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22nd Annual Meeting of the UK and Ireland Neuroendocrine Tumour Society 2024

Oral Communications

OC1

^{68}Ga68 DOTATATE imaging on a whole-body PET/CT scanner & optimising injected activity

Shaunak Navalkissoor, Adnan Chowdhury, Noel Santillan, Bruno Ferreira, Martyn Caplin & Gopinath Gnanasegaran
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Background
Currently there is limited availability of ^{68}Ga-DOTATATE in the UK due to limited radiopharmaceutical production. New whole-body PET/CT scanners with higher sensitivity may allow administered activities lower than the recommended 100-200MBq by international guidelines, potentially allowing more patients to be imaged from an elution vial.
Aim
To evaluate the feasibility of reducing administered tracer activity on a whole-body scanner in patients undergoing ^{68}Ga-DOTATATE somatostatin receptor scintigraphy for Neuroendocrine Tumours
Methods
Following preliminary re-binning of twenty patient data in those administered 100-150MBq of ^{68}Ga-DOTATATE, we established 0.75MBq/Kg would be potentially be feasible on the whole-body Siemens Biograph Quadra camera (minimum of 50MBq was selected). We evaluate the images of 10 consecutive patients who had previously undergone ^{68}Ga-DOTATATE PET/CT on Siemens Biograph Vision camera (4minutes/bed position + 5mins for bed over liver) reconstructed with TrueX + TOF (UltraHD-PET) and subsequently had a follow-up ^{68}Ga-DOTATATE PET/CT on the wholebody Siemens Biograph Quadra camera (10 minutes vertex to thighs acquisition) reconstructed with TrueX + TOF. We compared the injected activity, weight, body mass index (BMI) and liver signal to noise ratio (SNR) between these two studies.
Results
The mean injected activity was 58MBq (range 48-82MBq) on Quadra and 129MBq on the Biograph. The mean BMI was 28 and 26 at the time of the Biograph and Quadra study respectively. Semiquantitative analysis showed an improvement in mean SNR of 56% (range 33%-93%) on the Quadra.
Conclusion
Administered activity of 0.75MBq/kg on the Quadra results in superior liver SNR ratio (vs. standard administered activities on Vision) translating to better images. In general, limited availability of ^{68}Ga-DOTATATE doses results in long waiting times for patients referred for ^{68}Ga-DOTATATE imaging. Therefore, reduced administered tracer activity and faster imaging times would potentially allow imaging of 1-2 additional patients per ^{68}Ga elution, helping in reducing waiting times. There are added benefits of better image quality and reduced patient dose.

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OC2

The biopsychosocial impact of pancreatic enzyme replacement therapy shortages

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Background
Pancreatic Enzyme Insufficiency (PEI) is a recognised potential consequence of pancreatic pathology and / or somatostatin analog therapy. It is known to be detrimental to patient quality of life and nutritional status (1). Patients with PEI can experience gastrointestinal symptoms, vitamin and micronutrient deficiencies, malnutrition, and even reduced survival (2). Pancreatic enzyme replacement therapy (PERT) is the expert guideline recommended treatment for PEI, associated with both improved survival and quality of life (QoL).(1,2) However, over the last 12 months, there has been a significant supply issue to the UK, predicted to continue until 2026. A Patient Safety Alert was released in May 2024 (3). Neuroendocrine Cancer UK, undertook a patient survey to understand the impact shortages have had on the patient community.
Methods
An online survey was developed, comprising of questions about usual PERT supply and others to identify any changes since shortages were first reported. Results were collated, alongside a thematic analysis of free text answers on the impact on well-being.
Findings
A total of 148 responses were received - with all respondents answering all questions. 68% reported difficulties with PERT supply on 1 or more occasions: 75% were told this was due to no stock. Of the 61% offered an alternative, 50% had difficulty obtaining this: 38% have run out completely at least once. More than 65% have tried to manage supply by reducing dose: 42% have gone without eating. 66% report an adverse impact on well-being: common themes included increased anxiety, symptom exacerbation, isolation, impact on work and finances, intolerance of treatment, weight loss and fear: I am finding this frightening, and depressing, I am a very positive person, and feel I've handled my life with NET quite well, always being careful not to be too far from a loo, but now yes, I am fearful. Respondents also reported low awareness amongst GPs, clinicians and pharmacists about PSA recommendations (3,4) - leaving them unsupported in obtaining supply: I am exhausted and stressed at this unsustainable situation of trying to obtain PERT and feel unable to continue doing this. My quality of life has significantly reduced.

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OC3

Emergency and routine presentation of neuroendocrine neoplasia in England: determinants of diagnosis and survival outcomes

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Introduction
The mean time from onset of symptoms to diagnosis in NEN is around 5-7 years. Late stage NEN is often diagnosed during an emergency admission. The difference in overall survival (OS) between emergency and elective diagnoses has not been studied. This study assesses factors associated with emergency presentation (EP) versus routine presentation (RP), evaluates factors associated with late presentation, and correlates these with OS.
Methods
A retrospective population-based study using gastroenteropancreatic and lung NEN registered with England's national cancer database (excluding appendix) between 2012-2021. The Kaplan–Meier estimator was used to predict OS. Cox regression and machine learning (ML) models evaluated factors associated with worse OS. Logistic regression and ML models were used to identify factors associated with emergency and late (disease stage 3 or 4) presentation.
Results
A total of 21,345 NEN were included. 20.3% were EP. EP showed worse OS compared to RP in both models (aHR 1.64, $P < 0.001$). Factors associated with EP were male sex, advanced disease, increasing deprivation, and carcinoma. Compared to small intestine (SI), caecal, colonic, rectal, pancreatic, lung, and stomach NEN were associated with lower odds of EP. The ML model showed EP associated with advanced stage, SI- NEN, NEC, advancing age, caecal NEN, and colonic NEN in decreasing order of importance. Factors associated with late presentation (LP) included EP, male sex, advancing age, and NEC. Asians were significantly less likely for LP. Compared to SI, caecal NEN were associated with significantly higher odds of LP (OR = 1.69, $P < 0.001$), while all other NEN had lower odds of LP. The ML model showed NEC, SI- NEN, advanced age, caecal, colonic, and mixed race are associated with LP in decreasing order of importance.
Conclusion
Emergency and late presentation of NEN are associated with poor survival. Addressing causal factors may aid timely diagnosis, decreased emergency presentation and improved survival in NEN.

DOI: 10.1530/endoabs.105.OC3

OC4

Clustering of gastroenteropancreatic neuroendocrine neoplasms (GEP-NEN) using machine learning (ML) and comparison with Tumour, Node, Metastasis (TNM) staging: a retrospective, population-based study using Surveillance, Epidemiology, and end results (SEER)

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Introduction
TNM 8 is the staging system for GEP-NEN, guiding prognosis and treatment. However, it ignores important prognostic factors including age, sex, race, tumour site, and morphology.
Methods
35,347 adults diagnosed between 2011-2021 with GEP-NEN and had no missing data in any variables were extracted from SEER. Age, sex, race, tumour site, size, morphology, number of lymph nodes and metastasis site were used to create 3 clusters using K-means ML clustering model. Univariable cox regression, Kaplan Meier (KM) plots and overall survival (OS) estimates were produced for TNM stage (model-1) and clusters (model-2). Prediction of OS concordance index (CI) was compared between both models using survival XGBoost ML model. A decision tree was developed to cluster patients.
Results
KM plots and OS estimates for model-1 showed overlap between stages 0 and 1, and between stages 2 and 3, with only stage 4 having distinct OS. Cox regression showed only stage 4 had different OS from stage 0. Three clusters were formed using K-means ML model: high, intermediate and poor clusters. KM plots, OS and Cox regression for model-2 showed no overlap between clusters, showing distinct OS between them. The poor survival cluster was characterised by advanced age, male sex (56%), advanced stage, higher tumour size, higher number of regionally positive lymph nodes, metastatic disease, NEC morphology, cecal, colon, pancreas and small intestine NEN. CI for TNM stage and clusters were 68.8% and 65.9% respectively. CI using both TNM stage and clusters was even better (73.2%). A decision tree was developed to cluster patients with accuracy of 91.6% (F1 score 93.1%). The most important factors for OS according to ML were age, stage, metastasis, site, size, NEC, T stage, number of regionally positive lymph nodes, race, and sex in decreasing order of importance.
Conclusion
ML can be used to improve TNM staging for better prognostication of GEP-NEN patients by clinicians.

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OC5

Selective internal radiotherapy (SIRT) versus hepatic artery embolization (HAE) for the treatment of neuroendocrine liver metastases

Calum Lynch, Samuel Tingle, Georgios Kourounis, Rodrigo Figueiredo, Jeremy French, Peter Littler, Derek Manas, Sanjay Pandanaboyana, Georgia Priona, John Reicher, Rohan Takkar, Colin Wilson & Stuart Robinson

Introduction
Liver-directed therapies are an important component of palliative control of disease burden and carcinoid syndrome for unresectable liver metastases of neuroendocrine tumours. Hepatic artery embolization (HAE) and selective internal radiotherapy (SIRT) are both available loco-regional therapies however there is currently no consensus on which should be offered. We looked to compare HAE against SIRT and their impact on survival.
Methods
This retrospective cohort study compared patients who had SIRT to a historical cohort receiving HAE (2006-2024). Kaplan-Meier plots and cox regression was used to compare survival.
Results
Our cohort included $n = 18$ SIRT and $n = 31$ HAE patients. There was no difference in survival between HAE and SIRT (log-rank $P = 0.55$). This was also seen when patients with G3 disease were excluded (log-rank $P = 0.27$). In a cox regression model adjusting for age and grade, SIRT was not associated with a survival difference (aHR = 1.266, 95% CI:0.534-2.999, $P = 0.592$). Increasing age and grade were associated with worse survival. Radiological response rate was numerically higher with SIRT (82.4%) compared to HAE (62.1%), but this was not statistically significant (Fisher's $P = 0.19$). There was missing data on symptomatic response, with only 55.6% on SIRT and 83.9% HAE patients having complete data. However, of those, 10/10 of SIRT patients had symptomatic improvement compared to 17/26 with HAE (Fisher's $P = 0.039$).
Conclusions
There was no difference in survival between the HAE and SIRT cohort despite some suggestion of improved radiological and symptomatic response. This information can be used to guide palliative management of liver metastases from neuroendocrine tumours.

