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F O R E D R A G

Assessment of treatment response in known Crohn's disease – a prospective blinded study comparing the diagnostic accuracy of intestinal ultrasound, magnetic resonance enterocolonography, panenteric capsule endoscopy and faecal calprotectin

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Background and aims: Minimal invasive modalities may replace ileocolonoscopy (IC) in the follow-up of Crohn's disease (CD). The aim of this study was to evaluate intestinal ultrasound (IUS), magnetic resonance enterocolonography (MREC), panenteric capsule endoscopy (PCE) and faecal calprotectin (FC) for determining response to medical treatment in patients with ileocolonic CD.

Methods: This prospective, blinded, multicentre study included patients with endoscopically active CD. Patients were scheduled for IC, MREC, IUS, PCE and FC before and 12 weeks after treatment with corticosteroids or biological therapy. A ≥ 50% reduction of the *Simple Endoscopic Score for Crohn's Disease* (SES-CD) with IC defined treatment response.

Results: Fifty patients completed the pre- and post-treatment evaluation with IC, and endoscopic response was achieved in 25 (50.0%). PCE was omitted in 12 (24.0%) patients because of stricturing CD. All activity scores decreased in patients achieving endoscopic response: The Simple Ultrasound Score for Crohn's Disease 2.2 vs. 6.1 ($P < 0.001$), Magnetic Resonance Index of Activity 29.0 vs. 37.1 ($P = 0.05$), SES-CD with PCE 3.1 vs. 12.8 ($P < 0.001$) and FC 115.3 vs. 1339.9 mg/kg ($P < 0.001$). The sensitivity and specificity of IUS, MREC, PCE and FC was 80.0% (95% CI 56.3-94.3) / 77.8% (52.4-93.6), 65.2% (42.7-83.6) / 87.0% (66.4-97.2), 87.5% (61.7-98.4) / 86.7% (59.5-98.3) and 90.0% (68.3-98.8) / 86.4% (65.1-97.1), respectively.

Conclusions: IUS, PCE and FC are equally effective for determining endoscopic response in patients with active CD. PCE is limited by the occurrence of strictures in this group of patients.

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The Bilirubin-Albumin-Betablocker-Statin (BABS) Score Shows Potential for Hepatic Encephalopathy Risk Stratification

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Aims: Hepatic encephalopathy (HE) frequently complicates liver cirrhosis, leading to hospital admissions. Currently, no risk scores predict overt HE (OHE). The Bilirubin-Albumin-Beta-Blocker-Statin (BABS) score, validated in the US, was assessed for its efficacy in predicting OHE in Danish and German cohorts.

Methods: Clinical data from 698 patients (60 years, 61% male, MELD 10) in Germany (n=398) and Denmark (n=276) were analyzed. The BABS score, based on bilirubin, albumin, beta-blocker, and statin use, categorizes patients into low, intermediate, and high-risk groups. Incidence of HE, death, and liver transplantation were tracked over a mean follow-up of 2 years (range 8 months–5 years).

Results: HE incidence rates were 12.23 per 100 person-years in Denmark and 10.29 per 100 person-years in Germany. Key cohort differences included higher beta-blocker use in Germany (50% vs. 13%) and higher statin use in Denmark (34% vs. 10%). Age correlated directly with HE risk in Germany and inversely in Denmark. The BABS score Harrell's C-index for predicting HE was 0.7358 overall, 0.795 for German patients, and 0.6466 for Danish patients. Fifty percent were categorized as low- or high-risk, potentially bypassing psychometric testing.

Conclusion: The BABS score shows promise in predicting OHE but requires optimization for the studied cohorts. Data suggest a clinical approach where high-risk patients receive prophylactic treatment, intermediate-risk patients undergo psychometric testing, and low-risk patients undergo annual BABS scoring or re-evaluation upon clinical change.

No Effect of Methylnaltrexone on Acute Pancreatitis Severity: A Multicenter Randomized Controlled Trial

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Objective: Opioids used to manage severe pain in acute pancreatitis might exacerbate the disease through effects on gastrointestinal and immune functions. Methylnaltrexone, a peripherally acting μ-opioid receptor antagonist, may counteract these effects without changing analgesia.

Materials and methods: This double-blind, randomized, placebo-controlled trial included adult patients with acute pancreatitis and systemic inflammatory response syndrome at four Danish centers. Participants were randomized to receive five days of continuous intravenous methylnaltrexone (0.15mg/kg/day) or placebo added to the standard of care. The primary endpoint was the Pancreatitis Activity Scoring System score after 48 hours of treatment. The main secondary outcomes included pain scores, opioid use, disease severity, and mortality.

Results: In total, 105 patients (54% males) were randomized to methylnaltrexone (n=51) or placebo (n=54). After 48 hours, the Pancreatitis Activity Scoring System score was 134.3 points in the methylnaltrexone group and 130.5 points in the placebo group (difference, 3.8 [95% CI, -40.1 to 47.6]; *P*=0.87). At 48 hours, we found no differences between groups in pain severity (difference, 0.0 [95% CI, -0.8 to 0.9]; P=0.94), pain interference (difference, -0.3 [95% CI, -1.4 to 0.8]; P=0.55), and

morphine equivalent doses (difference, 6.5 mg [95% CI, -2.1 to 15.2]; P=0.14). Methylnaltrexone also did not affect the risk of severe disease (difference, 8% [95% CI, -11 to 28]; P=0.38) and mortality (difference, 6% [95% CI, -1 to 12]; P=0.11). The medication was well-tolerated.

Conclusion: Methylnaltrexone treatment did not achieve superiority over placebo for reducing the severity of acute pancreatitis.

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Study title

Treatment outcomes after first-line biological treatment in biological-naïve patients with inflammatory bowel diseases – a prospective, multicenter cohort study

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Study aims

Existing findings on outcomes of biological therapy in patients with inflammatory bowel diseases (IBD) are largely based on retrospective or tertiary center studies. In this study, we aimed to investigate outcomes of biological therapy and predictors of these outcomes in a prospective, biological-naïve IBD cohort.

Materials and methods

This study included 796 adult biological-naïve IBD patients who initiated biological therapy between May 1, 2019, and April 31, 2022, and followed prospectively for 125 weeks in median. Clinical response and remission were evaluated using clinical disease activity scoring indices at week 12. Loss of response (LOR) and major IBD surgery were evaluated during maintenance therapy. Predictors of outcomes were assessed using multivariable regression analyses.

Results

About half of patients (41.0% of patients with ulcerative colitis (UC); 52.3% of patients with Crohn's disease (CD)) initiated biological treatment within two years of their diagnosis. Overall, 67.7% of patients with UC and 74.3% of patients with CD achieved clinical response at week 12, while 46.0% of patients with UC and 48.0% of patients with CD also achieved clinical remission. During maintenance therapy, 30.0% of patients with UC and 24.8% of patients with CD experienced LOR, but only 5.3% and 8.3% underwent major IBD surgery. Severe clinical disease activity at baseline, concomitant corticosteroid treatment, and a negative smoking history predicted inferior outcomes in patients with UC, while short disease duration, colonic disease, non-stricturing behavior, and antimetabolite combination therapy predicted favorable outcomes in patients with CD.

Conclusion

Clinical remission was achieved in only half of patients at week 12, while another one-third of patients with UC and one-fourth of patients with CD experienced LOR despite being biological-naïve and having a short disease duration. Several clinical features were associated with outcomes and may be useful predictors of response to biological therapy.

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Brain dysfunction is prevented by alpha 2A adrenergic receptor antagonism in experimental metabolic dysfunction-associated steatotic liver disease

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Aim: Cognitive dysfunction is a recognised complication of metabolic dysfunction-associated steatotic liver disease (MASLD), yet approved treatments for this condition are lacking. We have previously shown that antagonising the alpha 2A adrenergic receptor (ADRA2a) modulates MASLD progression. This study aims to investigate the potential of ADRA2a antagonism as a novel target for treating brain dysfunction in MASLD.

Materials and methods: Two animal models of MASLD were used: 1) Male Sprague Dawley rats were fed a high-fat, high-cholesterol diet (HFHC) or a standard diet (controls) for 16 weeks, 2) Male C57BL/6NTac mice were fed a modified Amylin-liver non-alcoholic steatohepatitis diet (AMLN) or a standard diet (controls) for 36 weeks. Half of the MASLD animals received the ADRA2a antagonist Yohimbine in their drinking water for the final 10 weeks. Neurobehavioural tests were conducted in all animals. Inflammation in the liver-brain axis and brain tissue oxygen availability were assessed in the HFHC model, whilst brain perfusion was evaluated in the AMLN model.

Results: ADRA2a antagonism prevented impaired memory and depression-like behaviour in both MASLD models, in addition to anxiety-like behaviour in the AMLN model. The examinations of inflammation in the liver-brain axis using the HFHC model revealed that ADRA2a antagonism ameliorated liver inflammation and prevented elevated plasma cholesterol levels, decreased systemic inflammation and attenuated signs of neuroinflammation. The evaluations of brain perfusion showed that ADRA2a antagonism prevented a decrease in brain oxygen availability in the HFHC model and increased total cortex perfusion in the AMLN model.

Conclusion: Ten weeks of ADRA2a antagonism in two rodent MASLD models prevents cognitive dysfunction, decreases inflammation in the liver, systemic circulation and brain, increases cerebral cortex perfusion and maintains cortex oxygenation. This paves the way for further mechanistic studies and consideration of future clinical translation in MASLD patients at risk of cognitive dysfunction.

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Validation of Transient Elastography and the Enhanced Liver Fibrosis Test as Prognostic Biomarkers across the Spectrum of Steatotic Liver Disease

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Background: Steatotic liver disease (SLD) provides a consensus-driven, but not data-driven, approach to phenotype patients with hepatic steatosis. We aimed to validate the prognostic performance of transient elastography (TE) and the enhanced liver fibrosis (ELF) test in patients with SLD.

Methods & Materials: We included patients from an observational cohort (n=446) where all had a historic alcohol intake of ≥36 g/day for men and ≥24 g/day for women for ≥1 year, with no prior hepatic decompensation. We identified patients with SLD by ultrasonic and histological findings. Preceding three months alcohol intake subclassified into metabolic dysfunction-associated steatotic liver disease (MASLD), metabolic and alcohol-related liver disease (MetALD) and alcohol-related liver disease (ALD). We stratified by the TE ≥10 kPa and ELF ≥9.8 cut-offs. Hepatic decompensation (Baveno VII) and deaths were identified by review of medical records.

Results: We classified 143 MASLD, 75 MetALD and 90 ALD patients. Baseline median TE was 9.3/7.9/8.7 kPa and ELF 9.7/9.5/9.2 (MASLD/MetALD/ALD). 28 MASLD, 13 MetALD and 15 ALD patients experienced hepatic decompensation during follow-up. TE ≥10 predicted decompensation in MASLD (aHR=43.2; 95%CI: 5.8-319.0), MetALD (aHR=36.9; 95%CI: 4.8-285.8) and ALD (aHR=14.6; 95%CI: 3.3-65.1), while ELF ≥9.8 showed comparable prognostic performance. Majority (86%) of decompensations developed in patients with concordant TE ≥10 kPa and ELF ≥9.8. Death occurred in 80 patients, with hepatic decompensation preceding death in 39 (49%) cases. TE ≥10 was an independent predictor of all-cause mortality in MASLD aHR=4.1; 95%CI: 1.9-8.6, MetALD aHR=3.7; 95%CI: 1.4-9.9 and ALD aHR=6.9; 95%CI: 2.7-18.0. Stratifying

by the ≥9.8 cut-off, ELF predicted mortality in MASLD (aHR=3.6; 95%CI: 1.7-7.6) and ALD (aHR=6.8; 95%CI: 2.7-17.1) but not MetALD (aHR=1.6; 95%CI: 0.6-4.2).

Conclusion: Our study validates the TE ≥10 kPa and ELF ≥9.8 cut-offs in patients across the SLD spectrum, demonstrating their effectiveness in predicting hepatic decompensation and all-cause mortality.

Title: The risk of psychiatric disorders in patients with AIH: a nationwide registry-based follow-up study comparing with the general population

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Abstract

Aims: Many patients with autoimmune hepatitis (AIH) have impaired quality of life and symptoms of depression and anxiety. However, little is known about the long-term risk for psychiatric disorders in patients with AIH. We conducted a population-based follow-up study on the risk of psychiatric disorders in patients with AIH and compared with the general population.

Material and methods: From nationwide registries we identified all Danish patients diagnosed with AIH, 1994-2022, and matched comparators from the general population. We estimated the prevalence of psychiatric disorders at the time of AIH diagnosis. The patients were followed through December 2022, and we compared the risk of subsequent diagnosis of a psychiatric disorder for patients with AIH vs. matched comparators.

