ALTERED FC AND FAB GLYCOSYLATION STATUS IN PATIENTS WITH IGG4-RELATED SCEROSING CHOLANGITIS AND AUTOIMMUNE PANCREATITIS

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Introduction IgG4-related disease (IgG4-RD) is a systemic fibro-inflammatory condition characterised by an abundance of IgG4+ antibodies in the serum and tissue of involved organs. IgG glycosylation plays an important role in many chronic inflammatory and autoimmune conditions. We sought to assess the glycosylation status in patients with IgG4-RD and correlate with disease activity, damage and response to treatment.

Methods IgG Fc and Fab glycosylation status was assessed in patients with IgG4-RD involving the bile ducts (IgG4-sclerosing cholangitis, IgG4-SC) and pancreas (autoimmune pancreatitis) (n=22), disease controls with primary sclerosing cholangitis (DC n=22) and healthy controls (HC n=22). Disease activity, organ damage and response to treatment were assessed serially using the IgG4-responder index. Serum IgG and subclasses were quantified using an ELISA and nephelometry. IgG and subclass Fc glycosylation was assessed by mass spectrometry and Fab glycosylation by lectin (SNA) affinity chromatography. Statistics were performed using Prism.

Results IgG4-SC and AIP patients exhibited reduced total IgG Fc galactosylation and IgG1 Fc bisecton, and increased IgG4 Fc fucosylation and IgG2/3 Fc hybrid compared to HC. There was recovery of IgG1 Fc bisecton (increase) and IgG2/3 Fc hybrid (decrease) upon corticosteroid treatment. IgG Fc galactosylation and IgG2/3 Fc hybrid correlated with disease activity. IgG Fab glycosylation was higher in IgG4-RD patients, with an increase in IgG4-specific, and to a lesser extent IgG1-specific, Fab glycosylation compared to HC and DC.

Conclusions In the first study to assess glycosylation status in IgG4-RD, we demonstrated alterations in both IgG Fc and Fab glycosylation, which may play a role in pathophysiology and serve as a biomarker of disease.

WHAT IS THE YIELD AND CLINICAL UTILITY OF EUS IN PATIENTS WITH PRIOR NON-DIAGNOSTIC MRCP?

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Introduction The most effective investigation for suspected gallstones between MRCP and EUS is unclear. A 2015 Cochrane systematic review of their performance in common bile duct (CBD) stones concluded that the tests were of comparable accuracy. Conversely, a 2017 meta-analysis found EUS to be more sensitive. Any superiority of EUS may be due to comparable accuracy. Conversely, a 2017 meta-analysis found EUS to be more sensitive. Any superiority of EUS may be due to parable accuracy. Conversely, a 2017 meta-analysis found EUS to be more sensitive. Any superiority of EUS may be due to parable accuracy. Conversely, a 2017 meta-analysis found EUS to be more sensitive. Any superiority of EUS may be due to parable accuracy. Conversely, a 2017 meta-analysis found EUS to be more sensitive. Any superiority of EUS may be due to parable accuracy. Conversely, a 2017 meta-analysis found EUS to be more sensitive. Any superiority of EUS may be due to parable accuracy. 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Pancreatic cysts can be incidental findings on cross-sectional imaging of the abdomen. We examined the decision-making and outcome of patients with a pancreatic cyst(s) discussed at the Royal Derby Hospital HPB cancer MDT and compared practice against the 2015 American Gastroenterology Association (AGA) and 2017 International Association of Pancreatologists (IAP) guidelines on the management of pancreatic cysts. 

Methods
A search of HPB MDT meeting reports, from January 2016 to October 2017 (n=1144) identified 88 patient (51 female) reports relating to the first discussion of a pancreatic cyst. Electronic medical records were examined to collect data pertaining to subsequent investigations and outcome. Details of medical comorbidities were used to calculate a Charlson Comorbidity Index.

Results
The median age was 72 years (range 32–87) and the median estimated 10-year survival based on the Charlson Comorbidity Index was 53% (range 0%–98%).

86% of pancreatic cysts were judged to be an incidental finding. The median cyst diameter was 19.5 mm (range 4–110 mm). 43/88 (49%) patients proceeded to endoscopic ultrasound (EUS), with 33 having a fine needle aspiration (FNA). 4/88 (5%) patients had probably malignant (C4) or malignant (C5) cytology. All 4 patients had “high risk stigmata” on their initial CT/MRI. The final outcome for most patients was no further intervention (56%) or follow-up imaging (36%), with 5 (6%) patients offered surgery.

Applying the 2017 IAP management algorithm, 13 (15%) patients had “high-risk stigmata” on CT/MRI and except where their performance status or co-morbidity precluded further investigation/treatment (5), were recommended for surgery (1) or EUS (7). Of the remaining 75 patients, 45 (60%) had no worrisome features on CT/MRI and so would not have required EUS, 21/45 (47%) of these patients in our practice underwent EUS, but none demonstrated definite mural nodules, main duct involvement or suspicious/positive cytology.

The 2015 AGA management algorithm could only be applied to those patients who had undergone initial radiological assessment with MRI (n=11). None of these patients had two positive features on MRI, indicating a need for EUS. 6/11 (55%) patients did, however, have an EUS, with none identifying positive features or concerning cytology.

Conclusions
These findings suggest that a significant proportion (24%) of patients with pancreatic cysts underwent unnecessary EUS. Application of international guidelines can reduce the number of patients who require an endoscopic ultrasound.