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Poster Presentations

P1

Clinical outcomes of streptozocin (STZ) based chemotherapy in neuroendocrine tumours (NETs): a retrospective analysis of 26 patients from a single cancer centre - nottingham university hospitals (UK)

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Background
Neuroendocrine tumours (NETs) represent a diverse group of neoplasms arising from neuroendocrine cells. Streptozotocin (STZ) based chemotherapy regimens have been utilized in the treatment of NETs, yet comprehensive clinical outcomes remain to be fully elucidated.
Methods
We retrospectively analyzed median overall (mOS) & progression-free survival (mPFS) among 26 patients with pancreatic and non-pancreatic NETs and NECs treated with STZ-based chemotherapy from July 2014 at Nottingham University Hospitals. Data were identified from Multi-disciplinary Team health records and analyzed using SPSS Statistics, v28.0. Survival analysis utilized Kaplan-Meier curves for cumulative survival estimates, with the Log rank test for comparing rates.
Results
We included 26 patients (53.8% males; median age: 65). Out of 26 patients: 3 had Streptozocin/5 fluorouracil; 3 had Streptozocin/5 fluorouracil/Cisplatin and 20 had Streptozocin/5 fluorouracil/Carboplatin regimen. Median overall survival (OS) was 12.63 months (95% CI 7.5-17.6), & median progression-free survival (PFS) was 5.07 months (95% CI 1.66 – 8.47). No significant differences were found between pancreatic and non-pancreatic NETs, metastatic sites, functional status, or chemotherapy regimen. Statistically significant differences were found in survival outcomes between tumors positive and negative for octreotide receptor expression (mOS: 21.7 vs 4.6 months, $P = 0.05$) and Ki-67 expression levels ($\leq 50\%$ Vs $> 50\%$) (mOS: 19.96 vs 4.8 months, $P = 0.031$). Patients receiving > 5 treatment cycles had better survival compared to < 5 cycles (median OS: 33.3 vs 12.34 months, $P = 0.002$). Response rates at 3, 6, 9, and 12 months were 61.5%, 46.2%, 30.8%, and 26.9% respectively. 50% patients had STZ dose reduction, with no significant impact on survival. 7.7% discontinued STZ due to toxicity; G3 toxicities were Fatigue (7.7%) & Neutropenia (3.8%).
Conclusions
Our study although limited by size underscores the prognostic significance of biomarkers such as Ki-67 index and octreotide receptor expression, as well as the number of treatment cycles in managing neuroendocrine tumors. While consistent with phase 3 trial results, larger-scale controlled studies are warranted to better understand treatment regimen effects on clinical outcomes in NET management.

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P2

Insulinoma: an argument for rapid PRRT pathways in refractory disease

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Introduction
Islet cells within the pancreas regulate blood glucose through the production of certain hormones, including insulin. Pancreatic neuroendocrine tumours (PNETs) are rare tumours arising from these cells. They are classified as non-functioning (NF-PNET) or functioning (F-PNET). Functional neuroendocrine tumours cause significant symptoms due to the excessive secretion of hormones such as insulin, gastrin, or glucagon. The transformation of NF-PNETs to F-PNETs is a rare occurrence, happening in just 3.4%–6.8% of cases. Patients with metastatic insulinoma, a type of F-PNET, have a poor prognosis, with average survival rates of less than two years.
Case report
We present the case of a 52-year-old male who was admitted to hospital following severe and persistent hypoglycaemic episodes. Insulinoma was confirmed with C-peptide and insulin levels. Prior to diagnosis, he had a five-year history of NF-PNET with liver metastases, which was managed with octreotide, a somatostatin analogue (SSA), and everolimus, a mechanistic target of rapamycin (mTOR) inhibitor. After admission, diazoxide and sunitinib a second-line treatment with palliative intent were started due to the potential wait for peptide receptor radionuclide therapy (PRRT). This is an internal radiotherapy treatment used in symptomatic disease that has metastasised or when surgical excision is not an option. He experienced repeated life-threatening hypoglycaemia and endocrinology advised the use of UKI NETS Bitesize Guidance for the Nutritional Management of Insulinomas. This was implemented by dieticians alongside high-dose IV dextrose. We have outlined the medical challenges over a month, highlighting severe coexistent hyponatremia secondary to the dextrose and arranging PRRT at the nearest nuclear medicine centre. Following transfer the patient was no longer fit for treatment and passed away two weeks later.
Conclusion
PRRT can be difficult to facilitate quickly due to the need for specialist multidisciplinary team (MDT) opinion, octreotide scans, and medical optimization. Reducing local wait times for scintigraphy and obtaining early approval from specialist centres should be a key priority in critical situations. Although this case is extremely rare, it highlights the need for an emergency pathway between regional hospitals for rapid access to treatment. Patients with acute and refractory disease are a subgroup for special consideration.

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P3

Primary hyperparathyroidism in multiple endocrine neoplasia type 1 (MEN1): Northern Ireland's (N.I) experience

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Primary hyperparathyroidism (PHPT) is commonly the first and most frequent clinical manifestation in MEN1 occurring in up to 95% of patients. Surgery is considered the treatment of choice. Clinical course differs to that of sporadic PHPTH in terms of age of onset, complications, surgical management and recurrence rates. This study aims to review the challenges of PHPT in MEN1. Retrospective analysis of patients attending a dedicated MEN1 clinic in the Royal Victoria Hospital, Belfast, under long-term review was carried out ($n = 26$). 85% had PHPT ($n = 22$; male:female 9:13; age 49.9: range 28-70 years); making it the most common manifestation. It was the initial presentation in 17 of these 26 patients. Average age at diagnosis of PHPT was 31 years. At diagnosis, average calcium level was 2.86 mmol/L and PTH 106 pg/mL. Fourteen patients had DEXA scan; all reported either osteopenia (43%) or osteoporosis (57%). Renal calculi occurred in 22.7% of this cohort. All patients underwent parathyroidectomy. Main surgical technique used in the first operation was subtotal parathyroidectomy (3 or 3.5 gland removal) (20 of 22 patients). Limited parathyroidectomy (2 gland removal) was employed in 2 patients. Persistent and recurrent disease was diagnosed in 9% and 54.5% of these patients, respectively, after first surgery. Recurrence occurred on average 13 years after first surgery. Rate of remission after first surgery was low at 36.3%. Five patients required a second surgery (3 achieved remission) and 1 patient required a third operation (now in remission). Post-operative hypoparathyroidism was seen in 31.8% of patients. The experience in N.I of MEN1-related PHPT is similar to other studies. This is a multi-glandular disease of which management is challenging. Age of onset is younger in MEN1 related PHPT compared to sporadic PHPT. Recurrence rates are much higher compared with sporadic disease (54.5% vs 1 to 15%). Effects on bone health are more severe in MEN1 (57% vs 40% in sporadic PHPT). Occurrence rates of nephrolithiasis were found to be similar in this study. The timing of surgery requires multi-disciplinary involvement with close and long term follow up, ideally at a dedicated clinic to allow optimal outcomes.

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P4

Leak rates in pancreatico-duodenectomy procedures in pancreatic NETs compared to pancreatic ductal adenocarcinoma resections

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Introduction
Pancreatic resection for Neuroendocrine tumour is associated with a higher risk of anastomotic leak and post-operative pancreatic fistula (POPF).
Aim(s)
The aim of this study was to compare POPF rate after Whipple's operation for neuroendocrine tumour (NET) versus pancreatic ductal adenocarcinoma (PDAC).

Materials and Methods
We conducted a retrospective case control analysis of a prospectively maintained database. Patients who underwent pancreatico-duodenectomy for NET and PDAC over a 10 year period at our institution were included in the study. Drain amylase levels on day 3 and day 5 were compared in the two groups by Mann-Whitney U test with $p < 0.05$ considered a significant result. The definition of pancreatic fistula as defined by the International Study Group of Pancreatic Fistula was used.
Results
A total of 660 patients underwent pancreatico-duodenectomy over a 10 year period. Of these, 44 (20.4%) underwent a resection for neuroendocrine tumour. 28 were males (63.6%) and 16 females (36.4%) with a median age of 62.5. 3 patients (6.8%) out of 44 had duodenal NETs. The drain amylase level (X3 normal) was elevated in 28 (63.6%) of the resections for NET as compared to 7 (15.9%) of the resections for PDAC at day 3 post procedure ($p < 0.05$). On day 5 post operation, the drain amylase was elevated in 7 (15.9%) patients in the NET group as compared to 2 (4.5%) patients in the PDAC group ($p < 0.05$).
Conclusion
As expected the drain amylase levels after pancreatic-duodenectomy were significantly higher in the NET group than in the PDAC group. The caliber of the pancreatic duct, normal pancreatic consistency (so called 'soft pancreas') and loss of pancreatic exocrine function in a chronically (secondary to tumour) obstructed gland have been cited as reasons for this difference.
Keywords: pancreatic resections, whipple, pancreatic fistula, drain amylase
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P5

Management of cold sepsis in a patient receiving peptide radionuclide receptor treatment (PRRT): a case review
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The Beatson West of Scotland Cancer delivers all PRRT to patients in Scotland. Approximately 4 patients are treated per week in a ward specially designed for the administration of radionuclide treatments. Pre treatment assessment is an essential part of the care and the patient in this case was identified as fit, well with bloods within normal range and a performance status of 0. Within a few hours of treatment administration the patient became unwell and was found to have cold sepsis and an acute kidney injury. The Critical Care Outreach Team were contacted as per protocol and she required to be transferred off-site to the Intensive Care Unit across Glasgow. This case raised several issues relating to radiation protection highlighting significant lack of understanding and knowledge of staff not routinely involved in this treatment. As a consequence of this a new Standard Operating Procedure has been produced. This is to improve the management of acutely unwell adults who are hazard to others health due to radiation who require off-site management.

