FROM THE LITERATURE

**Frequency of Esophageal Adenocarcinoma After Radiofrequency Ablation in Barrett’s Esophagus**

To assess the incidence of esophageal adenocarcinoma (EAC) after radiofrequency ablation (RFA) utilized in treatment of Barrett’s esophagus (BE), and to evaluate the factors associated with the development of EAC and EAC-specific and all cause mortality who underwent RFA for BE from July 2007 to July 2011 from US Multicenter RFA Patient Registry, data was collected.

Patients were followed until July 2014. Kaplan/Meier Curves of EAC incidence were stratified by baseline histology. Crude EAC incidence and mortality (all cause and EAC-specific), were calculated and adjusted. All cause mortality was assessed. Logistic regression models were constructed to assess predictors of EAC and all cause mortality.

Among 4982 patients, a total of 100 (2%) developed EAC (7.8/1000 patient years) and 9 patients (0.2%) died of EAC in a mean 2.7 years. The incidence of EAC in nondysplastic BE was 0.5/1000 patient years.

Overall, 157 patients (3%), died during follow-up (all cause mortality 11.2/1000 patient years).

On multivariate logistic regression baseline (BE) length and histology (OR 5.8 and 50.3 for low-grade dysplasia and high-grade dysplasia, respectively), predicted EAC incidence. Among 9 EAC deaths, 6 (67%) had baseline HGD and 3 had baseline intramucosal EAC. The most common causes of death were cardiovascular (15%) and extraesophageal cancers (15%). No deaths were associated with RFA.

It was concluded that based on analysis of multicenter registry of patients who underwent RFA for BE, less than 1% died from EAC. The incidence of EAC was markedly lower in this study than in other studies of disease progression, with the greatest absolute benefit observed in patients with high-grade dysplasia (HGD).


**Withdrawal of Long-Term Therapy in IBD**

A systematic search of the literature was carried out to identify studies reporting after de-escalation (drug cessation or dose reduction), of anti-TNF agents and/or immunomodulators in patients in remission from IBD.

Focus was reviewed to include type of IBD and drug, rates of relapse, factors associated with relapse, and response to retreatment.

A total of 6315 unique citations were identified; findings were analyzed from 69 studies (18 on de-escalation of immunomodulator monotherapy, 8 on immunomodulators de-escalation from combination therapy, and 43 on de-escalation of anti-TNF agents, including 3 during pregnancy), comprising 4672 patients.

Stopping immunomodulator monotherapy after a period of remission was associated with high rates of relapse in patients with Crohn’s disease or ulcerative colitis (approximately 75% of patients experienced a relapse within 5 years after therapy was stopped).

Both studies of patients with Crohn’s disease who discontinued an immunomodulator after a combination therapy found that rates of relapse did not differ from those of patients who continued taking the drug (55 to 60% had disease relapse 24 months after they stopped taking the immunomodulator).

The only study in patients with ulcerative colitis supported continued immunomodulator use. Approximately 50% of patients who discontinued the anti-TNF agents after combination therapy maintained remission 24 months later, but the proportion in remission decreased with time.

Markers of disease activity, poor prognostic factors, and complicated or relapsing disease course were associated with future relapse.

It was concluded, based on systematic review, 50% or more of patients with IBD who cease therapy have a disease relapse. Further studies are required to accurately identify subgroups of patients who are good candidates for discontinuation of therapy. The decision to withdraw a drug should be made for each individual, based on patient preference, disease markers, consequences of relapse, safety and cost.


**Acute Pancreatitis and Diabetes Mellitus**

To assess the incidence of diabetes in acute pancreatitis (AP) survivors compared with matched controls, a study cohort drawn from Taiwan National Health Insurance Frequency of Esophageal Adenocarcinoma After Radiofrequency Ablation in Barrett's Esophagus...
FROM THE LITERATURE

claims data included 2966 first attack AP patients and 11,864 non-AP general controls individually matched on age and sex with an AP/non-AP ratio of 1:4.

Incidence rate was estimated under Poisson assumption. Relative risks of diabetes were indicated by Hazard Ratios (HRs), estimated from Cox Proportional Hazard Regression Models with partitioning of time at 3 months to account for proportionality.

In the first partition of time (less than 3 months), the incidences of diabetes were 60.8 and 8 per 1000 person/years in AP and control groups, respectively; representing a covariate-adjusted HR of 5.9. In the second partition (greater than 3 months), the incidences of diabetes were 22.5 and 6.7 per 1000 person/years in AP and control groups, respectively (adjusted HR 2.54).