Results: We included 1371 patients with AIH and 13,556 matched comparators with a median age of 54 years at the time of AIH diagnosis. At AIH diagnosis the prevalence of overall psychiatric disorders was the same in the patients with AIH and the comparators = 25.2%. In the patients with AIH the absolute risk for overall psychiatric disorder development was 12.4% (95% confidence interval [CI] 10.6-14.4) 10 years after AIH diagnosis. Depressive and anxiety disorders comprised the highest 10-year cumulative risk of 11.4% and 3.6%, respectively. Sixty-eight (5%) of the patients developed more coexisting psychiatric disorders. The overall risk of psychiatric disorders was similar in the comparators with an adjusted relative risk of 1.0 (95% CI 0.7-1.6) 10 years after AIH diagnosis, and this pattern applied to all groups of psychiatric disorders.

Conclusions: This nationwide study showed that the risk for hospital or medically treated psychiatric disorders was similar in patients with AIH and in general population comparators.

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Clinical course of biopsy-controlled alcohol-related liver disease

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Background and aims: Alcohol-related liver disease (ALD) is associated with high mortality but there is a lack of good prospective studies characterising the natural history of ALD in more detail than epidemiological studies. We aimed to investigate the clinical course of biopsy-controlled ALD.

Method: Prospective cohort of patients with excessive alcohol intake (men: ≥36 g/day, women: ≥24 g/day) and no prior decompensation. At baseline, we performed liver biopsies, genotyping of SNPs in PNPLA3, MBOAT7, TM6SF2, HSD17B13, and clinical investigations. We manually reviewed patients' medical records for new diagnoses, alcohol intake and all-cause mortality. Decompensation were defined according to the Baveno VII recommendations.

Results: We followed 459 ALD patients for 5.9 years (IQR 4.5-7.8). Mean age at baseline was 57±10 years, 76% male, fibrosis stage F0-1/F2/F3-4 = 57%/23%/20%, 15.5 years of excessive drinking. During follow-up, 67 patients decompensated, and 101 patients died. All-cause mortality increased with higher fibrosis stage from 1.4 deaths per 100 person-years for stage F0-1, to 5.0 deaths per 100 person-years for stage F2, and 9.3 deaths per 100 person-years for stage F3-4. The cause of death was hepatic in 38%, non-hepatic in 43% and unknown in 20% of cases. The incidence of later decompensations increased with baseline fibrosis stage: 5 out of 260 = 1.9% for stage F0-1, 17 of 107 = 15.9% for stage F2, and 45 of 91 = 49.5% for stage F3-4. Baseline fibrosis stage (HR = 3.11; 95%CI 1.54-6.30) and excessive drinking during follow-up (HR = 4.80; 95%CI 3.28-7.02) were independent predictors of decompensation. PNPLA3 and TM6SF2 were predictors of decompensation in univariable regression but did not exhibit independent prognostic information.

Conclusion: Patients with ALD experienced a high 5-year risk of decompensation and death, even in patients with only moderate fibrosis (F2) at baseline. Excessive drinking predicted decompensation independent of fibrosis stage.

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POSTERS

Longitudinal changes in liver stiffness measurements in a population-based screening cohort of 5,517 participants

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Background and aim: Liver stiffness measurements (LSM) by transient elastography (TE) <8 kPa effectively rule out advanced fibrosis and therefore often serve as a threshold in fibrosis screening. However, the longitudinal trends in LSM in both general and at-risk populations remain largely unexplored. We therefore aimed to assess the proportion of participants experiencing clinically significant changes in LSM in a population-based screening cohort.

Methods: This multicenter study, conducted in Barcelona, Spain (BCN), The Netherlands (NL) and Denmark (DK), prospectively enrolled adult participants from the general population (BCN and NL), as well as people with current or prior excessive alcohol consumption (DK). Participants initially underwent liver fibrosis screening using TE, and were invited to a follow-up investigation after a mean of 3.7 years. We defined a clinically significant LSM change as an alteration (increase/decrease) of ≥20%.

Results: We included 5,517 participants for baseline screening, with 3,266 participants (736 at risk of ALD) undergoing a follow-up investigation.
Among participants with baseline LSM <8 kPa, 3.0% increased significantly and to a final LSM ≥8 kPa, a trend consistent across all cohorts. This group more often comprised male participants with metabolic dysfunction. Overall, 1.1% participants increased from <8 kPa at baseline to ≥10 kPa at follow-up.
Of participants with baseline LSM ≥8 kPa, 8.8% increased significantly (BCN: 6.2%, NL: 10.4%, DK: 10.0%). Conversely, 72% of participants either decreased significantly or decreased to LSM <8 kPa, with the biggest difference between the two general cohorts.

Conclusions: An 8 kPa liver stiffness threshold provides relevant information for clinical decision making when monitoring steatotic liver disease in the population at intervals spanning 3-4 years. About 1% of individuals screening negative will progress to stages suggestive of advanced fibrosis, whereas nearly 10% of patients initially screening positive will experience a clinically significant increase in liver stiffness.

Title: Long-term risk of alcohol-related liver disease following treatment for alcohol use disorder: A Danish nationwide register-based cohort study

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Background and Aims: Screening for ALD (Alcohol-related Liver Disease) is suggested in individuals with a high alcohol consumption. Our aims were to estimate the 10-year risk of ALD in individuals attending treatment for Alcohol Use Disorder according to age-, and diabetes and their absolute risk of mortality due to alcohol-related causes compared to controls.

Methods: We used nationwide healthcare registries to identify individuals 18 years or older with no prior ALD diagnosis who attended community-based treatment for AUD in Denmark from 2006-2018. Individuals were followed for hospital diagnoses of ALD until 2021 and for cause-specific mortality until 2018.

Results: Of 58,408 individuals attending treatment for AUD, 3% had diabetes and they had consumed alcohol for an average number of 26 years. During 423,056 person-years of follow-up, 3,933 were diagnosed with ALD and 11,590 died. Overall, the 10-year risk of ALD was 5.7% (95%CI 5.5-5.9) and the highest 10-year risk was found for those aged 45-54 years (7% 05%CI 6.9-

7.8). The 10-year risk was higher in individuals with diabetes: For example at age 45-64 years, it was 11.8% (95%CI 9.0-14.6) for individuals with diabetes vs 6.9% (95%CI 6.5-7.3) for individuals without diabetes. The 10-year risk of death from any cause was 14.3%: 1.6% for death from ALD, 2.5% for death from other alcohol-related causes. In age- and sex-matched comparators the corresponding risks were 4.3% ,0.15% and 0.15%.

Conclusion: About 6% of individuals attending community-based AUD treatment were diagnosed with ALD within 10 years, although the risk was nearly doubled in those with diabetes. The 10-year risk of dying from ALD was less than 2%. These findings imply that in this population, the potential number of ALD attributed deaths avoided by screening for ALD, is likely limited. However if screening for ALD motivates abstinence other alcohol related deaths could potentially be avoided.

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11.

Time-trends in cholangiocarcinoma mortality – a Danish nationwide cohort study

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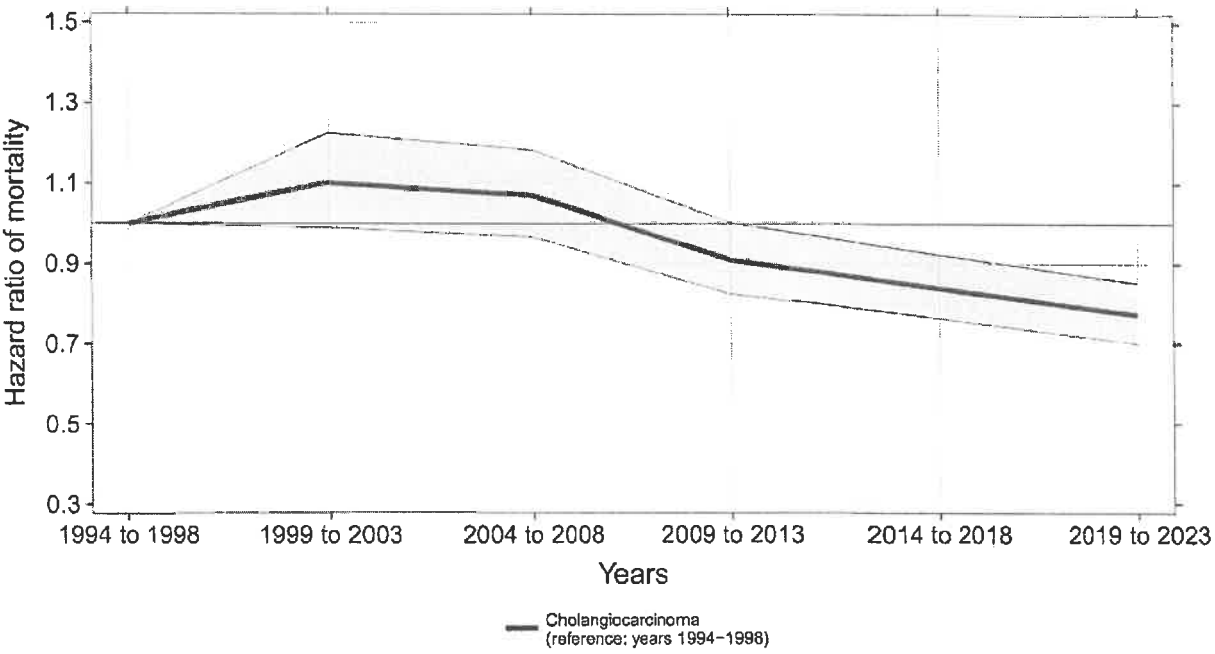
Aims: Cholangiocarcinomas (CCA) have a poor prognosis and the incidence of CCA is rising in Denmark. We set out to examine time trends in mortality of CCA in a nationwide Danish cohort.

Materials and Methods: We included all 6,300 Danish patients with a diagnosis of CCA (ICD-10 codes C22.1, C24.0, C24.8, C24.9) in 1994-2023 recorded in the Danish Cancer Registry or the National Patient Registry. We computed 1-year mortality and used Cox regression to estimate adjusted mortality hazard ratios (HR) by sex, age, year of diagnosis and type of CCA.

Results: Of the 6,300 CCA patients, 48% were men. The median age of patients diagnosed in 1994-1998 was 72 vs. 73 in 2019-2023. The 1-year mortality decreased between 1994 and 2023 from 78.3% (95% CI 75.3 – 81.2) in 1994-1998 to 66.6% (64.2-69.0) in 2019-2023, while 1-year mortality for the entire period was 71.3% (70.2-72.5). The 1-year mortality was: for 18-59-year-olds 56.1% (53.2-59.1), for 60-79-year-olds 70.1% (68.6-71.6), for patients over 80 years 86.6% (84.7-88.3), for intrahepatic CCA (iCCA) 70.5% (68.6-72.3), for extrahepatic CCA (eCCA) 68.4% (66.4-70.4), for unspecified CCA 84.1% (82.9-85.2), for females 72.5% (71.0-74.1), and for males 70.0% (68.3-71.7).
For year of diagnosis, adjusted mortality HRs decreased with more recent diagnosis year. Adjusted HRs of 5-year increase in diagnosis year were: overall 0.94 (0.92-0.95), for 18-59-year-olds 1.00 (0.96-1.04), for 60-79-year-olds 0.91 (0.89-0.93), for patients over 80 years 0.96 (0.93-0.99), for patients with iCCA 0.90 (0.87-0.93), for patients with eCCA 0.89 (0.87-0.91), for females 0.95 (0.93-0.98), and for males 0.92 (0.90-0.94); while for unspecified CCA it was 1.04 (1.01-1.07).

Conclusion: The 1-year mortality of Danish patients diagnosed with CCA in 2019-2023 was 66.6%, but it has decreased since 1994, overall and within subgroups defined by sex, age, or type of CCA.

Figure: (see next page)


Hazard ratio of mortality
1.5
1.3
1.1
0.9
0.7
0.5
0.3
1994 to 1998
1999 to 2003
2004 to 2008
2009 to 2013
2014 to 2018
2019 to 2023
Years
Cholangiocarcinoma
(reference: years 1994–1998)

12.

Post-discharge Mortality in Acute Pancreatitis:

A Nationwide Population-Based Matched Cohort Study

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Objective: To study in-hospital and post-discharge mortality in acute pancreatitis and how it has changed over time.