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P6

The experience of transarterial embolisation for metastsatic NET at queen Elizabeth Hospital Birmingham and future possible role of selective internal radiation therapy
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Introduction/Background
16th May 2024 NICE confirmed use of Selective Internal Radiation Therapy (SIRT) for neuroendocrine tumours that have metastasised to the liver, with arrangements in place for clinical governance, consent and audit. This was subject to Commissioners/providers implementing the guidance. Trans Arterial Embolisation (TAE) and Trans Arterial Chemo Embolisation (TACE) are two of the comparative therapies that the committee examined to come to their conclusion. The NET community is awaiting details on the commissioning of SIRT.
Aim
To examine the process and outcome of patients undergoing TAE at QEHB, looking at length of stay, complications, long term outcomes and compare this to the limited number of our patients receiving SIRT.
Method and Material
Experience of SIRT for NET at QEHB has been limited due to a lack of funding from the Commissioners. There have been 4 SIRT for NET in 2019 to 2023. In comparison there have been 20 TAE for NET from 2018 to 2023. Trust authority for the audit was obtained and retrospective analysis of hospital records was undertaken. The number of patients who had undergone TAE/SIRT for metastatic NET was ascertained. Further data was collected to enable discussion of the treatments and make comparisons. This data included demographics, rationale for treatment, disease burden, complications, length of hospital stay and survival.
Results/Discussion
From our series it appears that TAE is a procedure that can entail a hospital inpatient stay of several days and involve post procedure complications. The limited experience of SIRT demonstrated a shorter inpatient stay and fewer complications. With such small numbers however, it is difficult to infer any difference in survival.
Conclusion
The literature on SIRT and our own hospital experience with TAE suggest a different treatment journey. When looking at the allocation of hospital resources it would be helpful to calculate the difference in costings. However, it is difficult to do this as the costs of the therapeutic agent are commercially sensitive. The impact that SIRT will have on the provision of TAE in the future in uncertain.

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P7

Coeliac artery dissection in neuroendocrine neoplasms: coincidence or cause?
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Introduction
Incidental Coeliac artery dissection (CoAD) is an uncommon presentation of abdominal pain akin to post-prandial pain of mesenteric ischemia. Risk factors include hypertension, smoking, dyslipidaemias, pregnancy, atherosclerosis, trauma, or fibromuscular dysplasia. Imaging features of CoAD include an intimal flap, aneurysmal changes, mural thrombus, and (or) fat stranding. We report 2 novel cases of CoAD in patients with small bowel NETs with mesenteric masses.
Case 1
A 55-year-old male, presented with acute abdominal pain and distension. CT revealed a 50mm mesenteric mass. Biopsy confirmed Grade 1 metastatic well-differentiated NET. Urinary 5HIAA was 167 umol/24 hour and Chromogranin A was 265 ng/mL. This was intensely avid on Octreoscan SPECT-CT. Treatment with Lanreotide Autogel 120 mg deep SC every 28 days was commenced. Post-biopsy CT revealed a focal dissection flap, involving the coeliac trunk, a 12 mm coeliac artery diameter at the level of dissection with normal SMA and IMA. The Vascular multidisciplinary team reviewed the scan with a plan for serial follow-up scans. This was regarded an incidental CoAD with aneurysmal change.
Case 2
A 63-year-old male originally presented with severe carcinoid syndrome and carcinoid heart disease (he underwent PV and TV replacements) from a Grade 1 metastatic terminal ileum NET, with extensive liver metastasis. He underwent liver embolization which went uneventfully. Immediate post-procedure CT scan showed an 80% targeted liver lesion response. However, a follow-up scan four weeks later revealed a new dissection flap with aneurysmal changes at the origin of the coeliac artery, measuring 12 mm in diameter. The vascular multidisciplinary team has recommended conservative management with continued CT monitoring.
Conclusion
Coeliac artery dissection may be underreported due to the foregut collateral networks making the presentation variable and bowel ischemia infrequent. Treatment is most often conservative with endovascular or surgical management reserved for complicated cases. Complications include aneurysm formation, rupture, and arterial occlusion. We believe this is the first report of coeliac artery dissection associated with mesenteric mass in NETs, whilst this could be incidental it may relate to the fibrotic nature of the mesenteric mass and possibly implicated in causation.

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P8

The indolent behaviour of type 1 gastric neuroendocrine tumours smaller than 1 cm: a single western center experience
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Background
Gastric neuroendocrine tumours (g-NETs) constitute about 7% of digestive NETs, with type 1 g-NETs, linked to chronic atrophic gastritis, accounting for 80% of cases. These tumours are generally small, low-grade, and exhibit excellent long-term survival rates. Increased endoscopy and awareness have raised their incidence, prompting interest in management strategies. Current guidelines recommend either endoscopic surveillance or resection for type 1 g-NETs <10 mm, though these recommendations are largely based on expert opinion rather than strong scientific evidence. Most existing data come from Eastern populations, emphasizing the need for further research in Western populations. The study aims to evaluate the indolent behaviour of type 1 g-NETs <10 mm managed through endoscopic surveillance.
Methods
This study is a single-center, retrospective analysis of consecutive patients with type 1 g-NETs <10 mm, who were managed through endoscopic surveillance. The primary endpoint was progression-free survival. Statistical analysis was performed using MedCalc® software, with a p-value <0.05 considered statistically significant. A Cox proportional hazards regression model was applied to identify risk factors for disease progression.
Results
Of the 113 patients evaluated, 32 (28.3%) were excluded for not meeting the inclusion criteria, leaving a final cohort of 82 patients (72.6%) for analysis. The median patient age was 59 years, with 27 men (32.9%) and 55 women (67.1%). The median tumour size was 4 mm, with 92.7% classified as G1 tumours and 7.3% as G2, and a median Ki-67 index of 2%. Tumour progression (characterized by an increase in size >10 mm), was observed in 4 patients (4.9%) after a median of 75.5 months, necessitating further endoscopic treatment. No cases of metastatic progression were reported. Additionally, 3.6% of patients developed adenomas with low-grade dysplasia, and 1.2% developed early gastric cancer. Three patients (3.6%) died during follow-up, though none of the deaths were tumour-related. The median progression-free survival and overall survival were both 59 months [range 2-287]. No statistically significant prognostic factors for tumour progression were identified in the univariate analysis.
Conclusions
Type 1 g-NETs <10 mm are typically indolent and don't require invasive treatment at the time of diagnosis.

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P9

Clinical outcomes of patients with rectal neuroendocrine tumours smaller than 10 mm after endoscopic resection

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Background
Rectal neuroendocrine tumours (r-NETs) are the second most common neuroendocrine tumours in the digestive tract, with increasing incidence due to improved colonoscopy and cancer screening. These small, yellowish, low-grade lesions are often found incidentally during colonoscopies and generally have a favourable prognosis, with median survival sometimes exceeding 30 years. However, up to 20% of r-NETs may be misdiagnosed during endoscopy, risking inadequate treatment. Prognosis is influenced by factors such as tumour size (with a ≥ 10 mm cutoff), grading, staging, and lymphovascular invasion, leading to guidelines recommending endoscopic resection for small, low-grade lesions. The study aims to evaluate the clinical outcomes of patients with r-NETs <10 mm after endoscopic resection.
Methods
A retrospective single-center study was conducted, including patients with rectal neuroendocrine tumours <10 mm after endoscopic resection. The primary endpoint was progression-free survival. Statistical analysis was performed using MedCalc® software, with a p-value <0.05 considered significant. The Cox proportional hazards regression model was used to identify risk factors for disease progression.
Results
Out of 81 patients considered, 68 (83.9%) were included after excluding 13 for various reasons. The final cohort included 40 males (58.8%) and 28 females (41.2%), with a median age of 53 years and a median tumour size of 5 mm. Most tumours were grade 1 (92.6%). Endoscopic resections were inadequate (biopsy forceps or cold/hot snare) in 42 cases (61.8%) and advanced (EMR, ESD, or TAMIS/TEMS) in 26 cases (38.2%). Positive resection margins were observed in 47% of cases, and lymphovascular invasion was present in 1.4%. Tumour recurrence (local in all cases) occurred in 3 patients (3.4%). The median progression-free survival was 33.5 months, and the median overall survival was 35.5 months (range: 1-170 months). Only two deaths (2.9%) were recorded, neither of which were tumour-related, occurring after a median of 81.5 months. No significant prognostic factors for tumour recurrence were identified.
Conclusion
R-NETs <10 mm generally exhibit non-aggressive behaviour. However, more extensive prospective studies are required to gain a comprehensive understanding of these rare and heterogeneous tumours.

