ATU-10 QUPATH MACHINE LEARNING ALGORITHM ACCURATELY IDENTIFIES MLH1 DEFICIENT INFLAMMATORY BOWEL DISEASE-ASSOCIATED COLORECTAL CANCER

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Introduction Mismatch Repair (MMR) deficient colorectal cancers are an important cohort to study as these patients have a high neo-epitope load, suggesting they may respond well to immunotherapy. We previously reported deficient MMR due to loss of MLH1 expression occurs in >20% of all inflammatory bowel disease-associated colorectal cancers (IBD-CRC). Manually identifying MHL1 deficient tumours from immunostained samples is time-consuming and labour-intensive. Therefore, we aimed to train QuPath, a digital image analysis program, to accurately identify MLH1 deficient IBD-CRCs from a tissue microarray (TMA) containing normal colon and IBD-CRC.

Methods A TMA (n=162 cores) containing normal colon and IBD-CRC was immunostained for MLH1, digitalised and imported into QuPath. A representative sample (14 sections of 500µm x 500µm) was used to train a QuPath algorithm to identify tissue histology (normal epithelium, tumour, immune infiltrate or stroma) and MLH1 expression pattern. The algorithm was applied to the whole TMA. Accuracy level for histology and MLH1 classification was set at >75% of cells per category; cores where neither category met this threshold were flagged for review and these cores were histopathologically reviewed qualitatively. Data were exported to IBM®SPSS® (V25.0) for statistical analysis.

Results Tissue histology and MLH1 expression was correctly identified in 87/113 (77%) cases, misclassified in 1/113 (0.9%) case and flagged for manual review in 25/113 (22.1%) cases. Reasons cores were flagged for review included: small quantity of tissue, atypical morphology, excessive immune infiltrate, normal epithelium and patchy immunostaining. Of cores not flagged for review (n=88), the algorithm was highly sensitive (100%) and specific (98.6%) for identifying MLH1-deficient IBD-CRC, □=0.967 (95%CI 0.902-1.032) (p<0.001).

Conclusions MLH1 deficient IBD-CRC can be accurately identified using our QuPath algorithm, with an acceptable proportion of equivocal samples highlighted for manual evaluation. This process could be efficiently automated in conventional NHS IBD-CRC surveillance and treatment programmes to examine all colonic tissue and tumour specimens for MLH1 expression, thus identifying patients who may respond well to immunotherapy. This approach now needs to be validated using endoscopic biopsies.

Liver

ATU-7 INCIDENT ACUTE KIDNEY INJURY HAS A WORSE PROGNOSIS THAN BASELINE IN SEVERE ALCOHOLIC HEPATITIS

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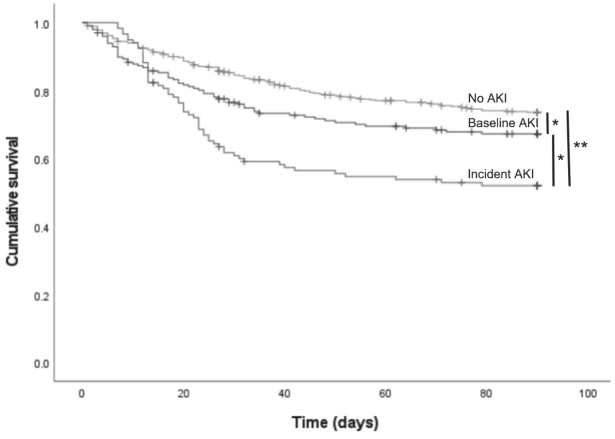
Introduction Alcoholic hepatitis (AH) is the most severe alcohol-related liver disease. Acute kidney injury (AKI) is associated with increased mortality. AKI may be present at the time of presentation (baseline) or develop subsequently (incident). We used data from the STOPAH (STeroids Or Pentoxifyline for Alcoholic Hepatitis) trial to describe the prevalence of AKI, its association with mortality and risk factors for its development.

Methods The primary endpoint in analysis was 90-day mortality. Patients from the STOPAH trial were classified as having a baseline or incident AKI (within 7 days of starting treatment; D7). AKI was defined as any of: i) creatinine ≥ 26.5 micromol/L above or ≥ 1.5x the lowest recorded creatinine; ii) creatinine ≥ 133 micromol/L; iii) renal replacement therapy. The effect of AKI on 90-day mortality was tested by Kaplan-Meier survival analysis. Factors associated with incident AKI were compared by Student's t-test, Mann-Whitney U test or Chi-squared test as appropriate.

Results Baseline creatinine was recorded in 1051 patients; 282 patients with a normal creatinine at baseline were alive at D7 but did not have a second creatinine recorded so were excluded from survival analysis. Baseline AKI was present in 198/1051 (19%) patients while 119/1051 (11%) developed an



Abstract ATU-7 Figure 1 Kaplan-Meier survival curves for patients with a baseline acute kidney injury (n = 198, 63 events), incident acute kidney injury (n = 119, 56 events) and normal baseline and day seven creatinine (n = 452, 115 events)
*Beslow (Generalised Wilcoxon) p < 0.05; **p < 0.001

incident AKI. Baseline AKI was associated with increased D90 mortality compared to patients without baseline or incident AKI. Incident AKI was associated with the highest mortality (Figure 1). There was no difference in mortality between patients with a baseline AKI that resolved by D7 or persisted (Breslow Chi-square 0.227, p = 0.633). Patients with incident AKI had significantly higher bilirubin (mean 374 mmol/L vs 281, p < 0.001), INR (2.0 vs 1.8, p = 0.001), and neutrophil count (8.1 vs 7.1, p = 0.031) than those without baseline or incident AKI. Prednisolone treatment was associated with a reduced risk of incident AKI (odds ratio 0.53, 95% confidence interval 0.34 - 0.81, p = 0.003). Age, gender, baseline observations and hepatic encephalopathy were not associated with incident AKI.

