
Poster Presentations

LIVER 2018



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Laparoscopic liver resections: An innovative approach to the liver in a single centre experience

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Laparoscopic liver resections (LLR) represent the new frontier of liver surgery. During the last decade indications for the laparoscopic approach to the liver have been widely extended, from peripheral benign lesions to malignant neoplasms, difficult localizations and major resections. Laparoscopic liver surgery was slower to develop than other fields of laparoscopic surgery because of a steep learning curve, and fear of uncontrolled bleeding or gas embolism. However, LLR is associated with significant advantages of laparoscopic procedures. The aim of this retrospective study is to evaluate the extent and safety of the learning curve for LLR. We retrospectively analysed 87 patients who underwent a LLR from July 2010 to November 2017 performed by a single senior surgeon. At the start of experience the indication was a single lesion, whereas in the last years an increasing number of patients were enrolled for laparoscopic intervention, according to the learning curve. Diseases included liver cancer, hepatic hemangioma, focal nodular hyperplasia, liver abscess, and metastatic liver cancer. The diagnosis was a malignant neoplasm for 53 patients (61%), a benign lesion for the remaining cases. In 45 patients a synchronous procedure was performed (four right colectomy, six left colectomy, eight rectal resection, two gastric resection, 21 cholecystectomy and four for other procedures). 35 patients were males and 42 were females,

with a mean age of 60 years (range 23-88). 81 patients (93%) had a good preoperative hepatic function, assessed with a Child-Pugh score. We performed 63 wedge resections (72%), two segmentectomies, four right lateral bisegmentectomies, 13 left lobectomies (15%), four left hepatectomies and one robotic right hepatectomy; the latter converted for intraoperative bleeding. Median operative time was 120 minutes (35-330). There were no intraoperative or postoperative deaths and 26% of morbidity (ascites in seven patients, fever in seven patients, pneumonia in four patients, one needed blood transfusion and three surgery-related complications occurred). Only one major complication (grade III of Clavien-Dindo classification) was observed, in a patient who received a synchronous proctectomy and needed reoperation for anastomotic dehiscence. The median time of discharge was five days (range 2-11). A negative histological margin (R0) was obtained in 88% of malignancy cases. In our experience laparoscopic surgery is a safe option for hepatic resection in benign such as malignant lesions, good patient selection and refined surgical technique are the keys to successful LLR, especially at the beginning of the learning curve as well as the experience of the surgeon in advanced laparoscopic procedures and hepatobiliary surgery.

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Characterization of laboratory and clinical findings of patients diagnosed with Drug-induced liver injury (DILI) as a tool to aid in diagnosis

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Background & Aim: Drug Induced Liver Injury (DILI) is a diagnosis the importance of which has become increasingly clear in recent years as a result of the combination of an increase in the number of reported cases each year and the potential for damage; DILI is the most common cause of Acute Liver Failure in the United States and a major cause of drug termination at various stages of development and marketing. Despite its importance, DILI is often underdiagnosed or suffers from a diagnostic delay, mainly due to a lack of a pathognomonic test, resulting in a Per Exclusionem diagnosis. Various attempts to find a more efficient diagnostic process met with partial success and the diagnostic challenge persists. The main objective of the study is to try to find unique characteristics for patients who have been diagnosed with DILI in order to try to create a basis for dealing with this diagnostic challenge.

Methods: A retrospective observational study was conducted on 50 patients hospitalized at "Shaare Zedek" Medical Center diagnosed with DILI.

Results & Discussion: In accordance with the literature on DILI, we found that the most common injury was hepatocellular (52% of the patients), that most of the cases were women (56% of the patients), that the prevalence increases with age (70% of the cases were over the age of 51) and that there is a relationship between the age and the sex of the patient to the type of injury. In accordance with studies conducted in the United States, the most common drugs described in our study as the cause of DILI are antibiotics (34% of the cases). The hepatocellular enzymes levels in patients with hepatocellular injury ranged from several hundreds to a thousand, and in the majority of the cases were higher

than 10 times the upper limit of the norm (AST in 80.8% of the cases and ALT in 53.8% of the cases). These ranges correspond to the ranges described in the literature for toxic liver injury. In our study, we have not been able to verify the worldwide trend of increasing prevalence of DILI. In general, the severity of the cases in our study was relatively mild, as expressed in the absence of mortality, in the absence of liver failure and in relatively low bilirubin levels. Previous studies have found that the most unfavorable outcome was of patients with hepatocellular injury. In contrast to that, in our study, the worst prognosis was of patients presented with mixed injury. In contrast to viral hepatitis, we found that the De Ritis (AST/ALT) ratio in DILI is generally greater than one (in 82% of cases).