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Testicular neuroendocrine tumour with carcinoid heart diseaseon the background of urological cancers: a trio of malignancies

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Introduction
Primary and metastatic testicular neuroendocrine tumours (por mTNETs) are rare and account for less than 1% of testicular tumours. Testicular mass is the commonest presentation, with radical orchidectomy being treatment of choice. Carcinoid syndrome is rare at 1-3 % of cases. Carcinoid heart disease is even more rare in TNET but notably the right testicular vein drains into inferior vena cava (IVC) and left testicular vein drains into left renal vein then IVC bypassing the liver. We report a rare case of carcinoid heart disease in TNET.
Case report
A 72 year old man, with a background of radical prostatectomy and cystectomy with ileal conduit formation, was found to have a testicular mass. This completely resected with radical orchidectomy with histology revealing a well differentiated NET, Grade 2, Ki 67 of 5 % expressing Chromogranin, CD56 and Synaptophysin. No germ cell (GCNIS) or teratoma were seen. CT and MRI Imaging showed solitary liver metastasis with biopsy confirming metastatic NET but Ki 67 was <2 %. Clinically he had signs of right sided heart failure with CV waves, a systolic murmur consistent with tricuspid regurgitation, pulsatile liver, and lower limbs pitting oedema. His urinary 5-HIAA was 276umol/24 hours (0-37) and Chromogranin A of 3941 ng/mL (0-105). Full staging was performed. Octreoscan SPECT-CT revealed a solitary liver lesion and no other primary. Echocardiogram confirmed a retracted and thickened tricuspid valve leaflets with poor mobility resulting in severe/torrential free flow TR and moderate PR with RV dilatation with good RV function with mild LVSD. Carcinoid syndromic features had improved since orchidectomy. Lanreotide Autogel 120 mg deep sc every 28 days was commenced, with significant improvement with no flushing or diarrhoea after 3 injections. Clinically RHF improved. He declined any further major surgeries.
Conclusion
TNETs are very rare form of NETs whether primary or secondary. Due to their venous drainage into IVC, carcinoid syndrome can develop as well as carcinoid heart disease. Given the rarity of pTNET full work up of the small bowel is underway to ensure there is not a primary or concomitant small bowel lesion.

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Is there a role for post-operative functional imaging in small intestinal neuroendocrine tumours resected with curative intent?

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Background
In southeast Scotland patients who have undergone resection of small intestinal neuroendocrine tumours (SI NETs) with curative intent are followed up by the NET team for recurrence. ENETs guidelines are that this should involve cross sectional imaging and hormonal assessment. During follow up we identified a number of patients with residual disease post surgery, rather than developing metachronous metastases. In 2019 we changed our policy to arrange post-operative (post-op) functional imaging in patients who had not had functional imaging in the pre-operative setting. During this time period we have moved from post-op tektrotyd scans to post-op Dotatoc PET imaging. We now review our first 5 years of post-op functional imaging.
Methods
We identified patients ($n = 64$) who had undergone a small intestinal resection since August 2019-2024 from MDT lists. This was then cross checked against a pathology database of patients with a NET identified in the small intestine, and one additional patient was identified. We looked at reports of imaging that had been performed and whether residual disease was found.
Results
We identified 64 patients who had undergone a resection from 2019-2024. In 17 patients surgery was with palliative intent, whereas 47 patients had undergone potentially curative surgery of which in 3 this included hepatic resection. In 12 patients no functional imaging was performed at any time due to comorbidity or patient request. Seven patients had undergone pre-operative functional imaging and no post-op functional imaging was arranged in these patients. Twelve patients underwent a post-op tektrotyd scan in which 4 had previously unknown residual disease found on scan (33%). Sixteen patients underwent a post-op Dotatoc PET scan in which unanticipated residual disease was identified in 9 (56%). We will present further analysis of these patients.
Conclusion
In patients where it is considered appropriate to perform follow up after resection of a SI NET, post-operative functional imaging should be performed.

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From PRRT to liver transplant: redefining boundaries and navigating multimodal management of metastatic duodenal NET

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Background
Liver transplantation is now recognized by ENETS as a valid indication for liver-metastatic gastro-entero-pancreatic (GEP) neuroendocrine tumors (NETs). Since 2021, the UK initiated a pilot program for selected patients — specifically, primary amenable to complete resection, low-grade, well-differentiated GEP-NETs, with 6-months stability and $<50\%$-liver-involvement.[1-3]
Case-summary
A 34-year-old woman, ECOG-PS-0, non-smoker, non-alcoholic, without significant medical or familial history, presented in March 2013 with transient severe right hypochondriac pain. Suspected of biliary colic, further evaluation was prompted by involuntary weight-loss, fatigue, and mild iron-deficiency anemia. By June 2013, imaging and duodenal-directed biopsy revealed a non-functional, well-differentiated ampullary NET with bilobar liver metastases, showing avid-uptake on Octreoscan. MEN-1 genetic testing was negative. She underwent Whipple's pancreaticoduodenectomy with synchronous left lateral hepatic segmentectomy. Histopathology confirmed pT4N1M1 ampullary NET, Ki-67-index 3%, involving 4/10 lymph-nodes and liver metastases. She commenced monthly Sandostatin-LAR® 20mg, well-tolerated. The plan included imaging-surveillance and potential liver-directed therapy for residual metastases. Recovery was uneventful aside from a superficial infection, with occasional nausea and mild exocrine insufficiency managed using dietary adjustments, Creon, and proton pump inhibitors. By March 2015 imaging revealed stable disease, but rising chromogranin-A and 5-HIAA levels prompted Lutetium-177 peptide receptor radionuclide therapy (PRRT) initiation. Four well-tolerated cycles completed from May 2015 to June 2016 — achieving maximum response by January 2017. Stable under Sandostatin-LAR® until October 2020, but subtle liver-metastases progression required dose increase to 30mg. Liver surgery and focal treatments were considered but deemed unfeasible due to extensive disease. Following liver-disease progression in April 2021, she started Everolimus 10mg daily — tolerating well despite mild skin rash and pruritus managed with low-dose topical steroids. After 24 cycles, given persistent liver-only disease with limited options, she successfully underwent liver transplantation (piggyback hepatic veins; Roux-en-Y hepaticojejunostomy) in October 2023. Histology confirmed multifocal well-differentiated NET, Ki67-index 7.7%, clear margins. Rapid recovery to PS-ECOG-0, reporting only intermittent mild intention tremors related to tacrolimus immunosuppression. By August 2024, follow-up MRI and Ga-68-DOTATATE-PET scans showed no recurrence, maintaining stable graft and kidney function.
Conclusion
This case highlights the importance of multidisciplinarity, opportune referral, and the life-saving potential of transplantation in selected patients with unresectable liver-metastatic NET.

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A pilot model of group education for nutritional/dietary advice and symptom management in neuroendocrine neoplasms (NEN) (GEDNEN course interim analysis)

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Background
Structured patient education has been used in chronic medical conditions such as diabetes mellitus, demonstrating both acceptability and improved outcomes. Here, we pilot the concept of group-based nutritional and dietary education in patients with NEN, delivered by specialist experts.
Aim
To evaluate 3 outcomes: 1) acceptability, 2) effectiveness and 3) improving accessibility to specialist experts in group education settings, advising on nutritional and symptom management for patients with NEN.
Methods
Patients were divided into two groups (small bowel NEN or non-functioning pancreatic NEN). Each group attended a 4-hour structured education session including an interactive session: 1) an overview of NEN by a NEN Consultant, 2) discussion of medical treatments such as somatostatin analogues and management of potential side effects by a NEN specialist nurse, 3) a mix of general nutrition education and more complex application to the nutritional considerations of NEN, presented by three NEN specialist dietitians. All participants completed established and bespoke pre and post course questionnaires.
Results
Of the 15 participants, 10 had small bowel NEN, and 5 had pancreatic NEN. Only 13% had consulted a specialist NEN dietitian prior to this, while 20% had previously seen a non-NEN specialist dietitian. In terms of outcomes: 1) 100% of participants supported the group education format and were open to attending the session again. 2) For the analysis of effectiveness, longer term follow up will be needed to ascertain if group education has lasting clinical benefit and this is planned. 3) In this course, all participants had access to experts with an open question and answer section to close the session.
Conclusion
This pilot model demonstrates that group education is an acceptable tool in patients with NEN. Over one third of patients found meeting others very beneficial. Further follow up and analyses are underway, and a larger multicentre study may be indicated. This education format could lend itself to an online platform and when optimised be available to other centres nationwide if needed. Based on this experience and feedback, the structured education program has been refined with plans to launch additional sessions in this patient group.

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Treatment of MiNEN with peptide receptor radionuclide therapy

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Introduction
Mixed non-neuroendocrine and neuroendocrine neoplasms (MiNENs) of gastrointestinal tract are rare tumours with characteristic histological features include at least 30% of both neuroendocrine and non-neuroendocrine components of the whole neoplasm. They are usually treated with surgical resection and chemotherapy in advanced disease. However, there is scarcity of data for the use of peptide receptor radionuclide therapy (PRRT) in these tumours.
Case presentation
An 82-year-old asymptomatic female referred to the neuroendocrine department in February 2023 following an incidental finding of liver lesions found on routine investigations for systolic murmur. Radiological investigations revealed bi-lobar liver metastases with unknown primary. Histology from the liver biopsy confirmed MiNENs with the predominant component (up to 60%) being grade 2 well differentiated neuroendocrine tumour (NET) with Ki67 of 19% and a smaller component (up to 30%) of well to moderately differentiated adenocarcinoma of pancreaticobiliary origin. Functional Imaging showed ^{68}Ga DOTATATE PET-CT avid bi-lobar liver metastases with no extrahepatic focus of activity, and there was no FDG PET-CT avid activity within the liver metastases. She was initially started on Lancreotide 120mg Auto gel every 28 days however the liver tumours progressed, and this was stopped in November 2023. After review in the MDT in view of the strong avid ^{68}Ga DOTATATE uptake she proceeded to four cycles of ^{177}Lu-DOTATATE therapy between November 2023 and June 2024. Post PRRT her repeat imaging showed reduction in the size of liver metastases (index lesions segment 4 and 3 reduced from 26mm to 18 mm and 21mm to 14 mm respectively). She remained well post PRRT treatment.
Conclusion
PRRT is currently not used in treatment protocol for the management of MiNEN, however, it could be a treatment option in patients with MiNEN where there is a predominant component of well differentiated NET with ^{68}Ga DOTATATE avid lesions.

