2 per 10,000 patient-years. A full-time general practitioner is likely to see a new case every 1–2 years.

Case presentation
An 86-year-old man presented to hospital with sudden onset visual loss in his right eye. His past medical history included chronic lymphocytic leukaemia, benign prostate hypertrophy and macular degeneration. Initial blood tests revealed a C-reactive protein (CRP) that was less than 5 mg/L, an erythrocyte sedimentation rate (ESR) of 30 mm/hour and a platelet count of 260 x 10^9/L.

He did not have any of the typical features GCA, eg headache, scalp tenderness, jaw claudication or constitutional symptoms. There was no associated PMR symptoms. An ophthalmology review was sought. Ophthalmological assessment revealed right eye anterior ischaemic optic neuropathy. This was followed by a temporal artery ultrasound showing widespread bilateral halo sign consistent with inflammation. This raised a strong suspicion of GCA, and the patient was subsequently treated with 3 days of intravenous methylprednisolone followed by prednisolone. This was given to protect the left eye from optic nerve ischaemia.

Temporal artery biopsy performed at a later stage showed adventitial chronic inflammation of uncertain significance.

The combination of ischaemic neuropathy and halo sign on ultrasound sufficed for a diagnosis of GCA to be made.

Discussion
The inflammatory nature of GCA typically results in raised inflammatory markers. Therefore, the American College of Rheumatology include an ESR of >50 mm/hr as one of its five classification criteria. CRP is a more sensitive marker than ESR for a positive temporal artery biopsy, which is diagnostic of GCA. In clinical practice, both tests are performed to evaluate for GCA.

This case is unusual as, at the time of presentation, the inflammatory markers were low to normal. Furthermore, the patient did not exhibit the classical symptoms of headache, scalp tenderness, jaw claudication or PMR-related symptoms. Rather, the patient presented directly with visual loss.

Notable learning points drawn from this case are that normal inflammatory markers should not exclude the diagnosis of GCA. If suspicion remains high, inflammatory markers should be repeated. It should also be
noted that GCA may not present with the typical symptoms of headache, temporal tenderness or jaw claudication; instead, it may present directly with visual symptoms.

Early treatment with steroids is essential to prevent progression of visual symptoms and to protect the contralateral eye.8

References
A case of acute lung injury due to an e-cigarette

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Introduction

Although considered to be by some as a safer alternative to smoking, electronic cigarettes (e-cigarettes) are associated with significant, even life-threatening, complications; for example, e-cigarette or vaping product use-associated lung injury (EVALI) especially in older patients with pre-existing respiratory and cardiovascular comorbidities. We present an interesting case of a patient who was admitted with confusion, fever, cough and breathlessness with raised inflammatory markers and bilateral radiologic abnormalities on chest imaging.

Case presentation

A woman aged in her 40s presented with 1-week history of fever, cough, shortness of breath and confusion. She was normally fit and well with past medical history of asthma, anxiety and Lown–Ganong–Levine syndrome. Her usual medications included salbutamol metered dose inhaler and sertraline. There was no history of recent travel, flu-like illness, use of recreational drugs or trauma. In the previous few months, she had started to vape an e-cigarette and she drank alcohol in moderation. On examination, she was alert but confused with no focal neurology and no signs of meningism. Chest auscultation revealed bilateral crackles. The rest of the examination was normal. Chest X-ray showed widespread, bilateral pulmonary infiltrates, consisting of a mixture of ill-defined and nodular opacities (Fig 1). Routine blood tests showed raised inflammatory markers with C-reactive protein (CRP) of 161 mg/L, white cell count of 11.3 x 10⁹/L and neutrophil count of 9.3 x 10⁹/L. There was patchy bilateral consolidation involving all the lobes in the computed tomography (CT) of the chest (Fig 2) along with enlarged bilateral hilar and mediastinal nodes. CT of the head, magnetic resonance imaging of the head and CT of the abdomen and pelvis were nil acute. Blood and urine culture had no growth. Viral respiratory panel; chlamydophilla; mycoplasma serology; anti-HIV antibodies; pneumococcal and Legionella urinary antigen; and vasculitic and connective tissue disease screens were all negative. Electrocardiography and 2D echocardiography were within normal limits. The patient was started on broad spectrum antibiotics and high-dose oral prednisolone with rapid clinical improvement. Repeat chest imaging was done after 2 weeks of onset of symptoms and this showed that the lungs were clear, with preserved volume and satisfactory mediastinal and hilar shadows.

Fig 1. Posteroanterior X-ray of the chest.
Fig 2. Axial computed tomography of the chest.

Results

Although EVALI is a diagnosis of exclusion, rapid resolution of symptoms and radiological findings with high-dose corticosteroids and ruling out alternative diagnoses confirmed the diagnosis of EVALI.

Conclusion

Due to variable presentation of EVALI, there is no consensus regarding its diagnostic criteria.⁴,⁵ Case definition stipulates that, to diagnose EVALI, there should be a history of use of an e-cigarette in the previous 90 days along with lung opacities on chest imaging, exclusion of lung infection based on negative influenza PCR, viral respiratory panel and urine antigen tests for Legionella and Streptococcus pneumoniae, blood cultures, sputum culture, bronchoalveolar lavage and testing for HIV-related opportunistic infections and absence of a likely alternative diagnosis (e.g., cardiac, neoplastic or rheumatologic).⁶ Even though underlying pathogenesis of EVALI remains elusive, multiple potential toxins have been highlighted including vitamin E acetate, tetrahydrocannabinol, nicotine and others.⁷,⁸ Risk factors for more severe disease include obesity, increasing age, history of asthma and cardiac disease.³ Due to widespread usage of e-cigarettes, clinicians should be vigilant regarding this serious respiratory illness that can be life threatening.⁹,¹⁰

References


Takotsubo cardiomyopathy or hidden cardiotoxic event by rituximab

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Introduction

Rituximab is a genetically engineered chimeric mouse/human monoclonal antibody representing a glycosylated immunoglobulin (Ig) with human IgG1 constant regions and murine light-chain and heavy-chain variable region sequences. The antibody is produced by mammalian cell suspension culture and purified by affinity chromatography and ion exchange, including specific viral inactivation and removal procedures.

It is used for:

- non-Hodgkin’s lymphoma
- chronic lymphocytic leukaemia
- granulomatosis with polyangiitis and microscopic polyangiitis
- pemphigus vulgaris
- Epstein–Barr virus infection.

Takotsubo cardiomyopathy is a syndrome characterised by transient regional systolic dysfunction, principally, of the left ventricle, mimicking myocardial infarction but in the absence of angiographic evidence of obstructive coronary artery disease or acute plaque rupture.

The onset of stress cardiomyopathy is frequently, but not always, triggered by intense emotional or physical stress (eg death of relatives, particularly if unexpected; domestic abuse; arguments; catastrophic medical diagnoses; devastating financial or gambling losses; natural disasters; or acute medical illness).

Infusion-related reaction by rituximab were reported in more than 50% of patients in clinical trials, and were predominantly seen during the first infusion, usually in the first one to two hours. These symptoms mainly comprised fever, chills and rigors. Other symptoms included flushing, angioedema, bronchospasm, vomiting, nausea, urticaria/rash, fatigue, headache, throat irritation, rhinitis, pruritus, pain, tachycardia, hypertension, hypotension, dyspnoea, dyspepsia, asthenia and features of tumour lysis syndrome. Severe infusion-related reactions (such as bronchospasm or hypotension) occurred in up to 12% of the cases.

Materials and methods

A retrospective study of a clinical case of cardiac reaction caused by rituximab infusion in a haematological day unit by history taking, physical examination, electrocardiography (ECG), blood tests and coronary angiography report was performed.

Case presentation

A 52-year-old man presented to haematology unit with a fever of unknown origin was found out to have Epstein–Barr virus active infection. He had previous medical history of unstable angina and treated acute myeloid leukaemia with allogenic stem cell transplant .Intravenous (IV) rituximab treatment was given according to multidisciplinary team discussion. 10 mins after the start of IV rituximab infusion (15 mL has been given already), the patient developed fever, rigors and hypotension that is normally found as an infusion-related reaction. However, contrary to usual reactions, the patient also complained of cardiac sounding chest pain with unstable haemodynamic status. ECG was performed and there was evidence of ST
elevation myocardial infarction. The patient was transferred immediately to a tertiary centre for urgent coronary angiography and later was diagnosed with Takotsubo cardiomyopathy with typical appearance of apical ballooning findings on left ventriculography in the absence of angiographic evidence of obstructive coronary artery disease or acute plaque rupture (Fig 1).

