Pattern of Alcoholic Consumption and Liver Fibrosis

To determine whether quantity, binge pattern consumption or type of alcohol was associated with liver fibrosis in patients with NAFLD, previous and current alcohol consumption was assessed in NAFLD patients undergoing liver biopsy. All subjects currently consumed less than 210 grams per week (male), or less than 140 grams per week (female). Binge consumption was defined as greater than 4 standard drinks (female), or greater than five standard drinks (male), in one sitting. Liver biopsies were scored according to the NASH CRN system with F3/4 fibrosis defined as advanced.

Among the 187 patients (24% with advanced fibrosis), the median weekly alcohol consumption was 20 (2.3-60)g over an average of 18 years. Modest consumption (1-70 g per week), was associated with lower mean fibrosis stage compared to lifetime abstainers and a decreased risk of advanced fibrosis (OR 0.33). The association with reduced fibrosis was not seen in subjects drinking in a binge-type fashion. Exclusive wine drinkers, but not exclusive beer drinkers, had lower mean fibrosis stage and lower odds of advanced fibrosis (OR 0.20), compared to lifetime abstinent subjects. No interaction between gender and alcohol quantity, type, or binge consumption on fibrosis was observed.

It was concluded that modest alcohol consumption, particularly wine in a non-binge pattern is associated with lower fibrosis in patients with NAFLD. Prospective longitudinal studies into fibrosis progression, cardiovascular outcomes and mortality are required before clinical recommendation can be made.

Mitchell, C., Jeffrey, G., Boer, B., et al. "Type and Pattern of Alcohol Consumption Liver Fibrosis in Patients with Non-Alcoholic Fatty Liver Disease." American Journal of Gastroenterology; Vol. 113, pp. 1484-1493.

BMI, Diabetes, and Cholangiocarcinoma Risk

Obesity and diabetes are associated with an increased liver cancer risk. To evaluate their relationship with intrahepatic cholangiocarcinoma (ICC), the second most common cause of liver cancer, a pooled analysis was conducted with a systemic review/meta-analysis of the literature. The liver cancer pooling project was a consortium of 13 U.S. based, prospective cohort studies with data from 1,541,143 individuals (ICC cases, N = 414). In this systematic review, 14 additional studies were identified and a meta-analysis was carried out, combining the results from LCCP with the results from the 5 prospective studies identified through September 2017.

In the LCPP, obesity and diabetes were associated with a 62% (HR = 1.62), 95% confidence interval and an 81% increased ICC risk, respectively. In the meta-analysis of prospectively ascertained cohorts and nested, case-control studies, obesity was associated with a 49% increased ICC risk (RR 1.49). Diabetes was associated with a 53% increased ICC risk (RR = 1.53).

Some heterogeneity was noted between studies, but subgroup analysis identified consistency. It was concluded that the findings suggested obesity and diabetes are associated with increased ICC risk as suggested in reference to etiologies of hepatocellular carcinoma. Additional prospective studies are awaited for verification.

Petrick, J., Thistle, J., Zeleniuch-Jacquotte, A., et al. "Body Mass Index, Diabetes, and Intrahepatic Cholangiocarcinoma Risk: The Liver Cancer Pooling Project and Meta-Analysis." American Journal of Gastroenterology 2018; Vol. 113, pp. 1494-1505.

Diverticular Hemorrhage and Anticoagulants

To analyze the incidence of and risk factors for recurrent diverticular hemorrhage and to determine whether discontinuing anticoagulation after diverticular hemorrhage is associated with ischemic stroke, a retrospective cohort study of patients enrolled in the OptumInsight Clinformatics database from 2000 to 2016 was carried out. Incidence rate for initial and recurrent diverticular hemorrhage was calculated by identifying patients who had hospitalizations with a primary discharge diagnosis consistent with diverticular hemorrhage.

The hazard ratios of second diverticular

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hemorrhage associated with anticoagulants or platelet aggregation inhibitors were calculated using Cox proportional hazards regression adjusted for demographics, comorbidities, and medication use. Hazard ratio for ischemic stroke among patients who discontinued anticoagulant after diverticular hemorrhage was calculated similarly.

In 14,925 patients with an initial diverticular hemorrhage, 1368 of these patients had a second episode. The unstandardized incidence rates of initial and second diverticular hemorrhage were 10.9 per 100,000 person-years and 3,625.6 per 100,000 person-years. Platelet aggregation inhibitors were associated with second episodes of diverticular hemorrhage (HR 1.47), whereas all classes of anticoagulant agents were not associated. Among patients with a potential indication for stroke prophylaxis, those who discontinued anticoagulation after the diverticular hemorrhage had an increased hazard of ischemic stroke (HR 1.93).

It was concluded in this retrospective study, that platelet aggregation inhibitors, but not anticoagulants were associated with recurrent diverticular hemorrhage. Discontinuing anticoagulation was associated with increased hazard for ischemic stroke.

Vajravelu, R., Mamtani, R., Scott, F., Waxman, A., Lewis, J. "Incidence, Risk Factors and Clinical Effects of Recurrent Diverticular Hemorrhage: A Large Cohort Study." Gastroenterology 2018; Vol. 155, pp. 1416-1427.

Antibiotic Resistance in H. Pylori Infection

A systematic review and meta-analysis was carried out to assess the distribution of H. pylori resistance to commonly used antibiotics and to measure the association between antibiotic resistance and treatment failure.