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Impact of somatostatin analogues on SSTR expression and Ki-67 expression marker in LCC-18 neuroendocrine tumour cells

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Introduction
Neuroendocrine neoplasms (NENs) represent a diverse group of tumours with varying clinical presentations and outcomes. Despite advancements in treatment, there remains a need to better understand the behaviour of somatostatin receptors (SSTRs) to monitor disease progression and therapeutic efficacy. Our study aims to evaluate the impact of octreotide acetate (OA), Lanreotide acetate (LA) and Pasireotide (P) on LCC-18 cells, investigating potential mechanisms behind the eventual loss of drug efficacy. Specifically, we focus on the changes in SSTRs 2, 3, 4 and 5, as well as the proliferation marker Ki-67 following drug exposure.
Materials and Methods
The LCC-18 cell line, grade 3 NEN from a colonic tumour, was cultured and treated for 2 hours with increasing concentrations of OA, LA and P (6.25 μM to 100 μM). Immunocytochemistry (ICC) and qRT-PCR was used to determine expression SSTRs 2, 3, 4 and 5 and Ki-67 following acute exposure to the respective SSTR analogues and 2 hours. Additionally, apoptosis induction was assessed for each drug to explore their potential cytotoxic effects.
Results
Preliminary results showed no evidence of apoptosis following exposure to either OA or LA; in contrast, P demonstrated a faint level of apoptosis, with a small percentage of cells undergoing apoptosis at 100 μM. The ICC and qRT-PCR data, which further reveal the impact of these drugs on SSTRs and Ki-67 expression, are still in progress and will provide valuable insights upon completion.
Conclusion
By focusing on early changes post-drug exposure, we aim to identify potential biomarkers that could predict therapeutic efficacy and guide clinical decision-making by elucidating the changes in SSTRs and Ki-67 expression. This research aims to improve future treatment strategies and more personalised approaches for patients with NENs, ultimately enhancing therapeutic outcomes by identifying early biomarkers of drug efficacy.

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Case report: immunotherapy for a well-differentiated rectal neuroendocrine neoplasm

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Introduction
Metastatic well-differentiated rectal neuroendocrine neoplasms (NENs) are heterogeneous and considered 'immune-cold.' Standard treatments include somatostatin analogues, peptide receptor radionuclide therapy and chemotherapy. We report a case where a patient responded to third-line immunotherapy, despite the absence of predictive biomarkers.
Case Presentation
A 60-year-old man was referred for colonoscopy following bowel cancer screening. A 3 cm rectal polyp, 5 cm above the dentate line, was identified and biopsied. CT and MRI showed this lesion was associated with mesorectal and para-aortic lymphadenopathy and indeterminate liver lesions. Gallium-68 DOTATATE PET CT showed avidity in the rectal primary and abdomino-pelvic nodes, but not in the liver lesions. FDG PET CT was negative at all sites. The liver lesions were too small to biopsy. An anterior resection with aortic lymphadenectomy confirmed a well-differentiated NET (Grade 2, Ki-67 7%), consistent with hindgut origin (ENETS pT2 N1 V1 L1 Pn1 R1). Three months post-operation, surveillance showed an increase in size and number of the liver lesions. Liver biopsy confirmed a NET G2 with a Ki-67 index of 8%, similar to the operative histology, with MMR proficiency and KRAS, NRAS, BRAF wild-type status. Following completion of 6 cycles of first line FOLFOX chemotherapy, repeat imaging demonstrated progressive liver disease. Symptomatic disease progression in the liver alone was again noted after 4 cycles of second line FOLFIRI. A repeat liver biopsy showed no histological change and dual PET scans remained non-avid. Given the disease's atypical behaviour and chemotherapy-resistance, the patient was offered participation in a Phase 1 clinical trial but declined. He was subsequently commenced on Ipilimumab/Nivolumab through a compassionate access scheme. Remarkably, he achieved a partial response after two cycles, though developed grade 2 immune-related arthritis. The patient's cancer (primary and liver metastases) are undergoing multi-omic evaluation to establish reasons for response that may refine the use of such therapies.
Conclusion
Dual checkpoint inhibition may be effective in chemotherapy-refractory patients with well-differentiated rectal NETs who are unlikely to benefit from somatostatin receptor-dependent therapies. This case underscores the potential role of immunotherapy and highlights the need for further multi-omic understanding of NETs to select patients for immunotherapy.

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P17

High prevalence of sarcopenia in patients with neuroendocrine tumours and carcinoid heart disease, but no effect on postoperative complications or survival

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Introduction
Patients with neuroendocrine tumours (NETs) and carcinoid syndrome are at risk of developing carcinoid heart disease (CaHD). Sarcopenia is a muscle disease, associated with poorer overall survival and post operative complications in other types of cancer. In patients with NETs sarcopenia is highly prevalent, if this effects complications and survival following surgery for CaHD is unknown.
The aim of this study is to describe the prevalence of sarcopenia and to assess its association with post operative complications and overall survival in patients with NETs and CaHD.
Methods
A single centre retrospective study was performed. Patients with CaHD and valve replacement surgery were included. An abdominal CT scan performed within 3 months of the surgery was analysed for sarcopenia. Additional data regarding post operative complications and overall survival were collected and analysed.
Results
A total of 27 patients, $n = 14$ (52%) male with a median age 62 year (IQR 52 – 70yr) were identified. The primary tumour was located in the small bowel in $n = 26$ patients (96%) and ovaries in 1 patient (4%). Eleven patients (41%) presented with heart failure as first symptom of a NET. In 18 patients there was sarcopenia present (67%), those patients were significant older (p-value 0.04) compared to the patients without sarcopenia. A median of 2 heart valves (IQR 2-3) were replaced. In 9 patients (33%) post operative complications were reported, 4 (44%) of these were severe. However, sarcopenia was not associated with post operative complications. Two patients died within 30-days postoperative. The median overall survival following surgery was 49 months (IQR 25 – 73 months). There were no survival differences in patients without or with sarcopenia (p-value 0.41).
Conclusion
In this small study population sarcopenia is highly prevalent in patients with NETs and CaHD, however it is not associated with post-operative complications or overall survival following surgery. Future studies should include a larger study population and investigate sarcopenia into more detail for example with muscle strength and physical performance to elucidate its true prevalence, once this is more clear the role of sarcopenia in patients with NETs and CaHD could be investigated further.

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Retrospective audit evaluating outcomes in patients post resection for pancreatic neuroendocrine tumours

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Background
Pancreatic Neuroendocrine tumours (panNETs) are usually sporadic and non-functioning, but occasionally associated with germ-line mutations causing multiple hereditary endocrinopathies. Small, non-functional lesions may be managed conservatively. For panNETs larger than 2 cm the mainstay of treatment is surgery (2). However, postoperative complications are common and can significantly impact patients' quality of life. The aim of this audit was to explore postoperative outcomes in a cohort of patients who underwent surgical excision of panNETs at an ENETS Centre of Excellence.
Method
Single centre retrospective review for a 5-year period, 2017 till 2022, of patients undergoing surgical resection for panNETs. Data collection was facilitated by informatics and database management tools. Data analysis was performed using Excel.
Results
There were 64 patients in total. Median age 57 (IQR 16.8). 53% were female. 28% were diagnosed incidentally, 20% presenting with symptoms such as diarrhea or of irritable bowel type. 9% had germ-line mutations. 27 (42%) patients had lesions $\leq$2cm, including gastrinomas or insulinomas. All the resections undertaken were in adherence to the ENETS guidelines (2). The average post-operative hospital length of stay was 8 days. Most common complications were weight loss (48%), diarrhoea (21%), and bile acid malabsorption (11%). Among patients who experienced weight loss, comparing pre-operative to latest follow-up review, the average weight lost was 9.3 kg. Eighty-one percent of the patients started new medications after surgery, with Creon being the most common. Twelve (19%) of the patients had post-op re-occurrence; 7 (56%) individuals with reoccurrence were started on SSA (in combination with surgery/chemotherapy), 2 patients received best supportive care, and 2 patients had further surgery. As of February 2024, 56 patients (89%) were still alive.
Recommendations
This review highlights generally positive patient outcomes, with 89% overall survival rate. Only one patient died within 1 year of the surgery, due to disease progression. However, surgery resulted in significant life-altering changes, particularly weight loss and bowel dysfunction that patients should be counselled about before their treatment. Additionally, there is a need for a study comparing outcomes with and without surgery.

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P19

Systemic anti-cancer therapy in gastroenteropancreatic neuroendocrine carcinoma (GEP-NEC): insights from national cancer registration and analysis service (NCRAS)

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Introduction
European Neuroendocrine Tumour Society guidelines advocate the use of platinum-based chemotherapy in combination with Etoposide as first line chemotherapy in advanced GEP-NEC. Following this regime, 30% of digestive NEC and 60% of colorectal NEC showed a lack of benefit or evidence of disease progression. Available retrospective evidence is from small studies. Other studies have shown BMI relates to survival in NEN. This study aims at studying chemotherapy regimens used in England in the last 10 years for patients with GEP-NEC.
Methods
Patients with primary GEP-NEC diagnosed between 2012-2021 were extracted from NCRAS and divided into chemotherapy (group-1) or no chemotherapy (group-2). Kaplan Meier estimated overall survival (OS) was calculated by site, chemotherapy regimen and body mass index (BMI). Logistic regression was used to evaluate for significant factors associated with receiving chemotherapy.
Results
2,636 patients with GEP-NEC were extracted. 38% received first-line chemotherapy. The most common site to recieve chemotherapy was pancreas (35.3%). 50.3% of patients in group-1 had performance status of 0 or 1. In total, 64 different regimens were used. The most common regimen was Cisplatin/Carboplatin + etoposide (66.1%). Carboplatin + 5FU + Streptozocin was used in 3.4% of patients. OS in the chemo group was higher in the first 12 months (48.1% vs. 41.5%). Small intestinal NEC and caecal NEC receiving chemotherapy had the highest and lowest OS respectively (73.5% vs. 31.9%). Appendiceal and colonic NEC not receiving chemotherapy had highest and lowest OS respectively (87.6% vs. 21.6%). Patients who received Carboplatin + 5FU + Streptozocin had higher OS compared to Cisplatin/Carboplatin + etoposide in all sites combined and in the colorectal NEC subgroup. Multivariable logistic regression showed routine diagnostic presentation (versus emergency presentation), younger age and advanced stage were more likely to receive chemotherapy. Small intestine and appendix NEC had lower rates of chemotherapy. No difference in OS of group-1 was shown between BMI groups.
Conclusion
Most patients with GEP-NEC do not receive chemotherapy. There is a large variation in chemotherapy regimens in GEP-NEC with Cisplatin/Carboplatin + etoposide being the most common regimen. Receiving chemotherapy is associated with younger age, advanced stage and elective diagnosis. BMI has no effect on OS of GEP-NEC.