Materials and methods: In a Danish nationwide population-based cohort study, we included all adults (≥18 years) discharged after an incident episode of acute pancreatitis between 2002 and 2017. For each patient, five individuals from the general population, matched by age and sex, were selected as controls. We used Cox regression analysis to evaluate the risk of all-cause mortality at 90 days, 1-, 2-, and 5 years post-discharge and to examine time trends in in-hospital and post-discharge mortality over the study period.

Results: Among 28,759 adults with incident acute pancreatitis, 956 (3.3%) died in hospital. The 27,803 patients discharged from acute pancreatitis were matched with 139,015 comparison individuals (mean age 58.1 years, 51.1% men). The cumulative post-discharge mortality at 90 days was 5.0% for the acute pancreatitis cohort and 0.55% for controls. The mortality risk was significantly increased in acute pancreatitis patients at 90 days post-discharge (adjusted hazard ratio [aHR] 7.62; 95% CI 6.86-8.45); the risk attenuated over time but remained elevated for up to five years. In-hospital mortality decreased over the study period (aHR 0.65; 95% CI 0.53-0.81) from 2002-2005 to 2014-2017, while post-discharge mortality risk remained stable (aHR 0.85; 95% CI 0.72–1.01). Gastrointestinal and cardiovascular diseases accounted for 59.4% of early (90-day) post-discharge deaths.

Conclusion: In-hospital mortality for acute pancreatitis has significantly improved in recent years. However, the risk of post-discharge mortality remains high, especially in the first 90 days after discharge.

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Endoscopic ultrasound-guided celiac plexus block only rarely leads to long lasting reduction of opioid consumption in patients with chronic pancreatitis and abdominal pain

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Background/aims

Chronic pancreatitis (CP) is often related with patient morbidity due to chronic abdominal pain. In CP patients with non-medically responsive abdominal pain, Endoscopic Ultrasound-Guided Celiac Plexus Block/Neurolysis (EUS-CPB/CPN) may reduce opioid consumption. This study aims to examine safety and effect of EUS-CPB/CPN in CP patients with severe abdominal pain despite medical treatment.

Methods

Retrospective evaluation of consecutive CP patients who underwent EUS-CPB/CPN at Odense University Hospital (OUH), Odense, Denmark, during a five-year period.

Results

Collectively, 77 EUS-CPB/CPN procedures were performed on 24 CP patients (18 males) for abdominal pain. Median age was 51 years (95% Confidence Interval (CI): 40-58) and 17/24 (71%) patients had alcoholic CP. Orally administered morphine (equipotent dosages of other opioids included) were consumed by 23/24 (96%) patients with median of 100 mg/day (95%CI: 20-315) prior to the initial EUS-CPB. EUS-CPB was performed with Bupivacaine (n=37). EUS-CPN was performed with Bupivacaine and alcohol (n=35) or alcohol alone (n=4).

Following the initial EUS-CPB procedure, 13/24 (54%) patients described reduced pain levels with median 4 weeks duration (95%CI: 1-36), and 6/24 (25%) reduced opioid consumption with a mean 43 mg/day (95%CI: 20-120).

Overall, 4/37 EUS-CPB and 3/39 EUS-CPN procedures reduced the level of pain lasting >6 months with reduced consumption of opioids.

Complications were registered in 3/77 (4%) of the EUS-CPB/CPN procedures and included chronic diarrhea (n=2) and postprocedural infection (n=1).

Conclusions

EUS-CPB/CPN only leads to reduced opioid consumption and pain relief, lasting >6 months, in a minority of CP patients. Despite low rates of complications, EUS-CPB/CPN has very limited clinical impact in CP patients.

Changes in endoscopic activity and classification of lesions with panenteric capsule endoscopy in patients treated for Crohn's disease – a prospective blinded comparison with ileocolonoscopy, faecal calprotectin and C-reactive protein

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Background and aims: Panenteric capsule endoscopy (PCE) is a minimally invasive modality that may replace ileocolonoscopy (IC) in selected patients with Crohn's disease (CD). This study aimed to evaluate the dynamics of repeated assessment with PCE in patients receiving medical treatment for ileocolonic CD.

Methods: This prospective, blinded, multicentre study included patients with endoscopically active CD. Patients were scheduled for IC, PCE, faecal calprotectin and C-reactive protein before and 12 weeks after treatment with corticosteroids or biological therapy. The endoscopic disease activity was assessed with the Simple Endoscopic Score for Crohn's Disease (SES-CD).

Results: 124 bowel segments in 31 patients were assessed with IC and PCE before and after medical treatment. The median SES-CD decreased from 14 (IQR 8-17) to 5 (IQR 0-14) ($P < 0.001$) and 14 (IQR 10-17) to 6 (IQR 3-12) ($P < 0.001$) with IC and PCE, respectively. The repeated measurement correlation between PCE and IC was very strong ($r = 0.77$, $P < 0.001$), strong compared to faecal calprotectin ($r = 0.42$, $P = 0.003$) and moderate compared to C-reactive protein ($r = 0.36$, $P = 0.005$). The mean score for ulcer size, ulcerated surface and affected surface was equal to that of IC before and after treatment. PCE had a sensitivity and specificity of 80.6% (CI 62.5-92.5) and 93.8% (CI 79.2-99.2) for ulcer healing compared to IC.

Conclusion: PCE is responsive and accurate for the assessment of ulcer healing in CD. PCE may serve as a minimally invasive alternative to IC in selected patients.

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Diagnostic accuracy of plasma calprotectin and serum calprotectin in patients with suspected Crohn's disease

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Background: Prior studies indicate, that serum calprotectin (SCal) and plasma calprotectin (PCal) can be used as biomarkers in IBD. The aim of this study was to investigate the diagnostic accuracy of SCal and PCal in patients examined for Crohn's disease (CD).

Methods: Patients with clinically suspected CD were enrolled in a prospective, blinded study examining non-invasive modalities for diagnosing CD. Patients had a standardized work-up including ileocolonoscopy, panenteric capsule endoscopy and blood samples within a 2-week period. SCal and PCal were analysed in batches using the calprotectin assay from Gentian (Moss, Norway) on the Cobas platform (Roche, Basel, Switzerland). A routine CRP was measured on the same day.

Results: 126 patients were enrolled in the study, and 57 (45%) were diagnosed with CD based on the result of ileocolonoscopy and panenteric capsule endoscopy. Patients with CD had a mean PCal of 0.50 mg/L (CI 0.38-0.62) compared to 0.35 mg/L (CI 0.27-0.44) in non-CD patients ($P = 0.03$). The mean SCal was 1.45 mg/L (CI 1.20-1.69) and 1.06 mg/L (CI 0.90-1.22) in patients with and without CD, respectively ($P = 0.01$). Receiver operating characteristics curves showed an AUC of 0.63 (CI 0.53-0.73) for SCal and 0.61 (CI 0.51-0.71) for PCal, which was inferior to CRP (0.76, CI 0.68-0.85, $P < 0.02$). In patients diagnosed with CD, SCal and PCal had a moderate correlation with CRP ($r_s = 0.47$ and 0.55, respectively, $P < 0.001$), and SCal had a weak correlation with the Simple Endoscopic Score for CD ($r_s = 0.29$, $P = 0.04$) and the Crohn's Disease Activity Index ($r_s = 0.36$, $P = 0.03$).

Conclusion: Levels of PCal and SCal are increased in patients with CD. However, SCal and PCal are insufficient biomarkers in patients with clinically suspected CD, and they are both inferior to CRP.

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Title:
Cause-specific mortality in patients with alcohol-related liver disease in Denmark: a population-based study

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Aims: Increased knowledge of the causes of death will be essential to prevent premature death in alcohol-related liver disease. We examined cause-specific mortality, including death due to specific cancers, in the 15 years after diagnosis of alcohol-related liver disease.

Material and method: We used nationwide health registries to identify patients with a first diagnosis of alcohol-related liver disease between Jan 1, 2002, and Dec 31, 2017, in Denmark and followed up with patients for their underlying cause of death up to Dec 31, 2019. We estimated the cause-specific mortality and investigated whether the cause-specific mortality differed by sex, age, alcohol-related liver disease severity at diagnosis, and presence of diabetes.

Results: The study included 23,385 patients with incident alcohol-related liver disease. Patients had a median age of 58 years, 68% were men, and 66% had cirrhosis. During 111,532 person-years of follow-up, 15,692 (67%) patients died. Liver disease was the leading cause of death, with a 5-year risk of death due to liver disease on 25.8% (95% CI 25.3–26.4). Beyond 5 years, causes other than liver disease combined became more common, and cancer, cardiovascular disease, and alcohol use disorder were the most common. Hepatocellular carcinoma was the dominant cause of cancer death (10-year risk of 2.5%, 95% CI 2.3–2.7), followed by lung cancer (1.9%, 1.7–2.1). The 10-year risk of death due to liver disease (around 30%) was similar for patients in all age groups and independent of sex and diabetes but was three times higher for those with decompensated cirrhosis than steatosis or unspecified liver disease.

Conclusion: Patients diagnosed with alcohol-related liver disease were at high risk of dying from liver disease many years after diagnosis, irrespective of age and sex. Each specific cancer contributed minimally to the total mortality in patients with alcohol-related liver disease.

Word count: 297
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Subclinical myocardial fibrosis is related to disease severity in patients with metabolic dysfunction-associated steatotic liver disease (MASLD)

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Background and Aims: Myocardial extracellular volume (ECV), derived from advanced cardiac magnetic resonance imaging (CMR), reflects connective tissue in the myocardium. Quantification of myocardial ECV is based on T1-mapping technique with a comparison between the pre- and post-contrast T1 relaxation times. An increase in ECV may signify increased fibrosis in the myocardium. We assessed myocardial ECV in metabolic dysfunction associated steatotic liver disease (MASLD) which is increasingly being recognized as a systemic fibroinflammatory disease and which is associated with increased cardiovascular morbidity.

Method: We included 39 patients with histologically verified MASLD without a history of cardiac disease and 11 healthy controls. All participants underwent contrast-enhanced CMR with T1 mapping and quantification of myocardial ECV. The patients were extensively characterized including non-invasive biomarkers of liver fibrosis: FibroScan, Fibrosis-4 index (FIB-4), Enhanced Liver Fibrosis Test (ELF), and Pro-C3.

Results: The FibroScan showed that 16 patients had advanced fibrosis with a median value of ≥ 12.5 kPa and that these patients had an increased myocardial ECV suggesting myocardial fibrosis (28% vs. 27% p = 0.031. Similar results were found for patients (n = 12) with increased ELF scores (29% vs. 26%, p = 0.036) and Pro-C3 (n = 11, 29% vs. 27%, p = 0.015). Patients with abnormal myocardial ECV, defined as ECV >27% had significant alterations in structural cardiac parameters including native T1 and T2 relaxation times (1216 vs. 1179, p=0.032 and 41 vs. 39 ms, p = 0.006) and functional parameters including increased end-diastolic volume (p = 0.034), and cardiac index (p = 0.010).

Conclusion: Myocardial ECV values and other structural and functional parameters may have prognostic implications that could be used for risk stratification in MASLD, and our findings suggest that CMR could be considered in the monitoring of patients and possibly in the assessment of pharmacological treatments.

Title: Intestinal Ultrasound Findings and Their Prognostic Value in Early Crohn's Disease – a Copenhagen IBD Cohort Study

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Summary

Aims:

This study aimed to characterize sonographic features of Crohn's disease at diagnosis and evaluate the prognostic value of intestinal ultrasound during the early Disease stage.

Methods

In a prospective, population-based cohort of newly diagnosed patients with Crohn's disease, patients were followed with intestinal ultrasound in conjunction with symptomatic, biochemical, and endoscopic evaluations.

Results

During the inclusion period (May 2021 – April 2023), 201 patients with adult-onset Crohn's disease were included. No associations were found between sonographic inflammation at diagnosis and diagnostic delay. The International Bowel Ultrasound Segmental Activity Score (IBUS-SAS) in the terminal ileum emerged as the best predictor of ileocecal resection during the first year, with an optimal threshold at 63 (AUC 0.92, sensitivity 100%, specificity 73%). After three months, transmural remission was achieved in 38% of patients, with colonic disease patients achieving transmural remission more often. Achieving transmural remission at three months was significantly associated with symptomatic remission at three months and all subsequent follow-ups within the first year. Transmural remission was also associated with a lower risk for treatment escalation during follow-up until 12 months (26% vs. 53%, p=0.003). At 12 months, 41% achieved transmural remission. Baseline Body Mass Index (BMI) negatively

impacted the likelihood of 12-months transmural remission significantly (overweight: [OR 0.34 (0.12;0.94)], obesity: [OR 0.16 (0.04;0.73)]).