**Fig 1.** Left ventriculography showing typical appearance of apical ballooning.

### Conclusion

An acute infusion-related reaction can be considered as a medical stress in causing Takotsubo cardiomyopathy, an unusual and hidden side effect of rituximab infusion. There was reported evidence of angina pectoris, cardiac arrhythmias (such atrial flutter and fibrillation), heart failure and/or myocardial infarction. Therefore, a patient with a history of cardiac disease and/or cardiotoxic chemotherapy should be monitored closely during rituximab infusion and also should have a proper and thorough pre-assessment of cardiovascular risks before rituximab infusion.

### References

Teriparatide therapy for medication-related osteonecrosis of the jaw: case report and literature review

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Introduction
Medication-related osteonecrosis of the jaw (MRONJ) is a recognised complication of antiresorptive therapy. Emerging evidence suggests impaired epithelialisation post-dental surgery, local pro-inflammatory response and inhibition of angiogenesis in its pathogenesis. Risk factors include old age, prolonged medication exposure, intravenous bisphosphonates (BP), smoking, glucocorticoid therapy, anaemia, obesity, diabetes and cancer.

Case presentation
We present the case of an 81-year-old woman with severe osteoporosis and ischaemic heart disease, who had been on alendronate 70 mg weekly for 3 years from when she had a tooth extraction. Three months later, she presented to maxillofacial surgery with non-healing extraction sites, facial pain and erythema, and a malodorous discharging sub-mantle sinus. She received a diagnosis of stage 3 MRONJ confirmed by orthodentography and computed tomography. She had Proteus mirabilis on tissue culture. She had no history of osteosarcoma or local radiotherapy.

For 14 months, she underwent conventional therapy with limited debridement of the exposed bone, long-term antibiotics and chlorhexidine wash of the exposed areas, but her condition deteriorated. On referral to rheumatology, her vitamin D deficiency was corrected, total procollagen type 1 N-terminal propeptide (P1NP) and C-terminal cross-linking telopeptide (CTX) were within normal limits. She was commenced on subcutaneous teriparatide 20 µg daily for 2 years.

Within 2 months, there was full soft tissue coverage of the intramural lesion, the fistula was lined with healthy oral mucosa and she did not require further debridement. Within 5 months, her P1NP doubled and CTX remained the same. She then underwent surgical closure of the orocutaneous fistula. This healed successfully, leading to improved appetite and gradual weight gain. She was then provided with upper and lower dentures.

Discussion
The incidence of MRONJ in the UK is 620 per year. At the time of treatment, we reviewed 11 case reports, two case series and one retrospective study using teriparatide to treat MRONJ that was resistant to conventional treatment in a total of 44 patients, where all but one patient found a favourable outcome.

The biological rationale for the benefit of teriparatide (is a recombinant parathyroid hormone (rPTH)) could be that rPTH increases the proliferation of T-cells, thereby increasing Wnt-10b protein production and enhancing osteoblast differentiation. Teriparatide enhances osteoblast RANKL production to drive osteogenesis and augments osteoclast recruitment. These cells are pivotal to bone healing and a prerequisite for the anabolic effect of teriparatide on osteoblasts.
Teriparatide induces and ‘anabolic window’ where there is early response of the bone formation markers with delayed catch-up of resorption marker in MRONJ patient within the first 9 months of treatment, leading to a positive bone balance and indicating a role for these in monitoring treatment response.\textsuperscript{8}

Over the past 2 years, a systematic review and an randomised controlled trial has finally established the beneficial effect of teriparatide in the treatment of MRONJ, which provides welcome relief to the rare patients afflicted with this condition.\textsuperscript{9,10}

References
Predicting outcomes for Crohn's disease using a molecular biomarker: profile trial

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Introduction

Crohn’s disease (CD) and ulcerative colitis (UC), the two major forms of inflammatory bowel disease (IBD), collectively affect 0.8% of the population in the UK. IBD can have a profound health and socio-economic impact on patients, typically affecting educational achievement, relationships and employment. However, the course of IBD varies substantially between individuals and accurate prognostic markers have historically not been available to guide clinical practice. It has, therefore, become widely recognised that no single treatment strategy would be optimal for all patients. Accordingly, there has been an aspiration for a more personalised approach in IBD, being named one of the key research priorities by a research priority-setting partnership group, which included patients, clinicians and other key stakeholders.

Previously, our group has described a transcriptional signature detectable within peripheral blood CD8 T-cells at diagnosis, identifying two subgroups of patients, correlating with subsequent disease course. We have sought to develop a biomarker that could re-capitulate the previously identified prognostic CD8 subgroups and then assess whether such a biomarker could improve clinical outcomes by appropriately matching therapy to disease course for individual patients.

Methods

From a training cohort of 69 newly diagnosed IBD patients, we simultaneously obtained a whole-blood PAXgene® RNA tube and peripheral-blood CD8 T-cell sample. Gene expression in both samples was measured by microarray. Statistical modelling was used to identify a transcriptional classifier in whole-blood gene expression data re-capitulating the CD8 findings and optimised into a multi-gene qPCR assay with independent validation in a second, independent cohort of 123 newly diagnosed patients.

The PROFILE trial has incorporated this classifier to compare relative efficacy of ‘top-down’ and ‘accelerated step-up’ therapy between biomarker-defined subgroups of 400 patients with newly diagnosed Crohn’s disease. PROFILE is assessing outcomes that have consistently been reported as important to patients: clinical remission and avoidance/reduction of steroids and surgery, as well as quality of life. Alongside the trial, a formal health economic analysis is being conducted, as well as a national evaluation by the National Institute for Health and Care Excellence (NICE). If clinical utility is demonstrated, then it is anticipated that this biomarker-stratified approach could be implemented into routine clinical care.

Results

Following application of statistical learning methods described, a 17-gene qPCR assay was developed and optimised. In the validation cohort, 123 patients could be classified into two distinct subgroups: IBDhi (high risk) and IBDlo (lower risk). Irrespective of the underlying diagnosis, IBDhi patients experienced significantly more aggressive disease than IBDlo patients, with earlier need for treatment escalation (hazard ratio 2.65...
(CD) and 3.12 (UC)). Subsequently, this biomarker has been used to stratify therapy in the PROFILE trial (395 enrolled), where recruitment has completed and follow-up due for completion in December 2022.

**Conclusion**

We have developed, optimised and validated a whole-blood qPCR classifier that predicts disease course from diagnosis in patients with IBD. This classifier is currently being assessed in the PROFILE trial, the first biomarker-stratified trial in gastroenterology and, if clinical utility of a stratified treatment approach is demonstrated, this would represent a major step towards personalised therapy in IBD.

**Funding statement**

This trial is funded by the Wellcome Trust via an investment in PredictImmune (200448/Z/16/Z)

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**Tumour-induced osteomalacia**

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**Introduction**

Phosphate is important for normal mineralisation of bone. Phosphate is important in its own right for neuromuscular function, and profound hypophosphataemia can be accompanied by encephalopathy, muscle weakness and cardiomyopathy. Hypophosphataemia can be due to intracellular uptake of phosphate from the extracellular fluid, reduced intestinal phosphate absorption, increased renal excretion, decreased renal tubular absorptive capacity and genetic defects in renal tubule phosphate transporters.

**Case presentation**

A 31-year-old woman presented with hypophosphataemia (0.62–0.66 mmol/L), an abnormality she had since 2012. Fibroblast growth factor-23 (FGF-23) was above the upper limit of normal (98 pg/mL) but parathyroid hormone, calcium, full blood count, renal function test, random blood sugar, vitamin D and liver function test were normal. Her medical history included asthma, previous Ewing sarcoma in the chest wall for which she received chemotherapy, adjuvant radiotherapy and multiple chest wall operations in 2011. She was an ex-smoker. Family history was unremarkable. Based on history, examination and investigation, tumour-induced osteomalacia was the most likely diagnosis.