Publication databases for studies were searched that assessed rate of H. pylori resistance to clarithromycin, metronidazole, levofloxacin, amoxicillin or tetracycline. Pooled estimates of primary and secondary resistance and 95% confidence intervals (CIs), were grouped by WHO region. The association between antibiotic resistance and treatment failure was measured by extracting data on treatment efficacy in patients with resistant and susceptible isolates and pooling odds ratios with 95% CIs.

A total of 178 studies were identified comprising 66,142 isolates from 65 countries. Primary and secondary resistant rates to clarithromycin, metronidazole, and levofloxacin were greater than 15% in all WHO regions, except primary clarithromycin resistance in the Americas (10%), and Southeast Asia region (10%) and primary levofloxacin resistance in the European region (11%).

There was considerable heterogeneity (greater than 75%) among all analyses. This might have resulted from a grouping of resistance rates by country. Increasing antibiotic resistance was observed in most WHO regions. Resistance to clarithromycin was significantly associated with failure of regimens containing that antibiotic (OR 6.97).

It was concluded that resistance of H. pylori to antibiotics has reached alarming levels worldwide, having a great effect on efficacy of treatment. Local surveillance networks are required to select appropriate eradication regimens for each region.

Savoldi, A., Carrara, E., Graham, D., et al. "Prevalence of Antibiotic Resistance in Helicobacter pylori: A Systematic Review and Meta-Analysis in World Health Organization Regions." Gastroenterology 2018; Vol. 155, pp. 1372-1382.

Misoprostol and Aspirin-Induced Small Bowel Bleeding

A double-blind, randomized, placebo-controlled trial was carried out to determine whether misoprostol can heal small bowel ulcers in patients with small bowel bleeding who require continuous aspirin therapy. The study was prospective among 84 aspirin users who required continued aspirin therapy in Hong Kong and Japan.

Small bowel ulcers or multiple erosions were detected by capsule endoscopy and randomly assigned to groups that received either misoprostol (200 ug 4 times daily; N=42), or placebo (N=42) for 8 weeks. All patients continued taking aspirin

100 mg daily. The primary end point was complete ulcer healing. At follow-up capsule endoscopy, secondary end points included changes in hemoglobin level and number of ulcers/erosions from baseline.

Complete healing of small bowel ulcers was observed in 12 patients in the misoprostol group (28.6%), and 4 patients in the placebo group (9.5%), for a difference in proportion of 19%. The misoprostol group had a significantly greater mean increase in hemoglobin than the placebo group (difference 0.70 mg/dL). The reduction in medium number of ulcers or erosions were significantly greater in the misoprostol group (from 6.5 to 2), than in the placebo group (from 7 to 4).

In this double-blind, randomized placebo-controlled trial, misoprostol was found to be superior to placebo in promoting healing of small bowel ulcers among aspirin users complicated by small bowel ulcer bleeding, who require continuous ulcer therapy.

Kyaw, M., Otani, K., Ching, J., et al. "Misoprostol Heals Small Bowel Ulcers in Aspirin Users With Small Bowel Bleeding." Gastroenterology 2018; Vol. 155, pp. 1090-1097.

Upper Gastrointestinal Bleeding with Oral Anticoagulants

To compare the incidence of hospitalization for upper gastrointestinal bleeding in patients using individual anticoagulants with and without PPI cotherapy and to determine variation according to underlying gastrointestinal bleeding risk, a retrospective cohort study in Medicare beneficiaries was carried out between January 1, 2011 and September 30, 2015. The agents studied included apixaban, dabigatran, rivaroxaban, or warfarin, with or without PPI cotherapy.

The outcomes and measures study included hospitalization for upper gastrointestinal bleeding, adjusted incidence and risk difference (RD) per 10,000 person-years of anticoagulant treatment, and incidence rate ratios (IRRs). A total of 1,643,123 patients with 1,713,183 new episodes of oral anticoagulant treatment were included in the cohort with a mean age of 76.4 years; 56.1% were for women and the indication was atrial fibrillation for 870,330 patient-years (74.9%).

During 754,389 treatment person-years without PPI cotherapy, the adjusted incidence of hospitalization for GI tract bleeding (N = 7119), was 115 per 10,000 person-years. The incidence for rivaroxaban (N = 1278) was 104 per 10,000 person-years, which was significantly greater than the incidence for apixaban (N = 279); 73 per 10,000 person-years; IRR 1.97; dabigatran (N = 629) was 120 per 10,000 person-years; IRR 1.19; RD 23.4 and Warfarin (N = 4933) was 113 per 10,000 person-years; IRR 1.27; RD 30.4.

The incidence for apixaban was significantly lower than that for dabigatran (IRR 0.61), RD 47.5 and Warfarin (IRR 0.64). With anticoagulant treatment with PPI cotherapy (264,447) patient-years, 76 per 10,000 person-years was compared with treatment without PPI co-therapy, risk of upper GI tract bleeding and hospitalization (N = 2245) was lower overall (IRR 0.66) and for apixaban (IRR 0.66), dabigatran (IRR 0.49), rivaroxaban (IRR 0.75).

It was concluded that among patients initiating oral anticoagulant therapy, incidence of hospitalization for UGI tract bleeding was the highest in patients prescribed rivaroxaban and the lowest for patients prescribed apixaban.

For each anticoagulant, the incidence of hospitalization for upper GI tract bleeding was lower among patients receiving PPI cotherapy.

Ray, W., Chung, C., Murray, K., et al. "Association of Oral Anticoagulant and Proton Pump Inhibitor Cotherapy with Hospitalization for Upper Gastrointestinal Tract Bleeding." JAMA 2018; Vol. 320 (21); pp. 2221-2230.

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