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P20

See the unseen: a rare presentation of metastatic small bowel NET with unilateral visual loss

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Introduction
Neuroendocrine tumours can metastasize to the bones, but rarely to the orbit. The majority of orbital metastasis are incidental findings on somatostatin receptor imaging. Symptomatic metastases are treated with external beam radiotherapy or

chemotherapy, seldom with surgical resection (1–4). Here we present a case who presented with visual disturbance due to an orbit metastasis which was resected and the histology showed a metastatic NET.

Case

A 56-year male patient, with no past medical history, presented in early 2023 with visual disturbance of his left eye, optician and ophthalmology review noticed ptosis. A MRI head demonstrated a well circumscribed lesion on left rectus muscle. Due to the unclear nature of the lesion a left lateral orbitotomy was performed. The histology showed a well differentiated NET with Ki-67: 3.8% and mitotic count 5 per $2mm^2$. After receiving the histology report a CT chest, abdomen and pelvis and subsequently a ^{68}Gallium-DOTATATE PET scan were performed which showed an ileocaecal primary with local lymph node metastases, peritoneal-, bilobar liver- and multiple bone metastases, which all showed avidity on the PET scan. The patient was referred to a NET expert centre. He recovered well from his left lateral orbitotomy. He denied any abdominal symptoms or symptoms of carcinoid syndrome. His performance status was 0. His urine 5-HIAA was 6 times upper limit of normal. He was commenced on monthly somatostatin analogue injections which he tolerated well. Unfortunately 6 months later his ^{68}Gallium-DOTATATE PET scan showed new avid peritoneal lesions. He was still asymptomatic and was referred for peptide receptor radionuclide therapy (PRRT). He recently had his first cycle.

Conclusion

Patients with an unclear nature of an orbit lesion could benefit from multi-disciplinary approach as a neuroendocrine tumour metastasis is in the differential diagnosis. Especially, when metastases are considered patients could benefit from early cross sectional imaging and referral to a cancer centre.

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P21

Size, but not the number of positive lymph nodes is associated with worse overall survival in patients with small bowel neuroendocrine tumours

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Introduction

Until recently, lymph node metastases (LNM) in small bowel neuroendocrine tumours (SB-NETs) were classified as absent (N0) or present (N1). However, the American Joint Committee on Cancer (AJCC) updated the classification to N0, N1 (<12 positive lymph nodes), and N2 (≥ 12 positive LNM and/or a large mesenteric mass (MM) ≥ 2 cm). This updated N-classification has not been evaluated in a real-world population of patients with SB-NETs. The aim of this study is to describe the prevalence of N1 and N2 in patients with SB-NETs and explore its association with recurrence-free survival (RFS) and overall survival (OS).

Methods

A single-centre retrospective study was performed, including all patients with a curative SB-NET resection. Histology reports were reviewed and reclassified using the new AJCC N-classification. Demographic data were collected from patient records. RFS was calculated from the histology date to the date of disease recurrence, and OS was calculated from the histology date until death from any cause.

Results

A total of 112 patients (52% male, median age 63.5 years) were included. Sixty-seven patients (60%) had N1-disease, 45 patients (40%) had N2-disease. Among the N2-group, $n = 35$ (79%) had a MM $\geq$2cm, $n = 8$ (17%) had ≥ 12 positive LNM, and $n = 2$ (4%) met both criteria. The median MM size in N2-group was 30mm. Recurrence occurred in 18 patients (26.9%) in the N1-group and in 17 (38.6%) in the N2-group. No significant difference in recurrence time was found between N1-group (83 months) and N2-group (61 months), p-value 0.29. There was no significant difference (p-value 0.16) in OS between N1-group (134 months) and N2-group (106 months). However, patients with MM $\geq$2cm had significantly shorter OS (102 months, $P = 0.006$), compared to patients with MM $\leq$2cm (median not reached). Multivariate analysis suggested MM $\geq$2cm points towards significant worse OS (HR 3.71, $P = 0.06$).

Conclusion

For patients with SB NETs N1 or N2 LNM do not affect RFS or OS, but MM $\geq$2cm points towards worse OS. This highlights the need for tailored surveillance, particularly for patients with larger MMs. Future multi-center studies are needed to clarify the impact of N1 and N2 LNM on survival outcomes.

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P22

Advocacy in practice: pancreatic enzyme replacement therapy

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Background

Pancreatic Enzyme Replacement Therapy (PERT) is the gold standard treatment for Pancreatic Enzyme Insufficiency (PEI), regardless of underlying aetiology. Historically, there have been intermittent PERT supply issues, however, over the past year (2023/4) this has become a more persistent and significant issue: leading to questions being raised in both UK and EU parliaments and main media reports. PERT is potentially life-saving: for those with certain conditions, including cancer, it can significantly influence prognosis, suitability for and/or tolerability of treatment.

Methods

Brought together through the impact PERT shortages are having on their patient populations, a third sector collaborative formed. The aim of the collaborative has been to work with all stakeholders including specialist dietitians, health service colleagues, the Department of Health and Social Care (DHSC), national medicines management team, Medicines and Health Care products Regulatory Agency (MHRA) and suppliers to: a) understand underlying root causes, b) find workable interim and longer-term solutions, c) provide guidance for clinicians/prescribers and dispensers, and most importantly d) information for our patient communities.

Results

Root causes identified: from raw source materials (and yield) issues, to manufacturing capacity, and single supplier reliance. Under the auspices of the Pancreatic Society of Great Britain and Ireland a Position Statement has been published - 3rd version (June 2024) - offering advice to both clinicians and patients. In May 2024, the MHRA issued a National Patient Safety Alert. Updated information is available via the Specialist Pharmacy Service website (https://www.sps.nhs.uk/) Third sector organisations have provided information dissemination and patient resources. Two free to access online healthcare professional-focused webinars* were held September 2024: with combined total attendance of more than 450 GPs, dietitians, CNSs and pharmacists.

Conclusion

Continued collaboration and horizon scanning is needed to better quantify current and future demand, maintain and sustain PERT supply, and provide accurate, accessible, and up-to-date information provision. We would like to thank our charity partners, Pancreatic Cancer UK (chair and lead of group), Pancreatic Cancer Action, Guts UK and Cystic Fibrosis Trust, and all stakeholders. (Webinar recordings* available via HCP page at https://www.neuroendocrinecancer.org.uk/hcp/)

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P23

Profound, durable benefit from external beam radiotherapy for primary, in transit and locoregional disease from Merkel cell carcinoma in the frail elderly: illustrative clinical vignettes

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Merkel cell carcinoma (MCC) is a high grade cutaneous neuroendocrine tumour. They are a rare and often aggressive form of skin cancer, with increasing incidence in the elderly. MCC often presents as a firm, red/purple – coloured painless nodule with a short, aggressive history of increasing size. Wide local excision recommends 1-2cm margins, and deep clearance beyond that usually advised for keratinocytic skin cancers, but can have major cosmetic and functional implications especially as up to 50% of lesions are in the Head and Neck area, and elderly patients in particular have comorbidities which may preclude a radical approach requiring reconstructive surgery and prolonged anaesthetics. Radiotherapy is an alternative approach in patients who are not surgical candidates, or in those with advanced, unresectable or metastatic disease. Usually in patients with small tumours, at low risk of recurrence, surgery is considered definitive, but adjuvant post operative irradiation (PORT) may provide additional benefit in terms of risk reduction depending on histopathological features, and improves local control. We present 3 clinical scenarios to illustrate responses to RT: firstly the more typical circumstance of a 78 y/o lady with a 3 month history of enlarging 'cyst' on her right cheek, resected in a non-hospital setting, which recurred less than 3 months later, with re-resection showing MCC, but peripheral and deep margins of clearance <0.1mm, given

PORT, with remaining disease-free at 9 months. Secondly, an 86-year-old lady with multiple co-morbidities who presented with extensive MCC of right cheek extending from right nasolabial fold, with in transit disease across the whole right cheek, with complete response to RT which remains durable after 8 months' follow up. Finally, a 96-year-old gentleman presented with MCC right infra-orbital area in 2022, treated with excision but with close margins so received PORT. In 2024 he developed recurrent disease to right parotid and level 1/ 2 neck nodes. Patient received high dose palliative RT with profound response within 2 weeks, which is ongoing. Our patients show that radiotherapy can offer profound responses in elderly patients with MCC, and can achieve durable disease control without risking adverse effects of surgery.