**Discussion**

FGF-23 plays an important role in the development of hypophosphataemic disease, such as tumour-induced osteomalacia, X-linked hypophosphataemic rickets/osteomalacia (XLH). It reduces serum phosphate by supressing proximal tubular phosphate reabsorption and intestinal phosphate absorption.

TIO is a rare cause of impaired bone mineralisation. Removal of the tumour resulted in rapid reduction in serum FGF 23 levels. In our patient with TIO and XLH, FGF23 was above the upper limit of the reference range in most patients irrespective of medical treatment.

Phosphate and active vitamin D can be used in excessive action of FGF23 including a patient with TIO with unresectable tumours, but it has limited effects and several adverse events. Burosumab can be used in XLH.

**References**

Rapid echocardiography in the primary angioplasty era for timely detection and management of acute Stanford type A aortic dissection: a case illustration

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Introduction

Acute Stanford type A aortic dissection (ATAD), comprising two-thirds of all captured aortic dissections (AD) in the International Registry of Aortic Dissection (IRAD) series, is a life-threatening cardiothoracic emergency. Inpatient mortality without surgical intervention is approximately 50%–60%, reducing to 18% with timely operative management. Presentation is with cardiac chest pain (CCP) sometimes in conjunction with neurological, abdominal or peripheral vascular symptoms. Ischaemia on electrocardiography (ECG) and elevated troponin are often seen, precipitating initial management for acute coronary syndrome (ACS). We describe two cases of cardiac catheter lab (CCL) activation for presumed ST-elevation myocardial infarction (STEMI), where rapid echocardiography clinched diagnosis of ATAD and allowed timely transfer for life-saving surgical intervention.

Case 1

A previously fit 50-year-old man presented with CCP, inferolateral T-wave inversion and high-sensitivity troponin T of 646 ng/L. Treatment for ACS including dual-antiplatelet therapy was commenced. Ongoing chest pain, despite high-dose morphine, triggered repeat ECG, which demonstrated dynamic inferolateral ST elevation and led to CCL activation though bilateral blood pressures and transthoracic echo (TTE) were also advised. These revealed a 30 mmHg blood pressure difference and a large dissection flap prolapsing into the ventricular outflow tract causing free aortic regurgitation (AR; Fig 1). Computed tomography (CT) of the aorta (Fig 2) was performed and the patient transferred directly to theatre at the regional cardiothoracic centre within 90 minutes of TTE diagnosis. He underwent aortic repair and mechanical aortic valve replacement (AVR).

Fig 1. Aortic dissection detected by transthoracic echo. a) Aortic root dissection flap. b) Colour flow showing severe aortic regurgitation jet. c) Dissection flap prolapsing into left ventricular outflow tract.
**Case 2**

A 69-year-old man with hypertension and hypercholesterolaemia, suffered severe CCP. Paramedic ECGs demonstrated widespread malignant ST-depression with ST-elevation in AVR, suggestive of critical left-main stem disease and triggering CCL activation. While preparing for emergent angiography in the CCL, revisitation of clinical history revealed symptoms of both transient visual disturbance at onset of chest pain and examination findings included a loud holodiastolic murmur. Rapid TTE was performed showing dilated aorta (5.8 cm) with mobile dissection flap intermittently compromising coronary ostia alongside free AR. Immediate onward transfer to cardiothoracic theatre occurred. At operation, dissection involvement of the left main ostium was observed, and treatment was with a 32 mm aortic interpositional graft.

**Discussion**

Annual incidence of AD is rare, reported at 4.4 per 100,000 person-years. Misdiagnosis of AD for ACS is unsurprising given the incidence of the latter is significantly higher, reported at 234 per 100,000 person-years. A recent study characterising aortic syndromes reported presence of aortic insufficiency and coronary ischaemia in 18.2% and 6.5% of all AD cases, respectively. Further, though CT was the primary modality of diagnosis (68.8%), echocardiography was successfully utilised in 16.9%. Study of TTE versus CT of the aorta for diagnosis of ATAD demonstrates accuracy, speed and ease of use of TTE and notes the value of additional information pertaining to complicating features of ATAD, such as aortic insufficiency and cardiac tamponade.

**Conclusion**

Utilisation of rapid TTE in the CCL prior to emergent angiography in ACS presentations where clinical suspicion for AD is triggered, can allow early detection of ATAD, prevent detrimental coronary angiography and expedite appropriate life-saving operative interventions.

**References**


Don't just fit and forget: incremental benefit of optimisation of medical therapy post-cardiac resynchronisation therapy

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Introduction

Cardiac resynchronisation therapy (CRT) is recommended for suitable patients with heart failure (HF) who continue to be symptomatic despite optimal medical therapy (OMT).1 In reality, only a minority of patients are able to tolerate target dosages of guideline-directed medical therapy (GDMT) prior to receiving CRT.2 Common reasons for the same include low blood pressure, bradycardia, pauses, kidney injury or a combination of these factors.2 The aim was to assess whether a review by the heart failure team (HFT) post-CRT resulted in further optimisation of medical therapy for HF. The effect of this intervention on hospitalisation for HF, incidence of ventricular arrhythmias and mortality was also assessed.

Materials and methods

Retrospective analysis of records of consecutive patients undergoing CRT implantation (n=83; CRT defibrillator 70/83 (84.3%); CRT pacemaker 13/83 (15.7%)) between March 2017 and February 2019. Follow-up duration was 12 months. Baseline medical therapy prior to CRT was assessed. Patients reviewed by the HFT within six months of receiving CRT were compared with those who were not. Optimisation was defined as upward adjustment of dosages of GDMT or introduction of a new disease-modifying drug that the patient was not initially suitable for pre-CRT.

Results and discussion

Mean age was 71.1 ±11.1 years and there were 58/83 (70%) men. Prior to CRT, the proportion of those on target dosages of angiotensin inhibitors, betablockers, mineralocorticoid receptor antagonist and sacubitril–valsartan was 27.7% (23/83), 24.0% (20/83), 8.4% (7/83) and 6.0% (5/83), respectively. Twenty-five (72%) patients reviewed by the HFT post-CRT had their medications optimised. Of the remainder (58/83; 69.9%), only 5.2% had their medications optimised. Beta-blockers were the most optimised medication. The proportion of patients experiencing ventricular arrhythmias (VTs) treated by the device, hospitalisation for HF and mortality was higher among those not reviewed by the HFT (Fig 1).

Fig 1. The 12-month outcomes for those reviewed and not reviewed by the heart failure team. ATP = anti-tachycardia pacing; GDMT = guideline-directed medical therapy; HF = heart failure.
The low proportion of patients on target dosages of GDMT is a reflection of the difficulty attaining the optimal recommended dosages prior to CRT. Our findings show that, in a vast majority of patients, there is room for optimisation of GDMT post-CRT. This may be because of an improvement in blood pressure following CRT as found in the COMPANION and CARE-HF trials. It may also be from protection against bradycardia, sinoatrial nodal pauses and slowing of atrio-ventricular conduction offered by CRT. The difference in VTs between the two study groups may have resulted from the higher proportion of beta blocker optimisation among those reviewed by the HFT. Background severity of HF, response to CRT, short duration of follow-up and other comorbid conditions may have contributed to the attenuation of differences in other clinical outcomes observed between the study groups.

Conclusion
We strongly recommend that all patients receiving CRT should have their medications optimised post-implant. In view of their expertise, this is best done by the HFT as attaining target dosages of GDMT remains a cornerstone of heart failure treatment, favourably influencing symptoms as well as possible prognosis.