In this second partition, the risk of diabetes was greater in men than in women (3.21 vs. 1.58). When the analyses were stratified by severity of AP, the results for mild AP were similar to those for all AP.

It was concluded that the risk of diabetes increases by two-fold after AP. Therefore, a long-term screening is necessary to evaluate diabetes after an attack, regardless of severity.


Prognostic Laboratory Tests in Acute Pancreatitis

To compare admission BUN, hematocrit and creatinine as well as changes in their levels over 24 hours, aiming to determine the most accurate laboratory tests for predicting persistent organ failure and pancreatic necrosis in severe acute pancreatitis (AP), study of clinical data of 1612 AP patients was carried out. They were enrolled prospectively in three independent cohorts and were abstracted. The predictive accuracy of the studied laboratories were measured using areas under the receiver operating characteristic curve (AUC) analysis. A pooled analysis was conducted to determine their impact on the risk for persistent organ failure and pancreatic necrosis.

A classification tree was developed on the basis of the most accurate laboratory parameters. An admission hematocrit greater than 44% and rise in BUN at 24 hours were the most accurate in predicting persistent organ failure (AUC 0.67 and 0.71, respectively), as well as pancreatic necrosis (0.66 and 0.67, respectively), outperforming the other laboratory parameters, acute physiology and chronic health evaluation II score.

In a pooled analysis, admission hematocrit greater than 44% and a rise in BUN at 24 hours were associated with an OR of 3.54 and 5.84 for persistent organ failure and 3.11 and 4.07, respectively, for pancreatic necrosis. In addition, the classification illustrated that when both admission hematocrit was greater than 44% and BUN levels increased at 24 hours, the rates of persistent organ failure and pancreatic necrosis reached 53.6% and 60.3%, respectively.

It was considered an admission hematocrit greater than 44% and rise in BUN at 24 hours may be the optimal predictive tools in clinical practice among existing laboratory parameters and scoring systems.


Hereditry in Hepatic Fibrosis and Steatosis

A cross-sectional analysis of a cohort of well-characterized twins residing in Southern California was carried out to include 60 pairs (42 monozygotic and 18 dizygotic); average age 45.7 and average BMI 26.4. Data was collected on medical history, physical examinations, fasting laboratory test results, and liver health. Participants underwent advanced MRI examination of the liver from January 2012 to January 2015.

Hepatic steatosis was quantified not invasively by MRI and determined based on the proton density fraction. Liver fibrosis was measured based on stiffness, evaluated by an MRI elastography.

A total 26 of the 120 subjects (21.7%), had NAFLD after exclusion of other causes of hepatic steatosis. The presence of hepatic steatosis correlated between monozygotic twins, but not between dizygotic twins. The level of liver fibrosis correlated between monozygotic twins, but not dizygotic twins.

In multivariable models adjusted for age, sex, and ethnicity, the heritability of hepatic steatosis was 0.52 and the heritability of hepatic fibrosis was 0.5.

It was concluded that this study of twins provides
evidence that hepatic steatosis and hepatic fibrosis are heritable traits.


Treatment of CHB During Pregnancy
A systematic review and meta-analysis to synthesize the evidence on the efficacy and maternal and fetal safety of antiviral therapy during pregnancy was carried out and a protocol was developed by the AASD Guidelines Writing Committee. Multiple databases for controlled studies that enrolled pregnant women with chronic HBV infection treated with antiviral therapy were created.

Outcomes of interest were reduction of mother to child transmission (MTCT) and adverse outcomes to mothers and newborns. Study selection and data extraction were done by pairs of independent reviewers.

A total of 26 studies were included that enrolled 3,622 pregnant women. Antiviral therapy reduced MTCT as defined by HBsAg seropositivity. No significant differences were found in congenital malformation rate, prematurity rate or Apgar scores.

Compared to control, Lamivudine or Telbivudine improved maternal HBV DNA suppression at delivery and during 4 to 8 weeks postpartum followup. Tenofovir showed improvement in HBV DNA suppression at delivery. No significant differences were found in postpartum hemorrhage, C-section and elevated CPK rates.

It was concluded that antiviral therapy improves HBV suppression and reduces MTCT in women with chronic HBV infection with high viral load, compared to the use of hepatitis B immunoglobulin and vaccination alone; the use of telbivudine, lamivudine, and tenofovir appears to be safe in pregnancy with no increased adverse maternal or fetal outcome.


Hepatic Fibrosis Present in Diabetes and Steatosis
To investigate the relationships, prevalence of and factors associated with liver fibrosis in the general population, a well-characterized cohort was evaluated by means of transient elastography (TE). The study was part of the Rotterdam Study, a population-based study among individuals 45 years or greater. All participants underwent abdominal ultrasound and TE. Liver stiffness measurement 8 or greater kilopascals (kPa) was used as a cutoff, suggesting clinically relevant fibrosis.