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P24

Challenging diagnosis of intra-pancreatic splenunculus mimicking neuroendocrine tumour

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Introduction
Many patients who present with symptoms of possible neuroendocrine tumour, start their journey with cross sectional scans to look for malignancy as part of their diagnostic workup. Often, especially with advances in functional imaging, subtle abnormalities are now visible causing diagnostic challenges. Our case details one such potential pitfall and acts as a reminder to consider broad imaging differentials when reviewing patients scans.
Case
Our patient (a 64-year-old Vietnamese gentleman) initially presented as a 2WW via Haematology due to concerns over B symptoms (hot sweats overnight and weight loss). Initial CT scan showed minor inflammatory changes in the lung, with an 'unusual appearance' in the tail of the pancreas. He went on to have an MRI abdomen which showed 'a 2.4cm focal enhancing lesion in the tail of the pancreas, in keeping with possible neuroendocrine tumour'. Due to this finding, he was referred to Gastroenterology who requested an Octreotide scan which showed 'increased tracer uptake within the pancreatic tail'. The patient went on to have EUS biopsy of the pancreatic tail which a confirmed a lobulated mass in the tail of the pancreas. Fine needle biopsy surprisingly confirmed the lesion as a splenunculus, with no evidence of neuroendocrine tumour.
Discussion
A splenunculus is a relatively common, benign condition where splenic tissue is found outside of the spleen. Congenital cases of accessory splenic tissue are usually solitary nodules and are found in the region of the gastro-splenic or spleno-pancreatic ligaments. Intra-pancreatic splenunculi are not as rare as previously thought and their incidence rate is estimated to 17% of those with accessory spleens in an autopsy series. They can show uptake in octreotide scans as the splenic tissue frequently expresses somatostatin receptors. This case highlights the important of getting a conclusive tissue diagnosis before committing the patients to radical surgery so as to prevent unnecessary surgical risks and morbidity. Additional imaging scans such as Technetium-99m heat damaged RBC or sulphur colloid scans can be helpful to confirm the suspicion of ectopic splenic tissue.

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P25

Management of carcinoid flare events following peptide receptor radionuclide therapy (PRRT) in neuroendocrine tumours (NET): our experience at the christie NHS foundation trust

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Background
We have seen an increasing number of carcinoid flare events following PRRT which is a recognised complication of medical/ surgical intervention. Flare events are less severe than carcinoid crisis but require prompt management to avoid patient morbidity and mortality. The rise in this complication is likely due to the complexity and advanced stage of disease at time of therapy commencement. There is very little in the literature about management of this cohort of patients and to the authors' knowledge, no universally accepted management algorithm. An additional and significant complicating factor in these patients is that they are radioactive.
Purpose
To create a management algorithm for patients who present with a carcinoid flare event during/ following PRRT.
Methods
We present a treatment algorithm for carcinoid flare events which also encompasses proactive treatment of high risk cases. We have had collaborative discussions with the critical care team to identify a suitable place for transfer in the event of acute deterioration to ensure both staff and patient safety. As this is an uncommon occurrence, regular study days have also been set up to ensure ongoing education of nursing staff and clinical technologists involved in radionuclide therapy.
Results
Since putting the protocol in place in November 2023, there have been two carcinoid flare events, neither of which required critical care input. These patients were subsequently able to complete all four treatment sessions with pre treatment optimisation and prophylactic short acting octreotide injections. Having a management algorithm has increased efficiency of treatment and confidence in the management of this entity. We would advocate this approach in an uncommon but serious complication of PRRT.

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P26

Challenges in diagnosis and treatment in an evolving pancreatic neuroendocrine tumour

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Introduction
Gastroentropancreatic neuroendocrine tumours (GEP-NETs) have been observed to manifest a variable degree of heterogeneity, resulting in varied progression, change in grade, and treatment response over time.
Clinical case
A 43-year-old male presented with anorexia, weight loss, vomiting, diarrhoea, and abdominal pain. Initial imaging identified a pancreatic mass with liver and retroperitoneal nodal metastasis. The liver lesions expressed Cytokeratin and A1AT along with the DPAS positive cytoplasmic granules which favoured a diagnosis of Acinar cell carcinoma. However, a strong expression of both Synaptophysin and Chromogranin was also seen with Mib-1 proliferation index of 10%, and this was classified as an Acinar cell carcinoma. The disease progressed despite chemotherapy directed at this pathology. The patient started to experience recurrent hyper-insulinemic hypoglycaemic episodes two and half years after presentation. A repeat liver biopsy revealed a well-differentiated Grade 2 Neuroendocrine Tumour (NET) with Ki-67 11% and focal positivity for Insulin, suggestive of metastatic insulinoma (initial biopsy negative immunohistochemistry for Insulin in retrospect). All disease sites were somatostatin receptor avid on Ga68 DOTATATE PET-CT scan. The hypoglycaemic episodes proved challenging to treat, despite, Diazoxide, steroids, and somatostatin analogue (SSA) therapy. He was treated with four cycles of Peptide Receptor Radionuclide Therapy (^{177}Lu-DOTATATE), with good symptomatic response which enabled an uncomplicated right hepatectomy. He continues SSA therapy and is planned to have distal pancreatectomy and splenectomy.
Conclusion
Heterogeneity and variable GEP-NETs progression has been reported, though is not fully understood yet. Our case highlights the diagnostic challenges and the change in functionality and behaviour of pancreatic NETs. Our case also demonstrates the multimodal therapies and multidisciplinary teams that are needed in the treatment of such challenging cases. Future research is needed to identify the predictors of this biological behaviour, aiming to provide personalised NET therapy.

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P27

Multifocal small bowel neuroendocrine tumours – experience of a single clinical centre

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Introduction
Small bowel NETs (SBNETs) are a group of heterogenous tumours that can exist as unifocal or multifocal disease. The current literature regarding multifocal SBNETs includes small patient cohorts and mainly focuses on histopathologic characteristics only. Data regarding the presenting symptoms and survival are lacking.
Aim
To present clinical characteristic, disease free survival (DFS) and overall survival (OS) in patients with multifocal SBNETs.
Method
A retrospective search in a prospective maintained database of all patients with SBNETs, between December 2010 and December 2023, was performed. Datasets of patients with multifocal tumours were included, and additional clinical data and survival data were collected.
Results
We identified $n = 88$ patients, out of whom 49 were male (56%) with median age of 67.5 (IQR 58 – 74). A total of 40 patients (45%) were found to have liver metastases and $n = 9$ patients (10%) had bone metastases at the moment of SBNET resection. The median number of tumours in pathology reports was 3 (IQR: 2 - 6) and the median maximum size of a tumour was 2cm in diameter (IQR: 1.5 – 3cm). In pathology reports, $n = 72$ (82%) patients had G1 tumour, $n = 15$ (17%) patients had G2 tumours and $n = 1$ patient (1%) had a G3 tumour. Mesenteric fibrosis was documented in $n = 43$ patients (49%). The presenting symptoms were: incidental finding in $n = 45$ patients (51%), abdominal pain in $n = 21$ patients (24%), symptoms of a NET in $n = 16$ patients (18%), and obstruction in $n = 6$ patients (7%). There was progressive disease found in $n = 35$ patients (40%), and the median disease free survival was 36.5 months (IQR: 17 – 79 months). The overall survival was 61 months (IQR: 26 - 90 months) with only $n = 5$ patients dying within the first 12 months after the surgery.
Conclusion
This study contains the largest cohort describing the presenting symptoms, characteristics and survival data of patients with multifocal SBNETs. Future research should focus on the differences between patients with unifocal SBNETs to offer patients with multifocal SBNETs the most appropriate treatment and follow up.

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P28

Case series: tuberous sclerosis associated pancreatic neuroendocrine tumours at a tertiary centre

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Background
Tuberous sclerosis (TSC) is an autosomal dominant condition which can increase the risk of pancreatic neuroendocrine tumours (pNETs) (1). Patients with TSC undergo screening for renal tumours which may include pancreatic imaging (2). There are no screening guidelines for pNETs in patients with TSC.

Table 1

	Case 1	Case 2	Case 3	Case 4
Gender	F	F	F	F
TSC diagnosed before pNET?	Yes	Yes	No	No
Age at pNET diagnosis	37	34	53	34
Tumour size (mm)	18 x 12	12 x 11	110	20
Tumour location	Body	Body	Tail	Tail
Resection	No	No	Distal pancreatectomy	Distal pancreatectomy
Medical management	SSA	No	No	No
Grade	G1	G1	G2	N/A
CgA level (<60 pmol/L)	19	24	**73**	19
Metastases	No	No	No	No
Progression or recurrence	No	No	No	Yes
Follow-up	4 years	6 months	12 months	22 years

Case presentations
We reviewed four female patients who had TSC and pNET (table 1). The mean age at pNET diagnosis was 39.5 years. TSC was diagnosed after the pNET in two patients. Three patients had tumours ≤ 2 cm, one tumour was > 10 cm. Tumours were low grade. Two patients had surgical resection, one under surveillance and one treated with somatostatin analogues (SSA). One patient who underwent resection had recurrence 17 years later. Follow-up ranged from 6 months to 22 years. There was no metastatic disease after average follow-up of 6.8 years.
Discussion
In our series all patients had low grade, well-differentiated NETs with no metastases which is consistent with the literature demonstrating a more indolent disease course (2). One patient who had been discharged had a late recurrence after 17 years suggesting that long-term surveillance may be warranted. Further research is required to determine optimal management for this group.
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P29

Phaeochromocytoma associated with neurofibromatosis type 1: a single tertiary care centre experience