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Pancreatic cancer with multiple liver metastasis complicating multi-organ infarcts from marantic endocarditis and Trousseau's syndrome

Authors: Mir Rahman, Alan Wiles and Raj Shekhar

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A middle-aged previously healthy and fit man presented with left sided weakness, slurred speech, left sided sensory neglect, mild headache and fever. He denied having any cough, shortness of breath, chest pain, palpitations, abdominal pain or bowel-bladder symptoms. He has smoked 5–10 cigarettes per day since adolescence and drank 1–2 cans of beer occasionally. He denied use of illicit drugs. He had two doses of COVID-19 vaccine and never had COVID-19. Repeated COVID-19 PCR swab was negative throughout the hospital stay. At admission, on systemic examination he only had left-side hemiparesis with mild left-side sensory neglect and upper motor neuron type of facial nerve palsy with no signs of meningism. Glasgow coma score was 14/15. Cardiovascular, respiratory and abdominal examinations were unremarkable. Vital signs were stable except for a mild rise of temperature of 37.8°C. Computed tomography of the head showed acute right-sided temporal ischaemic changes. He was not thrombolysed as the onset of symptoms was more than 4.5 hours. Blood tests showed high infection markers with C-reactive protein of 202 mg/L, normal haemoglobin, clotting screen and kidney function. Blood and urine cultures were negative. Electrocardiography showed sinus tachycardia and chest X-ray was unremarkable. Echocardiography showed low normal ejection fraction with mild mitral regurgitation. Transoesophageal echocardiography arranged on theatre that was documented as mitral valve vegetation. He was started on broad spectrum intravenous antibiotics for suspected infective endocarditis. He also complained of left leg pain for two months. Left leg ultrasound Doppler on this admission showed a large left leg deep vein thrombosis involving the femoral vein. Magnetic resonance imaging (MRI) of the head and magnetic resonance angiography of the carotids showed multiple cerebral and cerebellar infarcts with normal carotid arteries (Fig 1).

Fig 1. Magnetic resonance imaging diffusion weighted imaging of the head showing multifocal cerebral and cerebellar infarcts with cytotoxic oedema.
On the 9th day of admission, the liver function test was done and came back deranged with bilirubin of 13.7 μmol/L, alanine aminotransferase of 212 U/L, alkaline phosphatase of 188 U/L, gamma-glutamyl transferase of 415 U/L, albumin of 29 g/L with normal international normalised ratio and platelets. Previous liver function tests were normal. Computed tomography of the chest, abdomen and pelvis with contrast showed bilateral pulmonary embolism, kidneys and spleen infarction, and multiple liver metastasis with unknown primary. He was started on treatment dose of low-molecular weight heparin for pulmonary embolism. Magnetic resonance imaging of the liver showed multiple liver metastasis with primary mass in the tail of the pancreas (Fig 2).

**Fig 2. Magnetic resonance imaging of the liver showing primary malignancy in the tail of the pancreas (35 x 20 mm) with hypovascular liver metastasis; the scan was limited due to motion artefacts.**

Antiphospholipid antibodies, HIV, hepatitis and vasculitis screening were negative, and non-invasive liver tests (autoimmune liver antibodies, alpha-1 antitrypsin, serum ceruloplasmin and iron studies) were normal. Cancer screening showed high carbohydrate antigen 19-9, >10,000 U/mL, normal alpha-fetoprotein and prostate specific antigen levels. The patient’s mother mentioned that he had attended the general practitioner surgery 3 months previously for right leg sprain and the acute emergency care (AEC) unit in hospital 2 months previously for left leg cellulitis. D-dimer in AEC unit was very high, 6,500 ng/mL. The clinical events explained that he most likely developed Trousseau’s syndrome 3 months previously and the embolic phenomena were due to rare marantic endocarditis (non-bacterial thrombotic endocarditis) secondary to pancreatic cancer. The multidisciplinary team advised for ultrasound-guided biopsy of liver metastasis, but sadly the patient passed away the next day.
A case of central nervous system mucormycosis in a patient with uncontrolled diabetes mellitus

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A 38-year-old man with diabetes presented with lethargy, night sweats, weight loss, right-sided pleuritic chest pain, fever and rigors, and hyperglycaemia. Chest X-ray and computed tomography (CT) of chest demonstrated multifocal inflammatory changes within the lungs.

Differential diagnoses included atypical pneumonia and tuberculosis (TB). Intravenous (IV) antibiotics and insulin for uncontrolled diabetes were commenced. Bronchoscopy was requested to rule out TB. He subsequently developed left-sided weakness. An urgent CT of the head demonstrated bilateral, but more marked right-sided low-attenuation intra-cerebral lesions with vasogenic oedema. Magnetic resonance imaging of the brain confirmed ring enhancing lesions, likely tuberculomas (Fig 1). TB treatment and IV dexamethasone were initiated. He developed worsening neurology with meningism and bulbar weakness. A further CT of the head demonstrated worsening bilateral ring-enhancing lesions and vasogenic oedema (Fig 2). The neurosurgeons performed a mini-craniotomy and aspiration of the right parietal brain abscesses; polymerase chain reaction testing for TB was negative. Histology and cultures showed pauci-septate branching non-pigmented fungal hyphae and *Apophysomyces variabilis*. A diagnosis of central nervous system (CNS) mucormycosis was made; isavuconazole with IV liposomal amphotericin was commenced. Despite 4 weeks of treatment, deterioration continued, leading to his death.

Mucormycosis is an opportunistic fungal infection. Prevalence is low in developed countries compared with developing nations, like India, where prevalence is 70 times higher.\(^1\) Common causes for CNS involvement are intravenous drug use (62%) and uncontrolled diabetes (43%).\(^2\) Mortality has been reported as 46%, with 68% in disseminated infections.\(^3\) Histology and culture are essential for diagnosis. Treatment is liposomal amphotericin and surgical debridement with the duration guided by radiological and clinical response.

The need to consider fungal infections in immunocompromised patients with worsening symptoms despite broad spectrum antibiotics is highlighted. Prompt treatment is paramount due to high mortality.

**Fig 1.** Coronal T1 weighted magnetic resonance imaging with contrast showing multiple ring enhancing lesions (arrows) with surrounding oedema in the right parietal lobe and left cerebellum.
Fig 2. Axial compute tomography of the head with contrast 2 days after presentation showing worsening vasogenic oedema around the ring enhancing lesion in the right parietal lobe (arrow)

References

Age-adjusted versus cut-off for D-dimer to exclude pulmonary embolism audit

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Aim
The aims in our trust was to change the cut-off of 500 µg/L to age adjusted D-dimer (AAD) in patients who are aged 50 years or above, improve the documentation of pre-test probability in clinical notes and encourage our radiology department to mention the presence or absence of right ventricular heart strain in their reports.

Method
We retrospectively reviewed 400 computed tomography pulmonary angiographies (CTPAs) for patients aged 50 years or more; comparing age, gender, laboratory D-dimer, AAD, CTPA result and pre-test probability.

The D-dimer result was interpreted according to our conventional cut-off (500 µg/L), in addition, an age-adjusted cut-off was analysed, which is considered negative if D-dimer was lower than a patient’s age (in years) x 10.¹

Results
Of the 400 scans, 300 matched the criteria for the study. Pre-test probability was documented in 50/300 (16.6%) and D-dimer checked in 173/300 (57.6%) patients.

From 173 patients, 36 (20.8%) patients had a finding of pulmonary embolism (PE), all should have had the scan in accordance with AAD recommendations (100%).

One-hundred and thirty-seven patients had D-dimer over 500 µg/L but negative for PE and 24 (17.5%) patients had D-dimer over 500 µg/L but below AAD were all negative on imaging for PE (100%).

D-dimer was not checked in 127/300 and 22 (18.6%) patients had finding of PE.

Fifty-eight out of 300 patients had imaging findings of PE, only 37 (63.7%) patients had a mention of right heart strain within the imaging report.

We presented the findings in grand round and delivered multiple teaching sessions to junior doctors and specialist nurses.

Re-audit of 100 CTPAs for patients aged 50 years or more were reviewed; 23 (23%) were found to be positive on imaging for PE. Of the 23, three (13%) patients would not have been suitable for imaging if the AAD was the only factor considered when referring the patient for imaging. However, the pre-test probability was not reviewed for these patients and this could have been the indications for referring these patients for imaging.

Eleven (11%) patients were negative for PE and under AAD and would not have been referred for imaging if the principals of the AAD guidelines had been applied (assuming low probability score).
**Conclusion**

This audit highlighted the importance of documentation and full consideration of patients prior to referring for imaging. Initial audit found that, if AAD theory had been applied, then it would have prevented 24 patients from having CTPA. However, the re-audit demonstrated that 23 patients would not have fit the criteria for AAD, even though three patients were positive for PE on imaging.