Conclusions: Despite the increasing prevalence of DILI according to literature, we have not been able to confirm this trend. In our opinion this is partially due a logistic difficulty—the absence of a specific diagnosis code for DILI, *i.e.*, patients whose main diagnosis is DILI are coded under another major diagnosis and the DILI is "Hidden" under a general hepatic diagnoses such as "Elevated Liver Enzymes" or even under a non-hepatic diagnosis as a free text. We respectfully submit that the ICD coding system should include DILI as a major diagnosis. We suggest considering using the De Ritis ratio as a diagnostic aid. Our study did not include a control group of viral hepatitis patients, so we can rely only on information from the literature, but this information is consistent across a large number of studies—Viral hepatitis is characterized by a De Ritis ratio <1 , In contrast to that, most of the patients in our study are characterized by a De Ritis ratio >1 .

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The result of clinical trial for the new lonal drug for hepatoprotective effect in patient with drug induced steatosis: A randomized placebo-controlled double blind clinical trail

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The aim of the clinical trial was to determine hepatoprotective effect of the new Lonal drug in patient with drug induced steatosis. The research was considered such as clinical trial guideline for new drug issued by the World Health Organization's "Good Clinical Practice" based on permission given by Biomedical Ethical Community of the Health Ministry of Mongolia approved diagnosis patient with drug induced steatosis. The research design is *Randomized Placebo-Controlled, Double Blind Clinical Trial*. Lonal drug significant decreases hepatocellular and cholestatic injury. The Lonal drug was taken during 21 days and comparing the some results of metabolic syndrome before and after treatment, reduces TG ($p=0.03$). The participants have

taken the fibroscan and liver biopsy. That was compared to determine before and after treatment such as steatosis and fibrosis degree of participants liver. Before treatment degree of steatosis was S3, after treatment it was dropped S2 ($p < 0.05$). And before treatment, such as fibrosis degree F1-2, after treatment it was decreased F0 ($p < 0.05$). New Lonal drug is reducing hepatocellular injury, cholestatic injury and some criteria of the metabolic syndrome in patient drug induced steatosis. Also new Lonal drug reduces activation of inflammation, decreases the degree of liver steatosis fibrosis validated by liver biopsy and fibroscan.

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Green tea confers protection against cigarette smoke-induced biochemical perturbations in tuberculosis patients

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Cigarette smoking is common among persons with alcohol dependence. Smoking and alcohol consumption cause damage to body organs. Many studies have suggested that these two factors are also responsible for increasing effect of Mycobacterium tuberculosis in lungs and other organs of humans. Tuberculosis is a global health disease. The present study investigates the effect of green tea consumption on confirmed cigarette smokers of TB. Blood samples from 84 human volunteers categorized into seven groups viz., control, TB smokers, and TB smokers with Green tea were selected for this preliminary study to investigate changes in membranes of erythrocytes by consuming green tea. Data obtained from the study suggested a significant increase in the percentage of Haemolysis in experimental groups when

compared with control group and were in the order TB smokers > TB smokers with green tea > controls indicating an additive effect of green tea on cigarette smokers of TB. Liver function tests (LFTs) are commonly used in clinical practice to screen for the liver disease. The liver markers AST, ALT and GGT in TB smokers were increased and TB smokers with Green tea were significantly decreased. The present study divulges that green tea contains catechins can reduce the abnormalities of cigarette smoking effect by ameliorating the oxidative stress. This finding reveals that the possibility of green tea may provide protection from cigarette-caused changes in TB patients.

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Effect of the gurgum-7 traditional compound on alcohol induced chronic hepatitis

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Current pharmacological studies on medicinal plants, animal, mineral based raw material, pure or compound chemical substances of Mongolian traditional medicine are identifying their biological active components thus, linear cell growth, pharmacogenomics, proteomics and clinical studies shown positive results on their treatment rate. Alcohol induced chronic hepatitis are broad epidemic disease worldwide, as the pathogenesis of the Alcohol hepatitis deteriorates it leads to serious health complications such as hepatic steatosis, cirrhosis, hepatocellular carcinoma, thus alcohol hepatitis has a critical impact on economics and population health. Epidemiological research conducted on alcohol induced hepatitis shown results of mortality rate of the disease decreasing last couple of years. Our team of researchers has chosen the topic basing on current wide usage of the Gurgum-7 traditional compound on hepatic disorders and its indication of relieving symptoms of hepatic fever, toxicities, jaundice, injuries thus administering to a patients with alcohol induced hepatitis under the aim of proving the results with modern scientific methods. As the results after the experimentation and research according to the GHS classification the hepatotoxic characteristic of Gurgum-7 is relatively low. The result shown 160 mg/kg dose of Gurgum-7 is more efficient on lowering AST, ALT enzymes at 28th week of chronic ethanol toxicity, Comparing the quantity of Malondialdehyde (10.73 ± 0.68) of a second group of the test animals which administered 160 mg/kg with control group shown statistically relevant ($p \leq 0.05$) therefore 18.46% reductions of the enzymes. Also, a group of test