Conclusions

Intestinal ultrasound findings at diagnosis predict ileocecal transmural remission is an achievable outcome target for many newly diagnosed Crohn's disease patients and has a favorable clinical outcome.

Protein-based oral rehydration solutions for patients with an ileostomy: a randomised, double-blinded crossover study

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Aim Patients with an ileostomy are at increased risk of dehydration and sodium depletion. We aimed to investigate if protein type or protein hydrolysation affects absorption from iso-osmolar oral rehydration solutions (ORS) in patients with an ileostomy.

Methods This was a randomised, double-blinded, active comparator-controlled 3x3 crossover intervention study. We developed three ORS with whey protein isolate, caseinate or whey protein hydrolysate. The ORS contained 40-48 g protein/L, 34-45 mmol sodium/L and had an osmolality of 248-270 mOsm/kg. The patients ingested 500 mL/d during three 4-week periods with a >2-week washout. The primary outcome was wet-weight ileostomy output.

Results Thirteen patients were included in the analyses. Wet-weight ileostomy output did not change and there was no difference between interventions (p=0.38). A series of statistically significant improvements was observed following intake of whey isolate ORS, including decreased faecal losses of energy (-365 kJ/d, 95% confidence interval (CI), -643 to -87, p=0.012), magnesium (-4.0 mmol/L, 95%CI, -7.4 to -0.7, p=0.020), plasma aldosterone (-4,674 pmol/L 95%CI, -8,536 to -812, p=0.019), and eGFR (2.8 mL/min/1.73m^2, 95%CI, 0.3 to 5.4, p=0.03).

Conclusion Ingestion of 500 mL/d of three protein-based iso-osmolar solutions resulted in unchanged and comparable ileostomy outputs in patients with an ileostomy. Following whey isolate ORS, we observed discrete improvements in a series of absorption proxies in both faeces and blood. The protein-based ORS were safe and well-tolerated. Future studies are warranted to explore if different compositions or doses of protein-based ORS can improve absorption in patients with an ileostomy.

ClinicalTrials.gov study identifier: NCT04141826.

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[^{64}Cu]-Methanobactin (SB2) biodistribution and excretion examined in pigs by whole-body PET/CT – pharmacokinetics of a potential new treatment for Wilson disease

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Introduction: Wilson disease (WD) is an inherited disorder caused by malfunction of the copper-transporting protein ATP7B, essential for hepatic copper clearance. Methanobactins (MB), copper-chelating peptides, demonstrate potential in removing hepatic copper in WD animal models. MB exhibits exceptional copper affinity, which makes it suitable for characterizing ^{64}Cu-labeled MB's (^{64}Cu-MB) pharmacokinetic profile. We investigated the biodistribution and excretion of ^{64}Cu-MB in pigs.

Methods: Seven pigs were administered 50 MBq i.v. ^{64}Cu-MB (10 mg MB-SB2) and five pigs received 50 MBq $^{64}CuCl_2$. A 90-minute whole-body PET/CT was conducted after injection of ^{64}Cu-MB or $^{64}CuCl_2$. Time activity curves (TAC) were obtained by placing volumes of interest in the liver. Two of the ^{64}Cu-MB pigs were pre-equipped with surgically implanted flow probes on the hepatic arteries and portal vein and catheters placed in the portal- and liver vein to calculate ^{64}Cu-MB's hepatic extraction fraction.

Results: ^{64}Cu-MB-PET-scans demonstrated rapid hepatic excretion into the gallbladder and intestines, with the liver TAC showed a rapid increase to a standardized uptake value (SUV) of 11.38 ± 1.65 within 10 minutes, followed by a 72% reduction in SUV. Conversely, the PET-scans of the $^{64}CuCl_2$ pigs showed hepatic accumulation of $^{64}CuCl_2$ with minor excretion, with the liver TAC displayed a gradual rise, reaching a plateau with an average SUV of 9.34 ± 1.42 after 90 minutes. ^{64}Cu-MB was also excreted by the kidneys to the urinary bladder, whereas the $^{64}CuCl_2$ accumulated in the renal parenchyma. There was no notable biodistribution of ^{64}Cu-MB in other organs. After initial distribution, MB's hepatic extraction fraction was ~25% after 2 minutes.

Conclusion: ^{64}Cu-MB is excreted rapidly through the liver and kidneys, exhibiting a faster elimination rate than $^{64}CuCl_2$. This suggests an alternate hepatic elimination pathway distinct from the ATP7B-mediated mechanism. The lack of ^{64}Cu-MB accumulation in other organs reinforces that MB's primary pharmacological action is in the liver.

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Systematic assessment of primary sclerosing cholangitis using magnetic resonance cholangiopancreatography in newly diagnosed inflammatory bowel disease – a prospective population based inception cohort study

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Aims

To determine the occurrence of primary sclerosing cholangitis (PSC) in patients with incident inflammatory bowel diseases (IBD).

Methods

Between 2021 and 2023, all adult patients with incident IBD within a catchment area covering 20% of Denmark were invited for magnetic resonance cholangiopancreatography (MRCP) and hepatobiliary blood tests at IBD diagnosis. Cox proportional hazard analyses were adjusted for age, gender, smoking, and disease phenotype (aHR, 95% confidence interval).

Results

In total, 242 (74.2%) and 147 (73.1%) patients with ulcerative colitis (UC) and Crohn's disease (CD) underwent MRCP within a median of 2.4 months (interquartile range (IQR) 1.3-4.9) of IBD diagnosis. PSC-like lesions were detected in 33 patients (8.5%), including 17 (7.0%) and 16 (10.9%, p=NS) with UC and CD, respectively. Of those, 19 patients (4.9%) had definite PSC, including 11 (4.5%) with UC and 8 (5.4%, p=NS) with CD. No difference in PSC or PSC-like lesions was found according to CD phenotype; however, extensive UC (62.5% vs. 27.1%, p=0.04) and male gender (87.5% vs. 44.9%, p=0.03) were more prevalent in PSC.

Abnormal hepatobiliary biochemistry was more common in PSC (47.4%) or PSC-like lesions (57.1%) compared to those with normal MRCP (15.7%, p<0.01). Receiver operating characteristic analysis identified ALT≥25 U/L and ALP≥117 U/L to predict PSC best (accuracy and sensitivity: 0.65, specificity: 0.63).

During 2.1 years (IQR 1.6-2.6), PSC and PSC-like lesions were independently associated with increased risk of intestinal resections (aHR 5.69, 1.13-28.54), biologics (aHR 2.00, 1.04-3.86), hospitalizations (aHR 2.70, 1.02-7.12), and systemic steroids (aHR 2.45, 1.02-5.89) in CD but not in UC. No PSC complications were observed.

Conclusions

A considerable proportion with incident IBD had undetected PSC or PSC-like lesions, despite normal hepatobiliary biochemistry in half of these cases. The outcomes impacted the IBD course negatively, highlighting the importance of systematic screening.

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Avoidant/Restrictive food intake disorder (ARFID); En ny type af spiseforstyrrelse associeret til 'Disorders of gut-brain interaction' (DGBI).
Erfaringer fra en bio-psykosocial behandlingstilgang

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Formål
ARFID er en ny type spiseforstyrrelse[1], karakteriseret ved restriktiv spisning grundet bekymring for symptomer, førende til underernæring og /eller nedsat funktionsniveau. I denne case-serie beskrives forekomst og præsentation af patienter med ARFID ved DGBI, samt behandlingsmuligheder og effekt.

Materiale og metoder
LRK har varetaget ambulant funktion i bio-psykosocial udredning og behandling af DGBI fra 1.3.22-30.6.24.
Ved en bio-psykosocial anamnese afdækkes psykologiske og sociale faktorer. Behandlingen omfatter medicin, psykoedukation i DGBI, kognitiv adfærdsterapi (KAT) og henvisning til psykiatrien hvis relevant.
I KAT tages udgangspunkt i samspillet mellem symptomer, tanker, adfærd og følelser. I behandlingen af ARFID er behandlingsfokus eksponering for at spise mindre restriktivt [2].

Resultater
Af 25 patienter i ambulant forløb, havde syv ARFID og præsenterede sig således (*Køn; alder; diagnoser/symptomer; behandling; effekt*):

- Mand; 32 år; IBS, træthed, skizotypi; ønsker ikke bio-psykosocial behandling. Startes duloxetin, udtrapper selv; uforandret tilstand.
- Mand; 26 år; funktionelle mavesmerter, a. mesenterica superior syndrom, skizotypi, angst, vægttab, sondeernæring; psykoedukation, støtte til normalisering af spisemønster, amitriptyllin, henvisning psykiatri (risperidon og sertralin); normalt spisemønster, vægtøgning 15 kg, sjældent anfald af mavesmerter.
- Kvinde; 42 år; IBS, emetofobi, undervægtig, behov for proteindrik; psykoedukation, KAT, henvist til psykiatri (ikke overskud til behandling); symptomer uforandret, afklaret med diagnose.
- Mand; 32 år; pouchitis, socialfobi, undervægtig; psykoedukation, henvist til psykiatrien (sertralin); afventer effekt
- Mand; 57 år; IBS, vægttab, træthed; KAT; spiser varieret, 8 kg vægtøgning, symptomfri.
- Kvinde; 21 år; IBS, funktionel dyspepsi, funktionelle opkastninger, opmærksomhedsforstyrrelse, helbredsangst, vitamin/mineral mangel; KAT; mindre restriktiv spisning, bedring i symptomer, accept af funktionel diagnose.
- Mand; 19 år; synkebesvær, panikangst, undervægtigt, sondeernæring; KAT, henvisning til psykiatri (sertralin, gruppe- og individuel- terapi); spisemønster normaliseret, 18 kg vægtøgning, minimale symptomer, genoptager studieliv.

Konklusion

ARFID forekommer hos patienter med DGBI og kan forekomme i samspil med psykisk sygdom. ARFID kan behandles med KAT, medicin og henvisning til behandling af psykiatrisk komorbiditet.

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Referencer:
1: https://icd.who.int/browse/2024-01/mms/en#1242188600
2: Murray et al, International Journal of Eating Disorders, 2023;56:616-27

Diagnostics and insight in autoimmune hepatitis enabled by mass-spectrometry based proteomics

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Objectives

Autoimmune hepatitis (AIH) is a rare, chronic, life-threatening liver disease difficult to diagnose as no accurate biomarker exists; even histological assessment of liver tissue may not provide the diagnosis. Here, we performed mass-spectrometry based proteomic analyses of paired liver-plasma samples in patients with AIH to uncover potential new biomarkers.

Materials and methods

We recruited 19 newly diagnosed patients with AIH and 19 controls from our prospective cohort study FALL (NCT05335603). Snap frozen liver tissue and plasma were collected. Mass-spectrometry based tissue and plasma proteomics were performed using PASEF-DIA on Bruker TIMSTOF instrument. Differential abundance analysis was performed with the Limma package. A protein was considered differentially abundant if a false discovery rate adjusted p-value by Benjamini-Hochberg was < 0.05.

Results

A total of 7,116 liver proteins and 556 plasma proteins were detected, herein 329 proteins present both in liver and plasma. There were 2,589 and 227 differentially abundant proteins in liver and plasma, respectively, 58 of these proteins present in both liver and plasma. Among the latter, proteins involved in cell adhesion/activation (MSN, ICAM1, CDH1, HBB, PDLIM1, LBP, B2M), fibroblast migration (PDLIM1), glucose (ALDOB, PCK2, ENO1) and lipid (PCK2, LCAT, APOF) metabolism were identified.

Conclusions

Mass-spectrometry based proteomic analyses of paired liver-plasma samples in AIH patients enabled discovery of numerous potential novel biomarker candidates. If validated in an external cohort, proteomics may be a useful technology to identify AIH.

Optimised dosing of encapsulated faecal microbiota transplantation for *C. difficile*: a quality improvement study

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Introduction: Faecal Microbiota Transplantation (FMT) is highly effective for *Clostridioides difficile* infection (CDI), but real-world effectiveness data to guide treatment algorithms is lacking. At our centre, the effectiveness of a single capsule FMT treatment was lower than in randomised trials. We aimed to increase FMT effectiveness by introducing an optimised capsule FMT dosing regimen in a real-world clinical setting.

Methods: This multi-site Danish quality improvement study included patients with CDI treated with capsule-based FMT. Recruitment began on June 24, 2019, and is ongoing. Initially, in 2019, one-dose capsule FMT was the standard treatment. In January 2021, capsule FMT production was upscaled, allowing more patients at regional FMT sites to receive treatment. In November 2022, two-dose capsule FMT was introduced as the standard treatment at Aarhus University Hospital.

This regimen was recommended at all FMT sites starting in February 2024. The primary outcome was cure of *C. difficile*-associated diarrhea (CDAD) at week 8, evaluated using statistical process control percentage charts.