Overall, there was poor documentation regarding pre-test probability score and low assurance within the radiology reports regarding right heart strain, in keeping with the NCEPOD report.

Without robust documentation it has been difficult to assess the validity of the use of AAD in line with national guidelines. Further work is required to ensure robust documentation and improvement of training and then re-audit.

**References**

3. National Confidential Enquiry into Patient Outcome and Death. Know the Score: A review of the quality of care provided to patients aged over 16 years with a new diagnosis of pulmonary embolism. NCEPOD, 2019
The BSG/BASL bundle for patients admitted with decompensated chronic liver disease improves standard of care but utilisation is poor across the UK

Authors: The Trainee Collaborative for Research and Audit in Hepatology UK

Introduction

Standardised mortality for patients with chronic liver disease (CLD) has dramatically increased in the UK since 1970.¹ The National Confidential Enquiry into Patient Outcome and Death previously reported that less than 50% of inpatients admitted with alcohol-related liver disease (ARLD) received good care.² The British Association for the Study of Liver Disease (BASL) and British Society of Gastroenterology (BSG) commissioned the development of a care bundle to improve standards of care for patients with CLD within the first 24 hours of hospital admission.³ We aimed to audit the uptake of the bundle and assess its impact on patient outcomes across the UK.

Methods

This was a national trainee-led retrospective audit conducted through the Trainee Collaborative for Research and Audit in Hepatology UK (ToRch-UK).⁴ All patients admitted with decompensated cirrhosis between 01 November 2019 – 30 November 2019 were included in this study. Inclusion/exclusion criteria are defined in Fig 1.

Fig 1. Inclusion/exclusion criteria for retrospective audit of the uptake of the bundle for patients with chronic liver disease.

Admission clinical, demographic and laboratory data were collected with outcome data and trust-specific data. Univariate and multivariate analyses were performed.

Results

There were 1,179 admissions from 1,124 patients from 99 sites across the UK included, making this the largest audit of the BSG/BASL admission care bundle to date. Median age was 58.00 years (interquartile range (IQR) 48.00–68.00), 62.00% were men, 59.28% were admitted out of hours, 87.62% had an underlying diagnosis of ARLD or non-alcoholic fatty liver disease (NAFLD) and median model for end-stage liver disease (MELD) score was 16.50 (IQR 12.00–21.00). Patient admission mortality was 15.80%.
Uptake of the bundle was low at 9.41%. There was significant geographical variation in use between NHS regions, with NHS North East and Yorkshire being the highest users (26.92% of admissions). When comparing admissions where the bundle was used to those where it was not, it was significantly more likely to be used in admissions for patients with ARLD (90.09% vs 72.57%; p<0.0001), with jaundice as presenting complaint (25.23% vs 13.95%; p=0.003) and with higher MELD scores (19.00 (IQR 14.00–22.00) vs 16.00 (IQR 12.00–21.00); p=0.008). Bundle use was associated with improved standards of care within the first 24 hours of admission. Compared with admissions where the bundle was not used, there was significantly increased completion of necessary blood tests, septic screens, ascitic taps, alcohol history and care plan completion, and acute kidney injury care plan completion. Patients with a completed bundle were more likely to see a gastroenterologist/hepatologist within 24 hours. Mortality was higher in patients where the bundle was used. However, when adjusted for age and MELD scores, this was not significant (adjusted odds ratio 1.62 (95% confidence interval 0.93–1.75)).

Conclusions
The BSG/BASL admission bundle improves standard of care but is poorly utilised across the UK. Work is required to understand the barriers to use in order to improve inpatient care for patients with CLD.

Funding statement
Funding supplied by GUTS-UK.

References
Myasthenia mimicry

Author: Stephanie Teh

Betsi Cadwaladr University Health Board, Bangor, UK

Background

Bickerstaff’s encephalitis is a rare GQ1b-mediated polyneuropathy, considered to be a brainstem variant of Guillain–Barré syndrome and Miller Fisher syndrome. It is classically differentiated from Miller Fisher syndrome by an altered sensorium but similarly demonstrates ophthalmoplegia and ataxia. Other commonly described features include peripheral involvement and bulbar weakness. Myasthenia gravis is more common, a chronic autoimmune condition primarily characterised by muscle weakness and fatiguability, and is an important cause of neuromuscular respiratory failure.

Case presentation

This case reports a man aged in his late 60s who presented with dysphagia to solids and headaches, double vision and an unsteady gait. He had a history of an antecedent viral upper respiratory tract illness a week prior to the onset of his symptoms. On arrival at the emergency department, he was assessed to be ataxic, ophthalmoplegic and was mildly confused (scoring 8/10 on AMT-10) but with no other neurological signs. Shortly after arrival, he became floridly confused and agitated with marked intermittent stridor. An arterial blood gas demonstrated severe respiratory acidosis secondary to hypercapnic respiratory failure. He was intubated for airway protection and subsequent investigations including direct visualisation of his vocal cords, oesophago-gastro-duodenoscopy, computed tomography and magnetic resonance imaging all did not find a cause for his symptoms. Cerebro-spinal fluid (CSF) analysis showed albuminocytological dissociation and nerve conduction studies demonstrated absent proximal motor responses and possible conduction block.

The combination of ataxia, altered sensorium, ophthalmoplegia, bulbar palsy, nerve conduction and CSF results prompted an initial working diagnosis of brainstem encephalitis, Bickerstaff’s: a GQ1B-mediated Guillain–Barré variant. Autoantibodies were sent for GQ1B, myasthenia and voltage-gated calcium channels (VGCC).

He had a stormy clinical course with two failed primary extubations in his first week of presentation, and seeming improvement post-intravenous immunoglobulins (IVIG), with a recurrence of his symptoms 1 month later. A second IVIG course was restarted and autoantibody results was found later positive for anti-acetylcholine receptor, confirming a diagnosis of late onset myasthenia. Anti-GQ1B, VGCC and GM1 were all negative.

Key points

This case critically highlights the overlap of key GQ1B and myasthenia features and demonstrates the challenge of distinguishing between them in clinical practice. The concurrent presentation of both stridor and his postural worsening of symptoms is suggestive of both a diaphragmatic and bulbar palsy while his history of weight loss with negative investigations may relate to a more insidious course of tongue and palate muscle weakness.
Association of quality of life with performance status, circadian rhythm, and activity level of lung cancer patients using wearable devices as ambulatory monitoring

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AHospital Universitario Puerta de Hierro Majadahonda, Majadahonda, Spain; BUniversidade Nova de Lisboa, Lisbon, Portugal; CUniversidad Politecnica de Madrid, Madrid, Spain; University of Murcia, Murcia, Spain

Introduction

Lung cancer survivorship has two critical attributes: survival time or quantity and quality of life (QoL). After decades of efforts focusing on reducing lung cancer incidence and mortality, we are now challenged by the lack of understanding of the health conditions and QoL among people who survived lung cancer. Herein, we report on the first integration of clinical data, wearable devices and QoL questionnaires in order to determine the factors that predict poor health status and to design personalised interventions that will improve patients’ QoL, based on clinical and real-world data.

Methods

Patients diagnosed and treated at the medical oncology department at Puerta de Hierro University Hospital were included. Eligible patients were aged >18 years old, were diagnosed with non-small-cell lung cancer (all stages) and had an Eastern Cooperative Oncology Group score 0–1. Artificial intelligence (AI) and knowledge discovery (KD) techniques were used to integrate heterogeneous datasets and synthesise complex relationships within these large data sets. A watch-like wearable device (Kronowise 3.0, Kronohealth, Espinardo, Spain) was placed on a patient’s wrist for a whole week, registering temperature, physical activity and light exposure for 24 hours a day. Written informed consent was obtained from all patients prior to the initiation of the study. The EORTC core quality of life questionnaire (EORTC QLQ-C30), designed to measure cancer patients’ physical, psychological and social functions, was completed by all patients.