Of 3,041 participants age 66 average with reliable LSM, 169 (5.6%) had an LSM greater than 8 kPA. Age (OR 2.4), ALT (OR 1.24), smoking (OR 1.77), spleen size (OR 1.23), HBsAg or anti-HCV (OR 5.38), and combined presence of diabetes mellitus and steatosis (OR 5.2), all were associated with LSM greater than 8 kPa in multivariable analyses.

The adjusted predictable probability of LSM greater than 8.0 kPa increased per age and decade with probabilities ranging from 1.4% in age of 50 to 60 years to 9.9% in participants greater than 80 years. Participants with both diabetes and steatosis had the highest probabilities of LSM greater than 8 kPa (overall probability 17.2%), which did not increase with age.

It was concluded that in this large population-based study of older adults, LSM greater than 8 kPa, suggestive of clinically relevant fibrosis was present in 5.6% and was strongly associated with steatosis and DM in the context of an aging population and increased prevalence of DM and obesity. This study illustrates that liver fibrosis may become a more prominent public health issue in the future.


HCV Treatment With Mixed Cryoglobulinemia
A case series of patients with HCV-associated mixed cryoglobulinemia syndrome (HCV-MCS), who were treated with sofosbuvir-based regimens and historic controls treated with pegylated Interferon and ribavirin in a single healthcare network was carried out. HCV-MCS was defined as circulating cryoglobulin associated with systemic vasculitis symptoms. Renal involvement (7 patients) was established by kidney biopsy (5 patients), or by 2 or more of the following clinical findings: Reduced kidney function, proteinuria or hematuria with other causes excluded (2 patients). A total of 12 patients received direct-acting antiviral
therapy (VAA) between December 2013 and September 2014. Median age was 61 years. A total of 58% was male and 50% had cirrhosis.

Median baseline serum creatinine was 0.97 mg/dL. Four patients received rituximab concurrent with VAA therapy. SVR 12 was 83% overall. Patients with glomerular nephritis who achieved SVR 12 experienced an improvement in serum creatinine and reduction in proteinuria.

Cryoglobulin levels decreased in 89% of patients with median percent decreasing from 1.5% to 0.5% and completely disappearing in 4 of 9 patients who had cryoglobulin measured after treatment. Serious adverse events were infrequent (17%) in contrast to historical cohort treated with PEG Interferon and ribavirin experiencing only 10% SVR 12, with 100% experiencing at least one adverse event and 50% experiencing premature discontinuation due to adverse events.

It was concluded that SVR 12 rates for sobosfovir-based regimens in HCV-MCS were 83%, significantly higher than historic controls treated with PEG and ribavirin. Patients with glomerulonephritis experienced improvement in renal function, including those not concomitantly treated with immunosuppression.


**Statin Use With Hepatitis C-Related Compensated Cirrhosis**

Statins decrease portal pressure in patients with cirrhosis and increase survival times of patients who have bled from varices. To determine whether long-term statin use will be beneficial or detrimental for patients with cirrhosis, the effects of statins on decompensation and survival times in patients with compensated cirrhosis was carried out in a retrospective cohort, using the Veteran Affairs Clinical Case Registry with nationwide data from veterans infected with HCV.

Patients were identified from January 1996 through December 2009. Statin use was according to filled prescriptions. Cirrhosis and decompensation was determined from international classification of diseases using a validated algorithm.

Among 40,512 patients with HCV compensated cirrhosis, a total of 2,802 statin users were identified. A propensity score model was developed using variables associated with statin prescription and new statin users were matched with up to 5 non-users; 685 statin users were matched with 2,062 non-users.

Discrimination of the propensity score model was 0.92. Statin users had a lower risk of decompensation (HR 0.55), and death (HR 0.56), compared with non-users. Findings persisted after adjustment for age, FIB-4 index score, serum level of albumin, MELD and Child-Turcotte-Pugh scores (HR 0.55 for decompensation 0.55) and death (HR 0.55).

It was concluded that based on data from this registry, statin use among patients with HCV and compensated cirrhosis is associated with a more than 40% lower risk of cirrhosis, decompensation and death. Statin use should not be avoided in these patients.

Mohanty, A., Tate, J., Garcia-Tsao, G. “Statins are Associated with a Decreased Risk of Decompensation and Death in Veterans with Hepatitis C-Related Compensated Cirrhosis.” Gastroenterology 2016; Vol. 150, pp. 430-440.

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