Results: Preliminary data are presented. By the end of 2023, 1,009 patients had received 1,470 FMT treatments, with 618 treatments performed at Aarhus University Hospital. Before 2021, the mean cure rate at Aarhus was 66% (95% CI: 61-72%). From 2021 to October 2022, it dropped to 55% (95% CI: 48-61%). After introducing two-dose capsule FMT, the mean cure rate increased to 71% (95% CI 61-79%). At the other FMT sites, the mean cure rate from 2019 to 2023 was 55% (95% CI: 52-59%).

Conclusion: Introducing a two-dose capsule FMT dosing regimen as routine treatment in a FMT system may increase cure rates.

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"Unveiling Socioeconomic Disparities on Liver Disease: A Comparative Study of ALD, MASLD, and MetALD Patients"

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Background and Aims

Steatotic Liver Disease (SLD) is a significant public health issue, influenced by socioeconomic factors that affect disease progression. We aimed to describe socioeconomic disparities across Metabolic DysfunctionAssociated Steatotic Liver Disease (MASLD), MASLD with moderate-high alcohol consumption (MetALD), and Alcohol-related Liver Disease (ALD), and explore the impact of these disparities on liver fibrosis within these SLD subgroups.

Methods

We screened individuals from the general population and those at-risk using controlled attenuation parameter (CAP≥248dB/m) and transient elastography TE (significant fibrosis: TE≥8kPa; advanced fibrosis: TE≥12kPa). We classified participants by the nomenclature. Socioeconomic status was assessed through standardized questionnaires. To explore associations with socioeconomic factors, we compared MASLD, MetALD, and ALD against a non-SLD group.

Results

We screened 6444 individuals, median age 57 (IQR 52-63), 52% female. The distribution of non-SLD/MASLD/MetALD/ALD was 38%/46.0%/10.3%/5.6%. ALD patients more often had an income <40,000€ (55%), compared to non-SLD (34%), MASLD (38%), and MetALD (34%) (p<0.005). ALD patients were more often unemployed (56%), compared to non-SLD (32%), MASLD (35%), and MetALD (44%) (p<0.005). ALD patients also more often lived alone (34%), compared to non-SLD (23%), MASLD (22%), and MetALD (21%) (p<0.005). Of MetALD patients, 19% had a higher education level, compared to non-SLD (15%), MASLD (10%), and ALD (14%).

When adjusting for risk factors, the risk of TE≥8 was greater for men (OR 2.3; 95%CI 1.8-3.0), individuals with a low income (OR 2.0; 95%CI 1.3-3.1), and those living alone (OR 1.3; 95%CI 1.1-1.8), with increasing odds for TE≥12. This indicates that females, higher income, and cohabitation are associated with a lower risk of severe liver fibrosis.

Conclusion

Individuals with ALD are more likely to have lower income, be unemployed, and live alone. Those with MetALD have higher educational levels. Female gender, higher income, and cohabitation are associated with a lower risk of liver fibrosis.

Værdien af røntgen af thorax som screening for tuberkulose forud for biologisk behandling af inflammatorisk tarmsygdom

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Formål:

Det anbefales i DSGH's guideline, at der forud for start på biologisk behandling af patienter med inflammatorisk tarmsygdom (IBD) foretages blodprøve screening for tuberkulose (TB), hepatitis B og HIV, samt at der tages røntgen af thorax. Formålet med denne undersøgelse var at vurdere værdien af denne røntgen screening.

Metode:

Alle patienter på Afdeling for Medicinske Mave- og Tarmsygdomme, Aalborg Universitetshospital, der i perioden 1.1.2019-31.12.2023 fik foretaget screening forud for biologisk behandling blev identificeret, dels ud fra databasen GastroBio, og dels ud fra en gennemgang af patienter, der i samme periode havde fået foretaget en HIV-test. Ved journalgennemgang af disse patienter noteres resultater af røntgen thorax, IGRA-test (Quantiferon test), hepatitis B og HIV-screening, samt om patienten er behandlet for TB.

Resultater:

I alt 829 patienter med IBD blev screenet i perioden. Der fandtes 15 IGRA positive patienter, som alle startede antituberkuløs behandling. Kun en af disse havde forandringer på en CT fortaget før, men vedkommende var allerede i udredning ved lungemedicinerne inden screeningen og blev ikke opstartet i biologisk terapi grundet aktiv TB. 13 andre patienter havde forandringer på røntgen, der kunne være tegn på TB, men alle disse afkræftes ved yderligere billeddiagnostik og testning. Ingen af patienterne fandtes positive for hepatitis B, mens 1 patient havde positiv HIV-test, og IBD diagnosen blev på grund af fundet revideret hos denne patient.

Konklusion:

Denne undersøgelse tyder ikke på, at røntgen thorax bidrager med yderligere sikkerhed i diagnostikken ved screening for TB i forhold til IGRA-testen forud for biologisk behandling, og det må derfor overvejes, om denne undersøgelse kan udelades i screeningsprogrammet fremover.

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DSGH'S ÅRSMØDE 2024

E P O S T E R

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Abstract – DSGH 2024

Title:

Early experience of GLP-1 receptor agonist treatment in liver transplant recipients in Denmark

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Background:

Liver transplant (LT) recipients have a high burden of metabolic diseases such as post-transplant diabetes, dyslipidaemia, hypertension, and obesity. Furthermore, steatotic liver disease is found in approximately 30% of post-transplant liver biopsies. Treatment with glucagon-like peptide-1 receptor agonists (GLP-1ra) induces weight loss, reduction in HbA1c and has beneficial effects on steatotic liver disease too. However, little is known about GLP-1ra usage in LT recipients. We aimed to characterize the safety and efficacy of treatment with semaglutide in this patient population.

Methods:

We conducted a retrospective study and collected information from patient records on LT recipients in our outpatient clinic treated with semaglutide for at least 12 months. We registered the indication for semaglutide, dose and duration of treatment. As measures of efficacy, we registered body weight, haemoglobin A1c, ALT at baseline and after 12 months. We looked for liver biopsy results before and after 12 months of semaglutide treatment. As measures of safety, we registered all unplanned hospital admissions after initiation of semaglutide therapy and changes in whole blood trough concentration of

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Comprehensive genetic testing of Wilson Disease patients with only 0 or 1 known pathogenic *ATP7B*-variant.

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Background

Wilson Disease (WD) is known as a monogenic autosomal recessive disorder caused by variants in *ATP7B*. However, up to 25% of clinically diagnosed WD patients lack identifiable causal variants in *ATP7B*. This study aimed to genetically characterize WD patients with zero or one known variant using state of the art genetic testing.

Methods

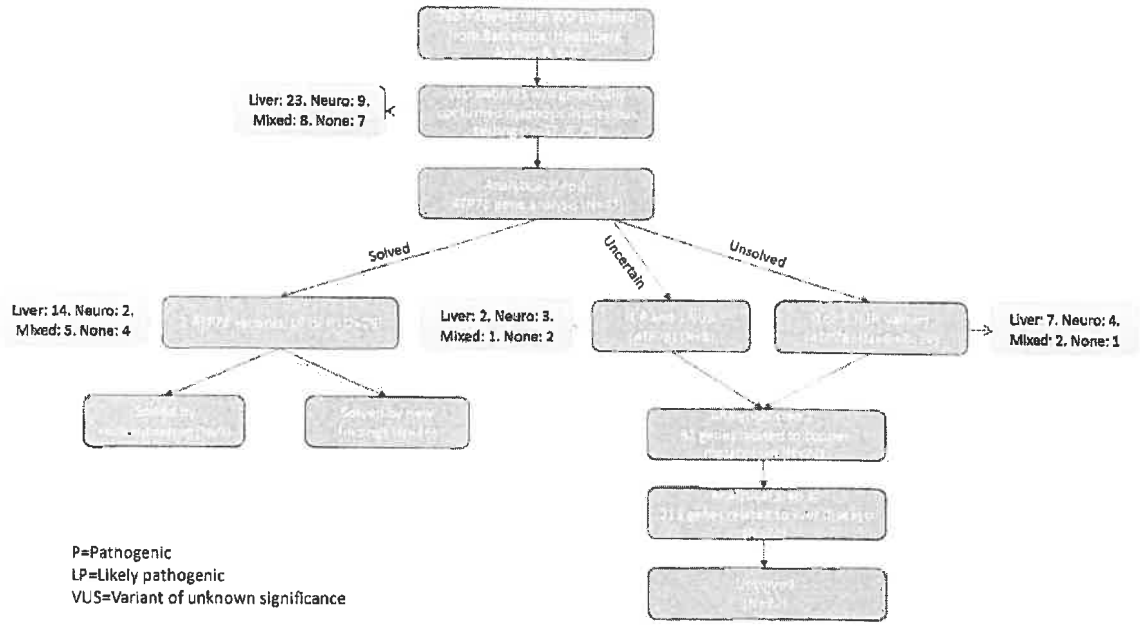
764 patients were screened for *ATP7B* variants in four different cohorts of patients with WD. A total of 47 patients with a clinical diagnosis of WD but with zero or one known *ATP7B* variant were included in this study. Whole Genome Sequencing (WGS) was performed, and results analyzed following a sequential diagnostic approach: Analysis for casual variants in (1) *ATP7B*; (2) in 82 copper-related genes; and (3) in 213 genes associated with liver diseases (Fig 1).

Results

6.2% (47 of 764) of the combined cohort had only 0 or 1 known variants in *ATP7B*. Of these, 24 (51%) were males. The median age at diagnosis was 20 years (range 0-68), with a median Leipzig score of 6 (range 1-11) before genetic testing. At diagnosis, 23 patients had liver-associated phenotypes, 9 had primary neurological phenotypes, 8 had mixed phenotypes, and 7 were asymptomatic. Analysis of *ATP7B* resolved 25 cases: 9 through reclassification of previously reported findings, and 16 were solved by identification of previously unreported *ATP7B*-variants. Interestingly, in 8 cases we identified one variant of uncertain significance (VUS) alongside one (likely) pathogenic *ATP7B* variant. Among the still unresolved cases, 8 had one pathogenic *ATP7B* variant and 6 had none. Comprehensive screening for causal variants in other genes of interest did not identify any alternative genetic causes.

Conclusion

Our findings suggest that reevaluation of *ATP7B* VUS is crucial when previous sequencing results are inconclusive. Resequencing methods capable of detecting structural and intronic *ATP7B* variants are recommended.


Liver: 23. Neuro: 9.
Mixed: 8. None: 7
Solved
Uncertain
Unsolved
Liver: 14. Neuro: 2.
Mixed: 5. None: 4
Liver: 2. Neuro: 3.
Mixed: 1. None: 2
Liver: 7. Neuro: 4.
Mixed: 2. None: 1
P=Pathogenic
LP=Likely pathogenic
VUS=Variant of unknown significance

tacrolimus as well as changes in the daily dosage hereof. Paired T-tests were used for statistical comparison before and after treatment.

Results:

We identified 13 patients that were treated with semaglutide with a mean age of 57 years (range 49-65). The indications were type-2 diabetes in five patients, obesity in three cases and in five recipients a combination of diabetes and obesity. Body weight (mean change -7.3 kg), hemoglobin A1c (-6.5 mmol/mol) and ALT (-15.7 U/L) were significantly lower after 12 months. In all patients we identified a historical liver biopsy taken prior to initiation of treatment, and in six biopsies steatotic liver disease was histologically confirmed. Three patients had a liver biopsy taken after at least 12 months of semaglutide treatment and in those no significant improvement in MAFLD histology scores was seen. We identified two unplanned admissions in two patients, which were unlikely to be related to semaglutide. There was no significant change in the ratio of tacrolimus concentration and daily dose over time.

Conclusion:

In this study, semaglutide safely and significantly reduced body weight, hemoglobin A1c and ALT in LT recipients. This observation calls for larger prospective studies investigating the benefit of GLP-1ra treatment in LT recipients with metabolic diseases, including steatotic liver disease.

Seks år efter kortvarigt intensivt styrketræningsforløb for patienter med cirrose ses fortsat kliniske fordele – en opfølgning efter et randomiseret klinisk forsøg

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Formål: Træning forbedrer den generelle sundhedstilstand ved en række kroniske sygdomme. Vi har tidligere vist, at når patienter med kompenseret cirrose deltager i et intensivt 12-ugers styrketræningsforløb, øges tiden til første akutte indlæggelse samt overlevelsen. Det gjaldt i op til 3 år efter deltagelse i forsøget; vi har nu fulgt op efter 6 år.
Materiale og metode: 39 deltagere med cirrose Child-Pugh A/B blev randomiseret til enten 12 ugers superviseret holdstyrketræning eller til en fortsat inaktiv livsstil. Der var ingen intervention efter studiet. Datoen for den første akutte hospitalsindlæggelse samt eventuel død blev uanset årsagen registreret fra randomisering og 6 år frem.