Results and discussion

A total of 140 patients were included in the study: 32 were diagnosed with localised disease (IA–IIIB), and 98 with advanced stage IIIC/IV receiving different treatments (radiotherapy, chemotherapy, immunotherapy, chemotherapy plus immunotherapy and tyrosine kinase inhibitors; Table 1). Results from QoL questionnaires showed that pain, dyspnoea and insomnia were the most common symptoms reported by lung cancer patients. Sixty-three per cent of patients reported mobility issues and 53% suffered from anxiety and depression. These results match the objective monitoring obtained from the wearable device, which showed sleeping disorders in 68% and lack of physical activity in 54% of patients, compared with healthy population parameters. Preliminary results suggest that wearable devices and QoL questionnaires are useful in detecting sleep disorders, inactivity and other factors that could influence the QoL during and after lung cancer treatment.

Table 1. Patients and classified by treatment
Conclusion

Design and validation of the effect of multidisciplinary interventions based on clinical and real-world data from the patients will ensure a personalised follow-up with a better assessment of their needs and eventually improve their quality of life, wellbeing and outcome.

Funding statement

This work was supported by the European Union Horizon 2020 Research and Innovation Program, under grant agreement number 875160 (Project CLARIFY).

References

Understanding prognosis and survival outcomes in patients with early-stage non-small-cell lung cancer

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Introduction

Lung cancer represents a significant global health problem, accounting for more than 1.7 million deaths worldwide in 2021.1 Despite advances in cancer treatment over the last decade, the 5-year survival rate is still around 50% for surgically resected non-small-cell lung cancer (NSCLC). Even for stage I patients, 20% showed recurrence within 5 years.2 Treatment modality, mostly dictated by stage and the patient's performance status (PS), directly determines disease survival. Adjuvant radiotherapy is no longer recommended after surgery and several recent large trials have confirmed the benefit in overall survival (OS) with adjuvant chemotherapy.3–6 Thus, the identification of patients with poor prognoses after surgery is of considerable clinical relevance.

We report the results of a study population survival analysis from patients diagnosed with early-stage NSCLC at Puerta de Hierro-Majadahonda University Hospital, a tertiary hospital in Madrid, Spain. Our objective was to determine their clinicopathological characteristics at diagnosis, analyse survival and develop a stratification model to identify poor prognosis factors.

Methods

A total of 560 patients with histological confirmation of NSCLC in early stages (I–II) were included. Statistical analysis was performed using R Software, version 4.0.5. Univariate survival analysis was performed using Kaplan–Meier curves and survival functions were compared using a log-rank test to check for differences. Statistical significance was set at p<0.05. To investigate the contribution of each characteristic in the survival time, Cox multivariate regression model was adjusted.

Results and discussion

Overall, there was a significantly greater number of men (77.5%) compared with women (22.5%). The median age at diagnosis was 60.6 years. Regarding smoking habits, 56% of the diagnosed patients were former smokers and 31% current smokers, with only 10.5% of never smokers; and 35% patients relapsed. The univariate analysis identified statistically significant differences (p<0.001) according to gender with greater survival in women, age with greater survival to youngest and smoking habits with greater survival in non-smokers (Fig 1). As for treatment, survival is strongly improved by surgery and surgery with adjuvant chemotherapy compared with radiotherapy. PS also stands as a statistically significant factor that impacts prognosis (Fig 2) along with relapse. Multivariable analysis shows that age, surgery, adjuvant chemotherapy, PS and relapse are the most significant variables, while gender, stage, comorbidities, smoking habit and radiotherapy are not statistically significant (p>0.05). Accordingly, we identified and integrated significant prognostic factors for survival in the patient cohort to build a model that could stratify patients by risk.

Fig 1. Survival analysis in the early stages according to gender, stage and age at diagnosis and smoking habit.
Fig 2. Survival analysis in the early stages according to treatment, performance status and relapse.

Conclusion
In this cohort study, patients predicted to be at a higher risk by the model were men, over 70 years old, former smokers, received radiotherapy, had a PS of 2 and had relapsed. The identified features for the low profile were being a woman, 20–50 years old, non-smoker, who underwent surgery and adjuvant chemotherapy, had a PS of 0, and no relapse. High-risk clinicopathologic features should be considered simultaneously when evaluating patients with early-stage NSCLC for improving prognosis.

Funding statement
This work was supported by the European Union Horizon 2020 Research and Innovation Program, under grant agreement Nº 875160 (Project CLARIFY).

References


Amlodipine induced hyponatraemia

Authors: Thein Zaw Tun, Cing San Nuam and Devaka Fernando

ASherwood Forest Hospitals NHS Foundation Trust, Sutton in Ashfield, UK

Introduction

Hyponatraemia (serum sodium <135 mmol/L) is a common finding in clinical practice. Patients with hyponatraemia have increased morbidity and mortality compared with patients without hyponatraemia. Hyponatraemia is often iatrogenic and avoidable. These can be classified into 5 main types: hypovolaemic hyponatraemia, euvoalaemic hyponatraemia, hypervolaemic hyponatraemia, hypertonic hyponatraemia and pseudohyponatraemia. Patients can be asymptomatic to severe cerebral oedema, leading to brainstem herniation, respiratory arrest and death.

Case presentation

A 73-year-old man was admitted with a chronic hyponatraemia (125 mmol/L). His serum osmolality was 259 mmol/kg (low). Clinically he was euvoalaemic. His urine sodium was 50 mmol/kg (>20 mmol/kg) and urine osmolality was 276 mmol/kg (low). He had a background history of hypertension controlled with amlodipine. Amlodipine was substituted with bisoprolol after exclusion of other causes of hyponatraemia with thorough history, examination and investigations. On his subsequence blood test, serum sodium level and osmolality returned back to normal (135 mmol/L and 275 mmol/kg, respectively). In the absence of other causes and the resolution of biochemical abnormalities after withdrawing amlodipine, a diagnosis of amlodipine-induced hyponatraemia was made.

Discussion

Dihydropyridines are calcium antagonists (nifedipine and amlodipine) that reduce the entry of calcium into cells via voltage-sensitive channels in smooth muscle, thereby promoting peripheral vasodilatation. It also has natriuretic and diuretic characteristics. Another mechanism of hyponatraemia may be via direct action on the renal tubules with resultant increased sodium excretion and inhibition of renal sodium absorption. This natriuretic property promotes antihypertensive actions and they may be the mechanism causing hyponatraemia. It is a very rare cause of hyponatraemia. A high index of suspicion is needed. Depending on severity of hyponatraemia, it can be treated with stopping the drug or, if needed, need extra fluid restriction.

References

A rare case report of granulomatosis with polyangiitis presenting with thrombus of the ascending aorta

Authors: Ioannis Tzanninis\(^A\) and Ahmed Elserwey\(^B\)
\(^A\)Queen Alexandra Hospital, Portsmouth, UK; \(^B\)Southampton General Hospital, Southampton, UK

Introduction

Granulomatosis with polyangiitis (GPA) is a rare multisystem autoimmune antineutrophil cytoplasmic antibodies (ANCA) positive vasculitis that, in rare cases, can affect the aorta causing aortitis, aneurysm and rupture.

Case presentation

A 50-year-old man presented with acute onset central chest pain, vomiting and haemoptysis with symptoms being preceded by arthritis of the right hand, ankle and knees. He was otherwise fit and well, non-smoker and without comorbidities.

Examination showed episcleritis and migratory arthritis without a rash. Electrocardiography was consistent with atrial fibrillation and serial troponins had a rising trend (42 ng/L to 376 ng/L to 1,300 ng/L). Repeated blood cultures were negative, but a vasculitic screen was positive for proteinase-3 (74 IU/mL).

An initial high-resolution computed tomography (CT) on admission was suggestive of right sided pulmonary haemorrhage (Fig 1).

Fig 1. Computed tomography suggestive of right sided pulmonary haemorrhage

A subsequent CT of the aorta 3 days later showed a new low-density filling defect in the aortic sinus, arising from the left/right coronary commissure and associated with minor thickening of the valve leaflets on that side. This was confirmed on echocardiography that showed a 1.79 cm x 0.64 cm lesion arising from the commissure of the left and right coronary cusps. This appeared to be attached to the aortic wall and moved independently of the valve leaflets.
The impression was that the mass was likely to represent a thrombus rather than an infective vegetation considering its position and time of appearance. The patient was commenced on intravenous (IV) heparin infusion with target activated partial thromboplastin time ratio (APTR) of 2 and IV methylprednisolone. Repeat CT of the aorta 3 days later showed reduction in volume of the low attenuation material. Overall, the appearances favoured thrombus that may had formed at a point of intimal inflammation or injury secondary to an underlying aortitis.