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Introduction
Neurofibromatosis type 1 (NF-1) (1/3000 live births) is a rare genetic cause for hereditary pheochromocytoma (0.1-5.7%) with unclear incidence and risk of malignancy. There is no current UK screening program for patients with NF-1 for pheochromocytoma/paraganglioma.
Methods
A retrospective review of patients who were diagnosed with pheochromocytoma in the context of NF-1 following referral to the adrenal multidisciplinary team at Oxford.
Results
13 patients with adrenal abnormalities in the context of NF1 were identified (2001-2024), 7/13 females, average age at date of surgery 51 years, range 29-70 years. 11 patients had histologically proven pheochromocytoma. Most patients were diagnosed incidentally on scans performed for an unrelated condition (7/8). Details available from the time of presentation show: only 1 patient presented with hypertensive symptoms, several were shown to be hypertensive on testing after the adrenal lesion was identified, 5 had significantly elevated plasma metanephrines (PMT) (normetanephrines 10,000 to $>$25,000 pmol/L) and 2 had significantly elevated urine normetadrenaline levels, 8/12 had tumour size $\geq$ 5cm, and 2/11 had metastatic disease (liver, lymph nodes) at presentation. 5/6 had a PASS score ≥ 4. Regarding outcomes, 12 surgical resections on 11 patients were performed; laparoscopic adrenalectomy $n = 9$, open adrenalectomy $n = 3$. 1 patient required 2 operations for bilateral disease. 2 patients had metastatic disease requiring further treatments (1 patient had debulking of recurrent disease followed by MIBG therapy, the second received MIBG therapy). Three patients have died. Of the other 2 patients, one had an adrenal abnormality radiologically in keeping with adrenal myelolipoma (normal PMT), one had a small nodule with mild PMT and is under observation.
Conclusions
Significant risk of large tumours and malignancy potential was observed with pheochromocytoma associated with NF-1. The majority were asymptomatic, but would have been identified with biochemical testing, raising the question about the potential need for a structured screening pathway to identify pheochromocytoma early among patients with NF-1 to enable timely intervention to prevent potential metastatic disease. Our case series highlights the need for larger studies (potential with a national registry) to identify risk factors for more aggressive disease and the need for greater screening for NF1 patients.

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P30

Malnourished patients with GEP-NETs, how does this develop in 5 years

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Introduction
Malnutrition is a common problem amongst patients with gastro-enteropancreatic neuroendocrine tumours (GEP-NETs). A recent study from our group reported 75% of patients with GEP-NETs treated with monthly somatostatin analogues (SSAs) are malnourished (1). Ideally, all malnourished patients are offered nutritional support. However, guidelines and support are often lacking. The natural course of malnutrition in patients with GEP-NETs is unknown.
The aim of this study is to describe a 5-year follow-up of a cohort of patients with GEP-NETs treated with monthly SSAs.
Methods
A prospective longitudinal single-centre cohort study was performed including patients with GEP-NETs treated with SSAs. The data of this cohort were analysed after 5-years. Baseline data were compared with 5-year follow-up. Analyses focussed on BMI, nutrition status using the malnutrition-universal-screening-tool (MUST), and vitamin-D deficiencies.
Results
The initial study population included 118 patients, after 5 years for 71 patients data were available and analysed. There were 29 male patients (41%) with median age of 69 years (IQR 60-76.5) and 16 patients (23%) had progressive disease. At baseline 35 patients (30%) had a positive MUST score (≥ 1) and 19 patients (16%) had a MUST score >2. After 5 years 28 patients (39%) had a positive MUST score (≥ 1) of which 19 patients (27%) had a MUST score >2. Overall, 41% of patients underwent dietitian review at any point from baseline. Patients deceased at the point of follow-up were more likely to have a positive MUST score (83% vs 31%, $p<0.05$). Although there was a trend towards increased prevalence of malnutrition in patients with progressive disease (53% vs. 31%), this did not reach statistical significance. At baseline, vitamin-D deficiency ($\leq$ 25 ng/mL) was shown in 5 (7.0%), and vitamin-D insufficiency (25-50 ng/mL) was shown in 32 (45%). At follow-up, vitamin-D deficiency was shown in $n = 8$ (11%), and vitamin-D insufficiency in 24 (32%) of patients.
Conclusion
This long-term follow-up study shows patients with GEP-NETs and monthly SSA treatment are at risk of malnutrition. Malnourished patients show a worse prognosis. This highlights the importance of nutritional support and guidelines. Future research should focus on improving nutritional status and developing nutrition guidelines.

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P31

Retrospective study evaluating factors influencing cancer recurrence following surgical resection of pancreatic neuroendocrine tumours (PanNETs)

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Introduction
Pancreatic neuroendocrine tumours (PanNETs) are the second most common form of pancreatic cancer. Lesions larger than 2 cm are commonly selected for surgical clearance according to the European Neuroendocrine Tumour Society (ENETS) guidelines. In this study, we assessed the variables that may affect recurrence following resection of PanNETs.
Methods
All the patients who underwent resection of PanNET over a 5-year periods between 2017 – 2022 at a NET COE were included. Variables assessed included age at diagnosis, lesion size, location of the mass, and post-operative complications. Univariate statistical analyses were performed, with independent t-tests used for continuous variables (age at diagnosis, lesion size) and a chi-square test applied for categorical variables (post-operative complications). Individuals with grade 3 NEC or known metastases prior to operation were excluded.
Results
A total of 58 patients who underwent resection for pancreatic cancer was analysed. Patients were categorised into two groups based on the presence (15.5%, 9 patients) or absence (84.5%, 49 patients) of cancer recurrence. Size of the lesion was significantly associated with recurrence ($P = 0.014$). Patients with recurrence had a mean lesion size of 7.11 cm (SD = 4.40 cm), compared to 3.71 cm (SD = 3.55 cm) in patients without recurrence. Age at diagnosis ($P = 0.289$) did not have a statistically significant influence on recurrence. Post-operative complications were significantly associated with recurrence ($P = 0.029$), with 77.8% of patients who experienced recurrence having complications. The most common complications included pancreatic leaks, adhesional obstructions, infections (sepsis, pyrexia) and incisional hernias.
Conclusion
Lesion size and post-operative complications appear to significantly influence the likelihood of cancer re-occurrence in patients undergoing resection for PanNETs. These findings will help in appropriate selection of patients for resection of PanNETs.

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P32

Perioperative short-acting somatostatin analogue use in patients undergoing neuroendocrine tumour excision – do we need a change in guidelines?

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Objective
Neuroendocrine tumours (NETs) are rare tumours and require treatment in specialist centres with familiarity management, particularly mitigation of perioperative risk from carcinoid crisis. This study retrospectively analysed the perioperative management of NET focusing on somatostatin analogue (SSA) utilisation. It aimed to evaluate compliance with local and UKINET guidelines and assess adverse outcomes from non-compliance. UKINET guidelines tailor SSA dosing to tumour activity, while local protocols recommend a standard continuous infusion for all.
Methods
A retrospective review of all patients (127) who underwent surgery for G1/2 small bowel NET (SI-NET) between January 2016 and September 2024 at a major tertiary centre. The compliance of SSA administration (intravenous octreotide), was compared to local and UKINET guidelines.
Results
Analysis of 127 patients showed 44.88% (57) to have secretory tumours. While 66.14% (84) of patients received octreotide in line with local trust protocols, only 4.7% (6) were managed in compliance with UKINET guidelines. During post-operative octreotide weaning, 96.8% of patients remained stable, with 3.14% being symptomatic or unstable, although none were formally diagnosed with carcinoid crisis. The data highlights differences in actual practice compared to local and UKINET guidelines with no clearly defined significant adverse events.
Conclusion
The results indicate variation in the use of perioperative octreotide administration with no defined significant adverse outcomes despite little compliance with UKINET guidelines. This study suggests that there is leeway for consideration of an individualised approach to SSA perioperative infusions in terms of timing and duration of administration. Such an approach may prove beneficial in optimising perioperative ward and ITU bed utilisation, reducing costs and maximising patient flow, whilst guarding against perioperative adverse events from carcinoid crisis.

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P33

Hidden hypoglycemia: a case series on diagnosing insulinomas

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Insulinomas are rare, functional neuroendocrine tumours (NETs) that secrete excessive insulin. They are often diagnosed late due to their variable presentation and rarity. While predominantly solitary and benign, a minority of insulinomas can present as malignant. Insulinomas typically carry a hallmark clinical presentation characterised by Whipple's triad; symptoms of hypoglycaemia (e.g., sweating, palpitations, headaches, confusion), documented low blood glucose levels and resolution of symptoms following glucose administration. However, this is not a specific syndrome and the intersection of NETs and insulinomas further contribute to deviation between textbook and real-world presentation. Furthermore, even with a multitude of imaging modalities, localisation is not

always possible in some cases, further complicating management. The following cases explore four patients initially diagnosed with non-functional or mixed-hormone secreting NETs, who later developed hypoglycaemic episodes, and were eventually diagnosed with insulinomas. In each case, patients first presented with non-specific symptoms typical of NETs, such as abdominal pain, flushing, or diarrhoea. These symptoms dominated the clinical picture, overshadowing early signs of hypoglycaemia. For example, Patient A, initially diagnosed with a well-differentiated NET of the pancreas, had reported sweating and dizziness at presentation, signs only later attributed to an insulinoma-induced hypoglycaemia. Similarly, Patient B experienced hypoglycaemic episodes months before his neuroendocrine tumour diagnosis, which were overlooked, culminating in a severe hypoglycaemic episode leading to a road traffic accident over two years later. Patient C experienced low blood sugars years after his initial diagnosis. Patient D had longstanding episodic fatigue and dizziness, initially dismissed until home readings revealed frequent low glucose episodes, leading to his insulinoma diagnosis. These cases highlight the diagnostic complexity of NETs and, more specifically, insulinomas. Consistently, hypoglycaemia in patients with neuroendocrine tumours is often late-presenting, missed or considered a secondary issue until it becomes severe or recurrent. The complexity of NET symptoms, combined with the overshadowing presence of primary tumour-related manifestation, contributes to delayed diagnosis. Clinicians must remain vigilant for hypoglycaemia in NET patients, as early detection and treatment of insulinomas can improve overall mortality and morbidity, namely complications of recurrent hypoglycaemia, including long-term neurological sequelae and critical incidents, such as motor vehicle collisions.

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