Fine and Gray-regression blev anvendt til at analysere risikoen for akut indlæggelse med død som competing risk og overlevelse blev estimeret ved Cox-regression. Analyserne fulgte intention-to-treat-princippet og blev justeret for Child-Pugh, alder, køn og komorbiditet (CirCom) ved randomisering.
Resultat: I løbet af 6 år blev 15 ud af 20 fra træningsgruppen og 18 ud af 19 fra kontrolgruppen indlagt akut minimum én gang. Risikoen for første akutte indlæggelse var efter 6 år lavere i træningsgruppen end kontrolgruppen: adjusted subdistribution hazard ratio: 0.46 (95% CI: 0.24-0.90) p = 0.02.

I alt døde 17 deltagere i løbet af de 6 år (7 fra træningsgruppen og 10 fra kontrolgruppen). Efter 6 år sås ikke længere en signifikant forskel i overlevelsen til fordel for træningsgruppen: adjusted hazard ratio 0,37 (95% CI: 0.12-1.09) p = 0.07.
Konklusion: 6 år efter et intensivt 12-ugers styrketræningsforløb for patienter med cirrose ses stadig en nedsat risiko for første akutte indlæggelse. Risikoen for død er nedsat, men ikke længere signifikant.
Hvilke mekanismer, der skaber denne langvarige kliniske virkning, er dog fortsat uafklaret. Et mindre tab af muskelmasse samt livsstilsændringer skønnes at være sandsynlige medspillere, men yderligere forsøg kræves for at belyse dette.

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ABSTRACT DSGH ÅRSMØDE 2024

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Beyond Diagnosis: Investigating Hospital Referral Impact on Biological Treatment Initiation, Hospital Admission, and Surgery Patterns in Inflammatory Bowel Disease – a Danish Population Based Study

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Objectives: Early biological treatment in patients with inflammatory bowel disease (IBD) is important in disease control. Previous studies have suggested that patients with IBD from Non-Academic Hospitals were less likely to receive biologics. The aims of this study were 1) to use the granular data in the clinical database, GASTROBIO, to study detailed differences in time from IBD diagnosis to first administration of biological therapy, hospital admission, and surgery in patients referred to Academic Hospitals versus to Non-Academic Hospitals, and 2) to explore differences in disease extent, behaviour, and indication for biological treatment.

Material and methods: This was a retrospective cross-sectional population-based study of patients with IBD initiating biologic treatment in the North Denmark Region between 2016-2018. Data from GASTROBIO were extracted, namely demography, time of diagnosis, biological treatments with indications, hospital admission, and surgery.

Results: Of the 146 patients included, 84 were from the Academic and 62 from the Non-Academic Hospitals. No significant differences in median time from diagnosis to 1) treatment, 2) hospital admission or 3) IBD surgery between the groups were observed. A higher percentage of patients with luminal Crohn's disease were treated with biologics at the Academic Hospital (78% and 66%).

Conclusions: Based on the findings of this population-based study, we found no evidence to suggest that the referral area had a significant impact on the duration from diagnosis to the initiation of biological treatment, hospital admissions, or surgery. However, the data suggested that fewer patients with luminal Crohn's disease were referred to biologics from Non-Academic Hospitals.

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TITLE
Treatment of primary biliary cholangitis patients with obeticholic acid: patterns of medicine dosing and delivery differ between UK hospitals

GOALS
Prior UK real-world studies of treatment of PBC with obeticholic acid (OCA) identified significant associations between dose titration history and discontinuation rates. We sought to assess whether patient dosing patterns differ by UK hospital and region.

MATERIALS and METHODS
Using the Homecare database which records OCA order histories for UK PBC patients, key dosing aspects (titration, frequency, compliance, deliveries) were tested for clustering by hospital using individual Kruskal-Wallis tests. Multilevel modelling methods were used to assess potential influence of dosing on patient retention, with hospital as the grouping variable. Hierarchical cluster analysis generated groupings agnostic to hospital – these were compared to actual hospital locations and UK regions using Chi-squared analyses.

RESULTS
We found marked differences between hospitals in all dosing aspects, which were each statistically significant. In the multilevel model, dose titration to 10mg had a significant impact on retention (HR=0.16, $p<0.001$) and hospital groupings improved model fit compared to a simple fixed-effects model (LR test $\chi^2=14.1$, $p<0.001$). Agnostic cluster analysis revealed groupings which aligned with some individual hospitals, although not perfectly.

CONCLUSION
Findings involving patient retention must be interpreted with caution, particularly from a commercial order database carrying no clinical information or context. Prior analyses have concluded that the factors most impacting patient retention on obeticholic acid are likely proxies for good patient management rather than directly impactful clinical parameters in their own right. However, we have shown that there is undoubtedly a distinct difference between the patterns of dosing we observe between some UK centres, and this may serve as an important discussion point between centres when sharing best practice.

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Tokyo Guidelines' performance in predicting acute cholangitis among Emergency Department patients

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Purpose: Acute cholangitis (AC) is a disease with a high mortality rate even among treated patients. Therefore, it is important to start the right treatment quickly to improve prognosis. This study investigated the discriminatory ability of Tokyo Guidelines 2018 (TG18) regarding presence of inflammation and affected liver parameters as a guide to proceed with imaging diagnostics to diagnose AC among emergency department (ED) patients.
Materials and methods: This study was a register-based, multicenter, cohort study of adult ED patient visits in the region of Southern Denmark. The cohort included patient visits collected from seven EDs between January 1, 2016, and March 20, 2018. Identified inflammation (fewer and/or increased CRP and/or abnormal leucocytes) and affected liver parameters (at least one) was used as the diagnostic exposure, and a hospital discharge diagnosis of acute cholangitis was used as gold standard.
We calculated the sensitivity, specificity, the positive likelihood ratio (LR+), and negative likelihood ratio (LR-) to examine the diagnostic accuracy of TG18.
Main results: We included 202,881 ED patient visits. The study found 19,816 patient visits, which fulfilled TG18 A and B criteria. A total of 440 (2.22%) patient visits had a discharge diagnosis compatible with AC. The TG18 criteria A and B had a sensitivity of 85.1%, specificity of 90.4%. The positive likelihood ratio was 8.9. The negative likelihood ratio was 0.16. The 30-day mortality for patients with AC was 15%.
Conclusion: TG18 A and B criteria had a high diagnostic accuracy among adult ED patients, which makes it relevant to use in the ED as guidance for further imaging diagnostic to confirm a diagnosis of AC. The high negative diagnostic value provides a safe rule out strategy regarding a diagnosis of AC.

Mind the Liver: Diagnostic and prognostic biomarkers in hepatic encephalopathy — presentation of an ongoing study

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Aim

The West have Criteria and psychometric testing is used in the diagnosis and grading of hepatic encephalopathy (HE). However, accurate diagnosis and monitoring can be difficult because HE is often intertwined with other cerebral disturbances, psychometric testing is relatively unspecific, and the West Haven criteria are subject to interobserver variation. The longstanding marker, venous ammonia, only has clinical value as a confirmatory test in patients with HE grades 3 and 4. Discovering and validating new and more accurate HE biomarkers would be of great value for clinical and study purposes, which is the aim of this study.

Design

The study is prospective and non-randomized and will include 150 patients with liver cirrhosis (50 patients with normal cognition, 70 patients with minimal HE, and 30 patients with HE grades 1 and 2) and 100 healthy controls. Participants will undergo a state-of-the-art workup at baseline, and will be followed for five years regarding hepatic encephalopathy and other adverse events. Patients with minimal HE will be treated according to guidelines.

Methods

The study visits include a clinical examination, portosystemic hepatic encephalopathy score (PHES), continuous reaction time (CRT), animal naming test (ANT), baseline portosystemic shunt measurement, and brain MRI. The following will also be obtained and correlated to cognition and to the development of hepatic encephalopathy:

Biobanking of cerebrospinal fluid and plasma— measurement of inflammatory and neuroaxonal damage markers in all, and untargeted metabolomics and proteomics in a subgroup.

EEG and CRT— simultaneous EEG and CRT will be performed in 60 patients to explore if the CRT measures can be optimised to achieve better HE specificity.

Results

So far, 100 participants have been included, and we have achieved funding and collaborators to succeed with the study aims.

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Title: The changes in alcohol drinking pattern after a diagnosis of alcohol-related liver disease: a clinical cohort study

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Aims: Alcohol use is the key driver of the progression of alcohol-related liver disease (ALD). We aimed to describe the changes in alcohol consumption up to and after an ALD diagnosis.

Materials & method: From July 2021-Dec 2023, we recruited patients with newly diagnosed ALD at Zealand University Hospital Koege. At baseline, we interviewed patients about alcohol use during life, current use, motivation to reduce alcohol use, and uptake of any treatment for alcohol use disorder (AUD). We measured the alcohol biomarker phosphatidylethanol. We followed patients for alcohol use for 3 months after baseline. We examined the use of alcohol on subgroups of sex and age.

Results: We included 80 patients with newly diagnosed ALD, of whom 70% had cirrhosis. The median age was 64 years, and 62 (78%) patients were men. The patients reported increasing use of alcohol from 30 years before until diagnosed with ALD. After the ALD diagnosis, 59% reported being abstinent and drinking patients reported a reduction in alcohol use from 35 drinks per week (IQR, 15-70) to 21 drinks per week (IQR, 14-49). However, the alcohol biomarker indicated that at least 58% were actively consuming alcohol after an ALD diagnosis. Of all, 65% expressed the highest motivation to reduce alcohol use at baseline, and 24% of patients reported receiving AUD treatment. After 90 days of follow-up, the reported use decreased further to a median of 14 drinks per week (IQR, 7-35), but concurrently, 41% (95%CI 29-58) of abstaining patients relapsed. Younger patients had higher alcohol intake up to ALD diagnosis and the lowest reduction in alcohol consumption after the ALD diagnosis compared to older patients.

Conclusion: Alcohol consumption increases before a patient is diagnosed with ALD, but around half succeed in stopping after that. Unfortunately, early relapse is common.

Word count: 294
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Association between quality of life and markers of inflammation and fibrosis in patients with primary biliary cholangitis during three-year follow-up

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Purpose: Patients with primary biliary cholangitis (PBC) consistently report low quality of life (QoL), but determinants of decreased QoL remain unexplored. We aimed to investigate the role of inflammation, fibrosis, and response to pharmacological treatment on QoL in a prospective PBC cohort.

Materials and Methods: We followed a cohort (n=130) of PBC patients for 3 years. Yearly visits included liver enzymes, transient elastography (TE), inflammation markers, sCD163, and two QoL questionnaires (PBC-40 and SF-36).

Results: Although the median QoL was not decreased, QoL was decreased in SF-36 Mental Component Summary (MCS)= 32% (CI95%: 24%-40%) and Physical Component Summary (PCS) 33% (CI95%:25%-42%) of patients. Fatigue, reported by 87%, was responsible for the largest symptom burden. QoL in patients with cirrhosis, not fibrosis, was decreased. We found weak and insignificant correlations between sCD163 and QoL. However, in UDCA non-responders, delta values from baseline to three years yielded a significant correlation between sCD163 and QoL where increasing sCD163 correlated with both decreasing QoL (ΔPCS and ΔsCD163 of Rho = 0.50, ($p<0.001$)), and increasing symptom burden in five of six PBC-40 domains.

Conclusion: In patients with PBC followed for 3 years we found that 30% of patients with PBC have impaired QoL with fatigue as the most severe symptom. Patients with cirrhosis exhibited worse QoL. Intraindividual 3-year changes in sCD163 and QoL correlated with changes in both PCS and five out of six PBC-40 domains. These findings suggest that that liver inflammation per se plays a role in the QoL of patients with PBC.

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Titel:
Orismilast for the Treatment of Moderate to Severe Ulcerative Colitis

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Purpose:
Ulcerative colitis (UC) is a chronic inflammatory bowel disease. Existing medications aim to induce and maintain remission, yet 30-55% of UC patients remain refractory in the induction phase, underscoring an unmet need for novel treatments (Zhao et al., 2022). Orismilast, a PDE4 inhibitor, is currently in development for the oral treatment of several dermatological diseases. PDE4 receptors have also been shown to be upregulated in UC. This study (UCORIS study) aimed to investigate orismilast as an oral treatment option in UC to guide future studies. Herein, we present the initial results.