The patient was then switched to warfarin to achieve target INR of 2 and was discharged with a reducing regimen of prednisolone. He also received a 6-dose course of cyclophosphamide as an outpatient. A repeat CT, 10 weeks later, showed complete resolution of ascending aorta thrombus lesion.

**Fig 2.** Computed tomography showing complete resolution of ascending aorta thrombus lesion.

**Discussion**

GPA is a small vessel vasculitis most commonly associated with PR-3 antibodies. In one-fifth of cases, myeloperoxidase antibodies can also be present. PR-3 antibody positivity provides aid to the diagnosis and is also a marker of disease activity.¹ The disease is characterised by granulomatous inflammation and necrosis of small and medium vessels, and most commonly affects the ears, nose, throat, respiratory tract and kidneys.² Cardiac manifestations of GPA are rare and can include pericarditis, cardiomyopathy, coronary arteritis, valvular lesions and conduction abnormalities.³ Large vessels may also be affected, despite it being classified as a small vessel vasculitis. Specifically for the aorta, which was affected in our case, this can present with aneurysmal formation, dissection, rupture, regurgitation or death. In those cases, a possible overlap between ANCA-associated vasculitis and large vessel vasculitis has been suggested.⁴

**Conclusion**

We have presented a rare case of GPA presenting with thrombus of the ascending aorta that resolved following effective anticoagulation and immunosuppressive treatment.

**References**


Risk factors for falls among elderly patients admitted to Colombo North Teaching Hospital, Sri Lanka: a cross-sectional analysis

Authors: Apsara Wijerathna, Shamila T De Silva, Indewarne E Gunaratna and PA Saranga M Weerarathne

A Luton and Dunstable University Hospital, Luton, UK; B Colombo North Teaching Hospital, Colombo, Sri Lanka; C Office of the Regional Director of Health Services, Galle, Sri Lanka

Introduction and objectives

Falls among the elderly lead to increased morbidity and mortality. Information on risk factors for falls among the elderly is lacking in Sri Lanka. This study aimed to describe characteristics of older adults admitted with falls to a tertiary care hospital.

Methods

Patients >60 years of age admitted with falls to surgical and medical wards of Colombo North Teaching Hospital between January 2021 – March 2021 were recruited. Data were gathered using an interviewer-administered questionnaire after obtaining informed written consent.

Results

Of 300 patients recruited, 99 were men and majority were between 60–74 years of age. Almost half of those recruited had diabetes (48.3%; n=145) and hypertension (54.0%; n=162), while 41% (n=123) were on more than three medications. Age >74 years (p<0.05) and use of long-term multiple medications (p<0.001) showed significant association with falls. Fear of falling (p<0.001), cognitive impairment (p<0.001), depression (p<0.001), high-risk mobility (p<0.001), postural hypotension (p<0.001) and reduced visual acuity (p<0.001) were also strongly associated with falls.

Conclusion

Multiple risk factors for falls were present in the study cohort, and many of those risk factors are modifiable. Therefore, interventions may be planned on an individual basis to reduce future risk of recurrent falls. The results of the study will be useful when developing future programmes for prevention as well.

References

2. Index Mundi. Sri Lanka Demographics Profile. Index Mundi. https://www.indexmundi.com/sri_lanka/demographicsprofile.html
**Ambulatory management of diabetic foot complications**

**Authors:** Kirsty Yates, Kiki Marinou and Alex Bunn  
Öxford University Hospital NHS Foundation Trust, Oxford, UK

**Introduction**

Diabetic foot infection (DFI) is the most common reason for diabetes-related hospital admissions and is the proximate cause in 60% of lower extremity amputations. With a strong evidence base and respected published guidelines, the foundations are in place for the provision of high-quality care to those presenting at hospital with DFI.

In 2015, our hospital trust opened an ambulatory emergency care (AEC) unit to provide hospital-level urgent medical services without the need for an overnight stay (referred to by NHS England as same day emergency care (SDEC) services). Early identification of patients requiring admission is key and, where this isn’t required, providing planned follow-up, 72 hour open access and hospital at home input minimises both admissions and re-admissions.

**Materials and method**

To ensure consistent and safe management of patients presenting to the AEC unit with active diabetic foot disease, we developed a scenario-based pathway to aid decision making and improve patient outcomes (Fig 1). In collaboration with our established multi-disciplinary diabetic foot team (MDFT), six key presentations are detailed with clinical questions and prompts to guide care processes in an interactive pathway that can be readily accessed by all staff groups working within the AEC unit (Fig 2).

**Fig 1. Scenario selection page**
Results and discussion

The clinical questions posed ensure rapid identification of those requiring admission for emergency interventions, facilitating this under the correct specialism. The accompanying training provided to the medical and nursing teams focused on the clinical decision making required to correctly identify these priority patients.

Where ambulatory management is appropriate, the pathway guides the user on initiation of immediate therapies and investigations with the inclusion of hyperlinks to antimicrobial guidelines. Improved resource usage and rapid access to relevant MDFT specialisms is facilitated by working through the scenarios. The pathway also enables appropriate outpatient follow-up once AEC is no longer required.

Successful management of diabetic foot disease requires a multi-disciplinary approach. The benefits of rapid assessment/treatment from relevant specialisms with the introduction of an MDFT and associated care pathways/protocols have been consistently demonstrated.² Our existing MDFT echoes these findings with overall reductions in major amputations, inpatient admissions and total bed days since its conception.³ The cross specialism working and principles developed through the MDFT are now embedded within our new ambulatory care pathway as they are transferable to the emergency care setting. This supports the

Fig 2. Scenario 1

<table>
<thead>
<tr>
<th>1. FOOT INFECTION WITH SIGNS OF SYSTEMIC SEPSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Evidence of sepsis where foot felt to be the source of infection</td>
</tr>
</tbody>
</table>

Requires Inpatient Management

• Start treatment as per sepsis bundle consulting antimicrobial guidelines for ‘Severe Diabetic Foot Infection’

You can discuss with Micro/ID team for antibiotic queries (Bleep 4076 for JR AAT, Bleep 9799 for Horton RAU)

• Does the patient require urgent foot surgery?

Deep collection/abscess, non-salvageable foot/digit, gas in tissues, source control

Monday – Friday 8am-4pm — Request time critical podiatry review (telephone advice within 1 hour and physical review within 4 hours) to determine if urgent foot surgery needed

After 4pm, weekends and bank holidays – Request urgent on call vascular team review (contact via switchboard) to support decision making

• If urgent foot surgery is not required...

• Does the patient have palpable foot pulses?

  • YES – Podiatry review only
  • NO – Referral to Vascular Team + Podiatry

(Urgent vascular review if signs of critical limb ischaemia)

Sepsis40421 or via switchboard

• Could the patient have osteomyelitis?

  • YES – request urgent foot x-ray +/- MRI. If positive, urgent referral to Foot & Ankle Team (Bleep 8740X) and liaison with Micro/ID team (#4076)
  • NO – Urgent podiatry review (will arrange inpatient MDT review as needed)

If not showing signs of improvement within 24 hours reassess management

If patient deteriorates urgent reassessment required due to high risk of requiring surgical management
recommendation by the National Institute for Health and Care Excellence for robust protocols and clear local pathways across all settings, including emergency care.\textsuperscript{5}

Conclusion

The introduction of a pathway for the ambulatory management of diabetic foot complications into our AEC unit has allowed us to embed an evidence-based approach to care. Using an interactive scenario-based approach has enabled early identification of those requiring admission for emergency interventions and facilitated doing so under the correct specialism. Where ambulatory management is appropriate, patients receive appropriate immediate therapies and investigations with rapid outpatient follow-up and ultimately better outcomes. The next step will be rolling out an adapted model within our non-ambulatory emergency care units (emergency department and emergency assessment unit).