Conclusions Incident AKI at D7 confers a worse prognosis than either no or baseline AKI. This highlights the need for proactive monitoring and treatment of factors predisposing to AKI in patients with AH, particularly for patients with markers of severe disease.

Gastroenterology service

ATU-4 E-HEALTH VERSUS STANDARD CARE IN INFLAMMATORY BOWEL DISEASE MANAGEMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction The increasing incidence and prevalence of inflammatory bowel disease (IBD) has fuelled the need for innovative models of care. We aimed to compare effectiveness of e-health interventions with standard care in management of IBD.

Methods We searched Medline, Embase, PubMed, CINAHL, PsychInfo, Clinical trials registry and Cochrane databases for randomized controlled trials published in the English language until November 2020, comparing e-Health interventions to standard care for patients with IBD. Primary outcomes included difference in disease activity and patients in clinical remission at the end of follow up. Secondary outcomes included differences in quality of life (QoL), IBD-knowledge & rate ratios (RR) for endoscopic procedures, total healthcare encounters, corticosteroid use, clinic visits and IBD related hospitalization or surgery. RevMan 5.4 was used for data analysis.

Results Nine studies (n=1841; 991- e-Health & 850-controls) were identified. There was no statistically significant difference between the mean disease activity scores for ulcerative colitis (UC)[standard mean difference (SMD) 0.22, 95% confidence interval (CI): -0.04-0.48] and Crohn's disease (CD)(SMD 0.02, 95% CI: -0.18-0.22) in the e-Health and standard care groups and no statistically significant difference in patients in clinical remission at the end of follow up between both groups (OR - 1.05, 95% CI: 0.76-1.45). Higher QoL (SMD 0.19, 95% CI: 0.05-0.34) and IBD knowledge (SMD 0.25, 95% CI: 0.12-0.37) scores were noted in the e-Health group compared to standard care. E-Health group had less clinic visits (RR 0.85, 95% CI: 0.78-0.93) while there were no statistically significant differences noted in the RR for endoscopic procedures, total healthcare encounters, corticosteroid use, and IBD-related hospitalization or surgery between both groups.

Conclusions E-Health interventions are comparable with standard care for impact on disease activity, remission, endoscopy utilization, total healthcare encounters, corticosteroid use, and IBD-related hospitalization or surgery. However, e-Health group had better outcomes with QoL, IBD related knowledge & fewer clinic visits.

ATU-5 PERCUTANEOUS LIVER BIOPSY TO CONFIRM ADVANCED METASTATIC CANCER: A STEP TOO FAR?

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Introduction Liver biopsy carries significant risks, including bleeding and death. It is routinely undertaken to confirm imaging evidence of hepatic metastases. However, establishing a cancer diagnosis beyond doubt is of limited benefit if a patient is not suitable for oncological therapy. We have therefore examined outcomes in patients undergoing liver biopsy for metastatic cancer.

Methods Hospital Episode statistics were examined to identify patients undergoing percutaneous liver biopsy between 2010 and 2019 and diagnosed with metastatic cancer. Multivariable logistic regression examined risk factors for mortality at 14 and 30 days and receiving chemotherapy.

Results 30992 patients underwent liver biopsy for metastatic cancer (median age of 67 (IQR 59-74) years, 52% female). 28% underwent biopsy during an emergency inpatient stay and 9% died within 14 days and 27.6% within 30 days of their biopsy. In contrast, only 2.2% of patients having an outpatient biopsy died within 14 days and 8.6% within 30 days.

Increased 30 day mortality was associated with: inpatient biopsy (odds ratio 3.37 (95%CI 3.15-3.61)) and increasing comorbidity (Charlson score 1-4: 1.21 (1.11-1.32)). Lower 30 day mortality was associated with all ages under 70 (for 18-29 yr olds: 0.35 (0.20-0.63)), a lymphoma diagnosis (0.69 (0.51-0.93)) and biopsy at a radiotherapy centre (0.89 (0.83-0.96)).

14,244 (46%) patients received chemotherapy within 6 months of liver biopsy; 53% of those undergoing outpatient biopsy but only 33% of those biopsied as an inpatient. 18% of patients received only one dose of chemotherapy and 18% died within 14 days of chemotherapy. Receiving chemotherapy was negatively associated with biopsy as an inpatient (0.45 (0.42-0.47)) and increasing comorbidity (Charlson score 1-4 0.85 (0.80-0.91)). All ages under 70 (for 18-29 yr olds: 3.79 (2.67-5.39)) and female sex (1.06 (1.01-1.11)) were associated with receiving chemotherapy. Medium and high volume providers of biopsies were also associated with receiving chemotherapy compared to the lowest volume providers (1.13 (1.04-1.22) and 1.51 (1.39-1.64), respectively).

Conclusions Mortality is high following liver biopsy to confirm metastatic cancer in patients admitted as an emergency. Only a third of such patients go on to receive chemotherapy. Clinicians should carefully consider the benefit of invasive