Materials and methods:
This is an ongoing phase 2, open-label, single-arm exploratory clinical study assessing the efficacy and safety of orismilast in patients with moderate to severe UC. Patients with a UC diagnosis currently on stable 5-ASA treatment and experiencing a flare (defined as a MAYO endoscopic subscore of 2 or 3) were eligible for inclusion. Orismilast were administered twice daily for 12 weeks. Responding patients could extend treatment to a total duration of 52 weeks. The primary endpoint was clinical remission based on the total Mayo score at week 12, defined as 2 points or lower with no individual sub-score above 1.

Results:
At present three patients have completed the first 12-week follow-up period. One patient reached the primary endpoint after 12 weeks of treatment and has continued treatment. Another patient achieved clinical and endoscopic remission but discontinued the treatment after 8 weeks due to an adverse event (headache). One patient discontinued after 6 weeks due to increased UC severity and a Norovirus infection. The most frequent adverse events were headache and nausea, consistent with previous studies.

Conclusion:
In conclusion, our preliminary data indicates that orismilast has a potential as treatment for UC, with one patient reaching the primary endpoint and another achieving total remission.

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Title: Intestinal Ultrasound as a Prognostic Tool in New Onset Ulcerative Colitis - a Copenhagen IBD Cohort Study

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Abstract

Aims:

This study aimed to assess the prognostic role of intestinal ultrasound (IUS) in determining the disease course of ulcerative colitis (UC) during the initial year post-diagnosis.

Methods

A prospective population-based inception cohort study was conducted on newly diagnosed patients with UC. Patients with left-sided or extensive UC underwent IUS assessments at diagnosis, three months, and 12 months, alongside symptomatic, biochemical, and endoscopic evaluations. Transmural remission was defined as bowel wall thickness ≤ 3 mm without color Doppler signal in all segments. Complete remission was defined as the absence of inflammation on any examination.

Results

From May 2021 to April 2023, 193 patients with left-sided or extensive UC were included. Inflammatory findings on IUS at diagnosis were significantly associated with symptomatic, biochemical, and endoscopic markers of inflammation but not with diagnostic delay. IUS-detected inflammation at diagnosis was an independent predictor for colectomy within the first three months, with bowel wall thickness > 6 mm as the optimal cut-off (OR 38, 95% CI 8-270, p<0.0001). At three months after diagnosis, 59% of patients achieved transmural remission, which was associated with higher rates of steroid-free clinical remission in all subsequent follow-ups alongside reduced need for steroids during follow-up (6% vs 19%, p=0.036).

Furthermore, transmural remission at three months increased the likelihood of steroid-free clinical remission as well as transmural and complete remission at 12 months.

Conclusions

Findings by intestinal ultrasound at time of diagnosis predict early colectomy risk in UC. Furthermore, our results underscore transmural remission as a feasible treatment target in early UC, significantly impacting the disease course.

TITEL:

Roux-en-Y Gastric Bypass improves liver steatosis and the plasma lipid profile more than Sleeve Gastrectomy: results from a 12-month follow-up study with paired liver biopsies and plasma lipidomics profiling.

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Aim

As Sleeve Gastrectomy (SG) has become the most frequently performed bariatric procedure in Denmark it is of interest to establish if SG offers the same improvement in metabolic dysfunction-associated steatotic liver disease (MASLD) as Roux-en-Y Gastric Bypass (RYGB). We aimed to investigate the effects of SG vs. RYGB on MASLD 12 months after bariatric surgery and extensively characterize the plasma lipid profile in response to surgery.

Material and methods

40 individuals (median age 44 years) with severe obesity undergoing bariatric surgery (RYGB: n=16, SG: n=24) at Hvidovre Hospital were included. Fasting blood samples were drawn immediately before surgery. Liver biopsies were collected at surgery and repeated 12 months after surgery. Liver histology was assessed using the NAFLD activity score (NAS) and Kleiner fibrosis score. Plasma was analyzed using a mass spectrometry-based lipidomics platform. Statistically significant lipids were determined using a mixed linear model.

Results

RYGB and SG patients were comparable at baseline. Mean (standard deviation, SD) NAS was 3.3 (0.9) in RYGB and 3.1 (1.4) in SG (p=0.560) with similar degrees of steatosis, inflammation and ballooning. Twelve months after surgery, NAS was significantly and comparably (p=0.241) reduced in both RYGB (-3.00 (95% CI -3.79 – -2.21), p<0.001) and SG (-2.25 (95% CI -2.92 – -1.59), p<0.001) patients but RYBG patients had a more noticeable reduction (p=0.007) in liver steatosis (-0.91 (95% CI -1.47 – -1.2) than SG patients (-0.33 (95% CI -0.54 – -0.13) and greater improvement in the plasma cholesterol profile. We observed decreases in all major lipid groups, but RYGB patients had more pronounced reductions in e.g., sphingolipids and phosphatidylcholine lipid groups 12 months after surgery.

Conclusion

Though RYGB and SG were equally good at improving MASLD, RYGB appeared to be superior in reducing liver steatosis which perhaps resulted in the greater improvement in the plasma lipid profile.

High Doses of Albumin are Associated with Increased Mortality and Complications in Patients with Cirrhosis Receiving Terlipressin: Insights from the ATTIRE Trial

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Background: The CONFIRM trial indicated potential harm with terlipressin in patients developing respiratory failure. The impact of concomitant albumin on terlipressin outcomes remains unclear. Using ATTIRE trial data, we compared the safety of serum targeted albumin infusions to standard-of-care in cirrhosis patients receiving terlipressin.

Methods & Materials: ATTIRE was a randomized controlled trial of albumin infusions in 777 patients hospitalized with cirrhosis and hypoalbuminemia (<30 g/L). Patients were randomized 1:1 to an active arm with serum targeted albumin infusions, aiming for a serum albumin ≥30 g/L, or the control arm with standard-of-care, where albumin was allowed per clinical guidelines. We studied mortality at day 15 and complications from trial SAE reporting. The primary outcome was a composite of 15-day complication-free survival (15-day mortality, respiratory failure, pulmonary edema and fluid overload).

Results: At baseline, 42 patients in the active arm and 41 in the control arm received terlipressin. Indications were variceal bleed (74%), hepatorenal syndrome (23%) and hypotension (3%). Patients in the active arm received more albumin compared to the control group (190g [140-260] vs. 0g [0-140], p<0.001). 15-day complication-free survival was lower in the active arm compared to the control (log-rank p=0.006). The difference persisted with the albumin intervention (aHR=5.63, 95% CI: 1.60-19.86, p=0.007), when controlling for baseline MELD (aHR=1.05, 95% CI: 1.02-1.08, p=0.002). Both mortality (active arm: 21% vs. control arm: 7%, p=0.068) and fluid-related complications (active arm: 19% vs. control arm: 5%, p=0.047) was driven the difference. Subgroup analysis for variceal bleed patients showed a markedly higher risk of the primary outcome in the active arm (n=6) compared to controls (n=0).

Conclusion: Serum targeted albumin infusions increase the risk of mortality and complications in patients with cirrhosis receiving terlipressin, independently of disease severity. Serum targeted albumin may be particular harmful in patients receving terlipressin for variceal bleed.

Incidence of osteoporosis and osteopenia in patients with newly diagnosed inflammatory bowel disease: a population-based inception cohort study

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Abstract

Aims

A high prevalence of osteoporosis has been reported among individuals with long-term Crohn's disease (CD) and ulcerative colitis (UC). We aimed to perform a population-based analysis determining bone mineral density (BMD) in UC and CD at diagnosis.

Materials and methods

All adult patients with incident UC or CD between May 2021 and May 2023 in an area covering 20% of the Danish population were invited for an assessment of BMD at the time of IBD diagnosis using dual-energy X-ray absorptiometry (DEXA).

Results

A total of 209 and 141 patients with UC and CD, respectively, were included in the study, constituting 67.9% and 70.1% of the overall population. Among postmenopausal women with UC, 15/42 (35.7%) had osteoporosis and 17/42 (40.5%) had osteopenia, while rates among CD patients were 6/21 (28.6%, p=0.57) and 8/21 (38.1%, p=0.86), respectively. Among elderly males (aged 50 years or above), the rates of osteoporosis and osteopenia were 5/38 (13.2%) and 17/38 (44.7%) in UC and (3/24 (12.5%, p=1.00) and 3/24 (12.5%, p=0.69)) in CD, respectively. Among premenopausal women with UC or CD, BMD below expected (Z-score of -2.0 or below) was found in 3/69 (4.3%) and 1/42 (2.4%, p=1.00), respectively, while the rates in young males were 3/60 (5.0%) and 8/54 (14.8%, p=0.11).

No significant differences in BMD or location of osteoporosis or osteopenia were observed according to IBD type or Montreal classification. Nutritional and inflammatory markers, including C-reactive protein, fecal calprotectin, Mayo Endoscopic Score, Simple Endoscopic Score for CD, or patient-reported outcome measures correlated significantly with the T-score.

Conclusions

In this population-based inception cohort, we found a large proportion of patients to have MBD at IBD diagnosis, specifically among males aged 50 years or above and postmenopausal women. The study highlights the importance of systematic MBD assessment in these patient groups with new-onset IBD.

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Title: Standardized Intended Learning Outcomes and Validated Multiple-Choice Questions for Intestinal Ultrasound Education: A Comprehensive Approach

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Purpose: This study aimed to establish standardized Intended Learning Outcomes (ILOs) for Intestinal Ultrasound (IUS) education and validate multiple-choice questions (MCQs) aligned with these objectives.

Materials and Methods: Our study followed a rigorous multi-phase approach. In the first phase, in-depth brainstorming sessions reviewed existing knowledge to create a comprehensive list of ILOs and focus points, specifying expected learning outcomes with action verbs from Revised Bloom's Taxonomy. A steering committee of four experts in IUS or ultrasound education refined these items. In the second phase, a modified Delphi method consensus voting involved experts with extensive IUS teaching or research experience to anonymously review and refine 50 statements, rating them on a Likert scale for relevance, importance, and achievability. The final consensus will update the IUS education curriculum. MCQs aligned with the ILOs were developed using guidelines like Revised Bloom's Taxonomy and Miller's Pyramid, and thoroughly reviewed by experts to ensure they were evidence-based, up-to-date, and grammatically correct.

Statements with >70% expert agreement and a mean score >3.5 were included. Cohen's Kappa coefficient evaluated inter-rater reliability. The same specialist group rated the MCQs, and the modified Angoff method set defensible scores.

Results: After the first round, 50 ILO statements were approved, and 44 were revised and circulated for a new voting round. Final results are expected in mid-August.

Conclusion: This study underscores the practical implications of standardized educational objectives and validated assessment tools, demonstrating their significant impact on enhancing and standardizing IUS education programs. These results will lay the foundation for introducing e-learning programs in IUS for international knowledge dissemination. Additionally, the MCQs were administered to two groups of trainees (hybrid and conventional workshops) under similar test conditions to ensure reliable results. Item Response Theory (IRT) was used to analyze the properties of the MCQs and individuals.

FAECAL MICROBIOTA TRANSPLANTATION (FMT) FOR CRYPTOSPORIDIOSIS: A CASE SERIES

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Background: Infection with *Cryptosporidium* and subsequent cryptosporidiosis may be challenging in patients who are immunocompromised due to e.g. solid organ transplantation. Treatment options are few and the standard treatment of nitazoxanide shows limited efficacy. Faecal microbiota transplantion (FMT) is safe and effective for *Clostridioides difficile* and could be considered for cryptosporidiosis.

Methods: We present a case series of 3 patients who were all renal transplant recipients and had cryptosporidiosis, treated experimentally with FMT. Patients received 1-2 FMT treatments consisting of 3-5 doses of capsules FMT in total. The first FMT was administered 10-20 days following the onset of diarrhea. Patient stool samples were collected prior to FMT treatment and follow-up samples were collected after FMT treatment. Stool samples were used for microbiome analysis.

Results: All patients achieved resolution of symptoms within days to a week following 3-5 capsule FMT doses. All patients achieved a negative stool test for *Cryptosporidium*. Two of the patients experienced mild and short-lasting adverse events such as diarrhea, abdominal pain and nausea. Microbiome analysis revealed major variation between patients prior to FMT. Overall, an increase in alpha diversity was observed following an FMT treatment series.

Conclusion: This is the first documented eradication of *Cryptosporidium* in humans with the use of FMT. These cases suggest that FMT may be a safe and effective treatment option for cryptosporidiosis. Further studies are needed to assess the generalizability of our findings.