References

**Rare case of overlap of myositis and myasthenia gravis**

**Authors:** Shabeena Zeb, Amol Sagdeo and Roshan Amarasena

The Shrewsbury and Telford Hospital NHS Trust, Shrewsbury, UK; The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust, Oswestry, UK

**Background**

Myositis and myasthenia gravis (MG) are both autoimmune disorders presenting with muscle weakness. So far, only fewer than 50 cases of co-existence of myositis and myasthenia gravis are reported in literature either as isolated cases or in case series. We report a rare case of overlap syndrome of myositis with myasthenia gravis.

**Case presentation**

We report a case of a 67-year-old woman with breast cancer and thymectomy, who was referred to rheumatology with pain in thighs and biceps after being started on aromatase inhibitor therapy that continued on after stopping this therapy. There was no proximal muscle weakness or tenderness. Impression of polymyalgia was made on initial review. Her blood tests showed elevated serum levels of creatinine kinase. Extended myositis spectrum antibody screen showed positive antinuclear antibodies and transcription intermediary factor 1-gamma antibodies. Magnetic resonance imaging indicated pelvic girdle and thigh muscle myositis. Electromyography didn't show any evidence of neuropathy. Muscle biopsy was consistent with necrotising myopathy. Computed tomography was performed to rule out active cancer. It was unclear whether inflammatory changes on biopsy are paraneoplastic in context of previous thymoma, so a conservative expectant approach was suggested. After a stable course of reducing creatine kinase levels and no muscle power deterioration for 3 years, the patient started deteriorating over 1 month and she developed proximal muscle weakness to that extent where she was unable to walk without support associated with bilateral ptosis and difficulty in swallowing towards the end of her meals. Clinical possibilities of myositis flare up and new onset of myasthenia was considered and acetylcholine receptor antibody test was sent. She rapidly deteriorated in the next 24 hours, developed bilateral ptosis, breathing difficulty and profound weakness of neck and proximal muscles while she was on steroids. She was admitted to the hospital where she underwent treatment with intravenous immunoglobulins, pyridostigmine and a high dose of steroids. Acetylcholine receptor antibody was reported high 7 days later. She improved rapidly within 1 week. Her dyspnoea and muscle weakness improved. She was discharged with a plan to continue escalating steroids till she made a full recovery or hit 90 mg (1.5 mg/kg) on alternate days and to stay on it for 2 weeks, and then to start reduction of prednisolone at the rate of 5 mg per 5th dose unless the symptoms recur where she should revert back to last dose or reduce until hits on 15 mg on alternate days.

**Conclusion**

This case illustrates need to consider myasthenia when a patient with inflammatory myositis deteriorates despite being on steroids.

**References**

Systematic review of mTOR inhibitor treatment, biomarkers and prophylaxis for tuberous sclerosis complex-associated seizures

Author: Jingwen Zhang

King’s College London GKT School of Medical Education, London, UK

Introduction

Tuberous sclerosis complex (TSC) is a major genetic cause of epilepsy, characterised by benign multi-system tumours (e.g., brain, kidney and skin) and neurological disorders (e.g., epilepsy, autism and learning impairment). Mutations in \( TSC1 \) and \( TSC2 \) genes result in hyperactivation of mammalian target of rapamycin complex-1 (mTORC1) pathway, linked to epileptogenesis in TSC.

Materials and methods

To examine research findings on anti-epileptogenic effects of mTOR inhibitors and predictive biomarkers in TSC, PubMed searches with keywords '"(((mTOR) OR (mTOR inhibitor) OR (everolimus) OR (sirolimus)) AND ((seizure) OR (epilepsy))) AND ((tuberous sclerosis) OR (TSC)))' and keywords '"((tuberous sclerosis) AND (epilepsy)) AND (biomarker)" were performed.

Results and discussion

For results of effectiveness of mTOR inhibitors in tuberous sclerosis complex-associated seizures see Table 1.

Table 1. Effectiveness of mTOR inhibitors in tuberous sclerosis complex-associated seizures

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Medication</th>
<th>Condition</th>
<th>Patients, n</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krueger et al, 2010</td>
<td>Everolimus</td>
<td>TSC-associated SEGA</td>
<td>16</td>
<td>Improved seizure control over 34.2 months. Patients with no seizures since last visit increased from 38.5% to 65.2%.</td>
</tr>
<tr>
<td>Krueger et al, 2013</td>
<td>Everolimus</td>
<td>TSC-associated refractory epilepsy</td>
<td>20</td>
<td>Well-tolerated with only mild and moderate adverse effects. Duration-dependent mechanism.</td>
</tr>
<tr>
<td>Cardamone et al, 2014</td>
<td>Everolimus and Sirolimus</td>
<td>TSC-associated refractory epilepsy</td>
<td>7</td>
<td>One, four and two patients had &gt;90%, 50%–90% and &lt;50% reduction in seizure frequency over 18 months (median), respectively.</td>
</tr>
<tr>
<td>Overwater et al, 2016</td>
<td>Sirolimus (adjunctive)</td>
<td>TSC-associated refractory epilepsy</td>
<td>23 (children)</td>
<td>Despite seizure frequency reduction, significant benefits could not be proven. Lacked precision to exclude sirolimus benefits.</td>
</tr>
<tr>
<td>French et al, 2016</td>
<td>Everolimus (adjunctive, low/high exposure)</td>
<td>TSC-associated refractory epilepsy</td>
<td>366 (aged 2–65 years old)</td>
<td>Greater response rate, median reduction in seizure frequency and number of seizure-free days. Duration response and dose response.</td>
</tr>
</tbody>
</table>

SEGA = subependymal giant-cell astrocytoma; TSC = tuberous sclerosis complex.
Everolimus
Long-term safety: 94% of 48 TSC patients with refractory epilepsy maintained improved seizure control over 4 years; safe and tolerable. Adverse effects decreased over time.\(^1\,^2\)

White matter modification: Everolimus pharmacologically modifies the genetic defect of TSC (including normal-appearing white matter) in 28 patients for 12–18 months. Longer exposure and younger age (<10 years old) are associated with greater effects.\(^3\,^4\)

Dosing and response: 5–7 ng/mL initially and 5–15 ng/mL if inadequate clinical response. It is more difficult for patients with higher baseline seizure frequency to respond.\(^5\,^6\)

Patient stratification for treatment with mTOR inhibitors
Age: mTOR inhibitors are more effective in those <18 years old, with greatest effects observed in those <6 years old. Longer exposure and early initiation are associated with long-term efficacy, especially when given in critical time windows. More calcification in cortical tubers with age is associated with resistance to treatment.\(^7\,^10\)

Baseline seizure frequency: Higher baseline seizure frequency is associated with more difficulty becoming a responder to adjunctive everolimus.

Calcification in cerebral parenchyma: Patients with cerebral parenchymal calcification in epileptic discharge sites are more likely to be resistant to appropriate antiepileptic drugs (AEDs) and adjunctive rapamycin.

Refractory seizures: Higher diffusivity increase is seen in refractory TSC-associated epilepsy, ie greater response to everolimus.

Predictive, diagnostic and prognostic biomarkers of epilepsy in TSC
Predictive biomarkers: Electroencephalography (EEG), genetics, miRNAs and inflammation

Diagnostic biomarkers: Interictal scalp fast ripples (FR); alpha-[\(^{11}\text{C}\)]-methyl-L-tryptophan (AMT) as the only molecular probe in positron emission tomography capable of localising epileptic foci in the interictal state

Prognostic biomarkers: Cyst-like tubers, predominance of poorly organised tubers, increased tuber count, white matter mean diffusivity and cerebellar lesions

Conclusion
Clinical trials have proven the efficacy and safety of mTOR inhibitors, principally everolimus, for seizure control in TSC. Effects of everolimus were shown to be mediated by duration- and dose-dependent mechanisms and more pronounced in patients with young age, low baseline seizure frequency, low level of cerebral parenchymal calcification and refractory seizures. Predictive biomarkers (including EEGs, genetics, miRNAs and immuno-inflammation changes) could identify high-risk patients and prompt initiation of prophylaxis. Diagnostic and prognostic biomarkers could confirm diagnosis and monitor response to treatment and disease progression. Widespread effects of mTOR blockade are unknown and case reports of everolimus prophylaxis in TSC patients were inconclusive. Future clinical trials are needed to study everolimus prophylaxis in young, asymptomatic patients and in combination with other AEDs.

References