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Portosystemic Hepatic Encephalopathy Scores (PHES) differ between Danish and German healthy populations despite their geographical and cultural similarities

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Aim: Minimal hepatic encephalopathy (MHE) is common in liver cirrhosis and is identified by psychometric tests. The portosystemic hepatic encephalopathy score (PHES) is the most widely used and serves as an inter-study comparator. PHES has not been standardised for use in the Danish population, where German normal values have been applied until now based on the notion that the populations are comparable. This study aimed to evaluate if German PHES normal values can be applied in the Danish population and establish Danish normal values if needed. **Methods:** 200 Danish and 217 German healthy persons underwent Number Connection Test A and B (NCT), Line Tracing Test (LTT), Digit Symbol Test (DST), and Serial Dotting Test (SDT), and based on performance, PHES was calculated. **Results:** German and Danish PHES performance declined with age in all subtests but more rapidly in Danes. Both German and Danish norms were impacted by gender and education, but to a different extent in the single tests of the test battery. Accordingly, there was a need for specific Danish normal values, which are presented here. Applying the new Danish normal values instead of the German in patients with cirrhosis yielded a lower percentage of out-of-norm performances (58% vs. 66%) and, hence, a lower prevalence of MHE. **Conclusion:** Danes and Germans perform differently on PHES, and therefore, normal German values cannot be used in Danish patients. Danish normal values are presented here and yield a lower number of 'out of norm' performances.

Mental sundhed blandt patienter med inflammatorisk tarmsygdom sammenlignet med den generelle danske befolkning under den første bølge af COVID-19.

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Formål

At sammenligne mental sundhed hos patienter med inflammatorisk tarmsygdom (IBD) med den generelle population (GP) under den første bølge af COVID-19 pandemien i 2020.

Materiale og metoder

Spørgeskemaundersøgelser inkl. spørgsmål vedr. demografi, mental sundhed og IBD relaterede faktorer gennemført under første bølge af COVID-19 pandemien. Patienter med IBD tilknyttet Herning Hospital og et sample af Danmarks GP blev inviteret til at deltage, sidstnævnte som en del af det nationale initiativ "Standing Together— at a Distance". Livskvalitet-skala angav høj mental sundhed ved høj værdi, øvrige skalaer angav nedsat mental sundhed ved høj værdi. Livskvalitet-skala angav høj mental sundhed ved høj værdi, øvrige skalaer angav nedsat mental sundhed ved høj værdi.

Resultater

Et sample fra GP på 968 personer og 400 patienter med IBD besvarede spørgeskemaer. Median alder for GP var 52 år (IQR) (32;66), og 48 år (IQR) (37;68) for IBD-patienter. Sammenlignet med GP var var IBD-patienter oftere kvinder (59% *vs.* 51%), oftere forældre, ofte erhvervsuddannet/faglært (34% *vs.* 23%), modsat lang videregående uddannelse (4% *vs.* 14%), og oftere på arbejdsmarkedet (59% *vs.* 47%).

Median score (IQR) for IBD-patienter og for GP var: livskvalitet (skala 1 – 10) 8 (5;9) *vs.* 7 (6;8), social isolation (skala 1 – 10) 3 (1;6) *vs.* 4 (2;6), angst (skala 4 – 20) 5 (4;6) *vs.* 5 (4;7), og søvn (skala 1 – 5) 2 (2;3) *vs.* 4 (3;4). Bekymring for COVID-19 (skala 1 – 10) var for de to grupper 5 (3;7) *vs.* 5 (3;7). Median score (IQR) for patienter der betragtede deres IBD som moderat/svær var 5 (5;8) for livskvalitet, 5 (2;7) for social isolation og 6 (5;8) for angst.

Konklusion

Ingen tydelig forskel i mental sundhed under den første bølge af COVID-19 imellem IBD-patienterne og GP. Patienter der betragtede deres IBD som svær viste en tendens imod påvirket livskvalitet, isolation og angst sammenlignet med. den generelle population.

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Behavioural risk factors in patients with Clostrioides Difficile Infection.

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AIM

We aimed to explore behavioural risk factors that might be a point of interest in further interventions against recurrence of Clostrioides Difficile Infection (CDI).

The morbidity and mortality in CDI are significant as is the risk of recurrence. Behavioural risk factors such as smoking, nutrition, alcohol, physical activity (SNAP) may play a role in CDI.

METHODS

We included patients > 18 years attending the out-patient clinic for fecal transplantation against CDI related to use of antibiotics.

Questionnaires answered at baseline, at week 8, -26 and -52 assessed frailty, qualitive of life, worries for CDI, gastrointestinal symptoms and attitudes towards SNAP. Patients were provided with vancomycin capsules 125 mg and instructed to start prophylactic vancomycin treatment in case they were prescribed any other treatment with antibiotics.

RESULTS

15 patients were included. Median age was 70 years and 47% were female. Baseline median score was 50 for General health VAS (1 - 100), 3 for Clinical frailty scale (1-9), 10 for Worried for CDI recurrence (1 - 10), 11 for 5-level EQ-5D (5 - 25), and 3 for Gastrointestinal symptom severity scale (11 - 7). Self-perceived status for behavioural risk factors ranging from "1" (poor status) to 10 (very good status) were 10 for smoking, 8 for nutrition, 10 for alcohol, and 5 for physical activity.

CONCLUSION AND PERSPECTIVES

Physical exercise may be a point of interest in frail patients recovering from CDI. Feasibility for providing prophylactic vancomycin to patients in risk of recurrent CDI may be further evaluated via follow-up data from this study.

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Validation methods for encapsulated faecal microbiota transplantation: a scoping review

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Background: Faecal microbiota transplantation (FMT) is an emerging treatment for diseases associated with a disrupted intestinal microbiome, mainly *Clostridioides difficile* infection. Encapsulated FMT is a patient-friendly application form that improves accessibility. Capsule processing may be standardised, but validation protocols are warranted. This review aimed to describe published validation methods for encapsulated FMT.

Data sources and methods: On September 1st and 29th, we conducted a comprehensive scoping review by implementing a systematic search strategy in the PubMed, Embase, and Web of Science databases. Original studies with encapsulated faecal formulations were included regardless of indication. Studies were excluded if they did not address processing or validation or used non-donor-derived capsules. Processing data and validation methods were registered during full-text analysis.

Results: The searches identified 283 unique studies, of which 41 were included for data extraction and analysis. We identified seven validation covariables: donor selection, pre-processing,

preservation, anaerobe processing, microbial count, viability, and engraftment, from which we constructed a model for quality assessment of encapsulated FMT that exhaustively categorised processing details and validation measures in the studies. The model consisted of three domains: 1. Processing (donor selection and processing protocol), 2. Content analysis (microbiota measures and dose measures), and 3. Clinical effect (engraftment and clinical outcomes). No studies presented a reproducible capsule protocol, and the validation strategies of the studies were sparse and divergent. **Conclusions:** The validation of FMT capsules is heterogeneous, and the processing requires relevant standardisation protocols, especially focusing on capsule content analysis. Future clinical studies should investigate how measures of validation covariables impact the clinical effect, underlining the need for standardisation in the field.

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Word counts: 264 words

Assessing the steatotic liver disease diagnoses over time.

A prospective cohort study

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Background and Aims: Steatotic liver disease (SLD) includes several subclasses including metabolic-dysfunction associated steatotic liver disease (MASLD), metabolic and alcohol-related liver disease MetALD and alcohol-related liver disease (ALD). However, these criteria may be sensitive behavioral changes making the SLD diagnoses dynamic. Our aim was to investigate the dynamics of SLD diagnoses over time.

Method: We performed a prospective cohort study among individuals from the general population and individuals at risk of SLD. We defined presence of steatosis as CAP >275 dB/m and presence of advanced fibrosis as TE >12 kPa. Subclassification of SLD was based on the presence of at least one CMRF and self-reported current alcohol intake. The SLD classification was assessed at baseline and after 2 years follow-up.

Results: We included 994 participants, mean age was 57 (±10) years, 633 were male (64%) and 361 (36%) female and 54 (5%) had advanced fibrosis. At baseline, 551 (55%) had SLD (CAP >275 dB/m and/or TE >12 kPa) while 443 (45%) did not have SLD. Among the patients with SLD, 337 (61%) met the criteria for MASLD, 133 (24%) for MetALD and 79 (14%) for ALD, and 2 (0%) were classified as crytogenic SLD. Median time between baseline and follow up visit was 25 months (IQR 25-31). At follow-up, 382 (38%) of the 994 participants were reclassified. Among the 443 participants that did not have SLD at baseline, 113 (26%) met the criteria for SLD at follow-up. Among the 551 participants classified as having SLD at baseline, 269 (49%) were reclassified of which 186 (69%) did not meet the criteria for SLD at follow up and 83 (31%) changed SLD subclass.

Conclusion: SLD and the subclassification hereof is highly dynamic, especially driven by changes in alcohol use and steatosis. This affects eligibility for clinical trials and clinical practice for patients with SLD.

Abstrakt

QUICKFACT, effektiv fæces prøvetagning

Forfattere;

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Formål; hvert år indsamles og analyseres over 130.000 fæcesprøver, ifm. udredning for diarre, mange af disse prøver tages under indlæggelse, og som udgangspunkt, er patienterne hvorfra prøverne tages fra, isolerede fra indlæggelse og indtil resultatet af fæcesanalyse foreligger.

Standardmetoden til at indsamle egnede fæcesprøver, er at opsamle i et bækken, uden kontaminering med andet biologisk materiale (typisk urin). Denne metode er ofte tidskrævende, til gene for den indlagte patient, der hyppigt er svækket, samt ressourcekrævende for personalet. Desuden medfører proceduren med opsamling af fæces fra et bækken, i et urent skyllerum/andet vådrum, en ikke ubetydelig risiko for kontaminering af omgivelser og smitte spredning.

Det ovenfor beskrevne procedureforløb giver ofte anledning til flere forsøg på opsamling, og dermed forlængelse af isolationsperioden.

Materiale og metode;

På baggrund af ovenstående blev der udviklet et prøvetagnings device (se illustration), der rektalt kan opsamle adækvate fæcesprøver.

Dette device blev indledende testet på fantomer og anæsteserede forsøgsdyr (svin).

Devicet blev herefter godkendt af lægemiddelstyrelsen, videnskabsetisk komité, datatilsynet, anmeldt via Clinical Trials og GCP overvåget,

Det kliniske forsøg blev udført på patienter indlagt og isoleret på mistanke om infektiøs diarre.

Efter 12 testede patienter, foretog gruppen bag projektet en evaluering, baseret på en formodning om at dimensionerne på device skulle justeres (3 patienter havde oplevet moderate gener, ingen komplikationer), og efter indhentede tilladelser, blev diameter af device reduceret med cirka 1,2 mm.

Resultater;

Der blev inkluderet 50 patienter.

Med følgende resultat;

Succesfuld indføring og prøvetagning på 47 patienter (94% af test population), ifm. med 3 forsøg på prøvetagning, kunne device ikke indføres pga. tekniske vanskeligheder (alle 3 var med oprindelig større diameter).

Der blev udhentet materiale hos 46 ud af 47 patienter (96% af prøver).

Tid fra ordination til prøve klar til afsendelse;

1 time	2 timer	3 timer	≥ 4 timer	Følgende døgn
28 patienter	8 patienter	3 patienter	3 patienter	4 patienter

Tidsforbrug i forbindelse med selve den kliniske prøvetagning;

1 minut	2 minutter	3 minutter	4 minutter	5 minutter	7 minutter
6 patienter	22 patienter	8 patienter	2 patienter*	7 patienter	1 patient

*Opsamling lykkedes i 2. forsøg

Har man kunne dyrke på det tilsendte prøvemateriale?

Ja: 44 ud af 46 patienter(96% af prøver).

Nej: 2 patienter (for lidt prøvemateriale i det tilsendte)

Påvisning ved dyrkning og resistensbestemmelse;

Clostridium difficile	Astrovirus	Negativ / intet påvist	For lidt prøvemateriale
9 patienter	1 patient	34 patienter	2 patienter

Gener ved prøvetagning (baseret på VAS score)

Score	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Antal pt.	**22**	**7**	**4**	**4**	**9**	**1**	**1**	**1**		**1**	

Gennemsnitlig VAS;

Smerter ved prøvetagning (baseret på VAS score)

Score	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Antal pt.	**21**	**10**	**2**	**6**	**6**	**1**	**1**	**3**			

Gennemsnitlig VAS;

Konklusion;

Det testede device kan hurtigt, sikkert, uden væsentlige gener og effektivt anvendes til fækal prøvetagning, og sparer indlæggelsestid i isolation.

Devicet kan formodentlig med fordel anvendes til prøvetagning på andre indikationer end infektiøs diarre.