animals which administered Gurgum-7 by 160 mg/kg dosage showed the result of difference of statistically relevant ($p \leq 0.05$) which is more close to the healthy group. These results tell us the Gurgum-7 has an antioxidant effect. First stage of clinical study Gurgum-7 showed no side effects and liver, kidney functions are remained healthy. Second stage of the clinical study showed the decreases on laboratory test results of the main and control groups as ALT 52.3% ($p < 0.01$), AST 45.5% ($p < 0.01$), gamma glutamyltransferase 43.9% ($p < 0.01$) thus indicating the compound is decreasing the breakdown of hepatocytes, bile duct obstruction during alcohol hepatitis and toxicity. Blood coagulation test showing the Gurgum-7 is decreasing the breakdown of hepatocytes therefore effecting blood clotting factors including I, II, V, VII, X, fibrinogen, protrombine, vitamin K deficiency positively. The decrease of hepatocyte breakdown leads to the regaining of the normal liver function and blood clotting factor II, V, X so the blood coagulation disorders are fixed. Therefore, we are connecting the result mentioned above to a short course of treatment. Because of the short course of treatment it may have not showed any difference on macro structure level, as identifying the liver fibrosis rate by APRI method before and after the treatment, Gurgum-7 effectively decreasing liver fibrosis.

Speaker Biography

Bayarsaikhan O has completed his MSc from MNUMS, Mongolia. He is the Teacher of University MNUMS, Mongolia. He has over 16 publications with citations over 16 times.

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Non-alcoholic fatty liver disease and its development to hepatocellular carcinoma in patients with obesity and metabolic syndrome

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Background: The rates of obesity and the metabolic syndrome are increasing worldwide, therefore clinical studies have been undertaken to examine for links with Nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH) and hepatocellular carcinoma (HCC). NAFLD represents the hepatic manifestation of the metabolic syndrome. It is associated with the presence of insulin resistance and type 2 diabetes mellitus. HCC has been registered as a most frequent type of cancer in type 2 diabetes.

Methods: Age, obesity, insulin resistance, and overall development of metabolic syndrome are the major risk factors associated with development of NAFLD. From longitudinal studies performed in the Western countries, it has been shown that rates of HCC from NASH are similar to those of HCC from infection with the hepatitis C virus. Liver biopsy is an invasive procedure and is not a suitable option as a routine screening tool for this common disease and a new diagnostic procedures and scoring systems that could non-invasively distinguish simple steatosis from NASH are emerging.

Results: Visceral body fat is related to the degree of inflammation and fibrosis in NASH. The pro-inflammatory environment can impact the liver and other tissues and patients with more visceral fat had higher rates of HCC recurrence. Part of patients who are initially diagnosed as clinically non-cirrhotic NAFLD could be at high risk of

HCC development, and employing only standard follow-up procedures for cirrhotic patients would not be enough. Although current guidelines recommend regular HCC surveillance for cirrhotic patients, HCC can develop in the absence of cirrhosis in NAFLD.

Discussion: With the increasing prevalence of NAFLD it is becoming clear that it will contribute to increasing incidence of HCC as well. Identifying a high-risk subpopulation in HCC development among non-cirrhotic NAFLD patients is imperative. Obesity almost doubles the risk of HCC. The diagnosis of HCC might be considered in obese and/or diabetic patients with liver nodules, even if they do not have others manifestations of chronic liver disease. Research reported in this press release presentation was supported by the Ostrava University, The Czech Republic, under grant award number SGS03/LF/2018.

Speaker Biography

Toman D has completed his MD in 2012 from the University of Pavol Jozef Šafárik, Faculty of Medicine, Košice, Slovakia. He is in his final year of residency program of General Surgery. He has Pre-graduation experience from different European countries (internships in Spain and Italy) and Post-graduation experience with internship in the USA (Ryder Trauma Center, University of Miami, Miami, Florida, USA 6/2014) and has given presentations at International Liver Conferences (7th APPLE conference in Hong Kong 2016, The Liver Week 2017 in Seoul – The travel award winner). Since 2016, he is a student of PhD at the Faculty of Medicine, Ostrava University in Ostrava, The Czech Republic, and he focus on the study of NAFLD and HCC in patients with obesity and/or metabolic syndrome.

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Dysregulation of GCLC by NRF2 signalling disrupts anti-oxidant pathway central to most cancers and RAC1 protein modifications in cancer

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Background: NRF2 is ubiquitously expressed transcription factor regulating cytoprotective genes such as *SOD*, catalase, *TRX* and *GPX*. NRF2 is additionally known to be a crucial regulator of cell survival and oncogenic pathways and is found to be up-regulated across most cancers. Ergo, investigating the gene expression status and exome sequencing of upstream and downstream neighbours of NRF2 is imperative to understand the oncogenic manifestation central to NRF2. *RAC1* and *GCLC* are such upstream and downstream molecules whose regulation status is unknown across many cancers.

Methods: We estimated the *GCLC* and *RAC1* transcripts from the RNA isolates from 15 cancer samples of different kinds. cDNA was constructed and authentic-time quantitative PCR was performed utilizing SYBR green assay and the fold change was calculated to understand the regulation status.


Results: The upstream gene *RAC1* and downstream genes *GCLC* were found up-regulated across samples with a fold change >5 fold. We identified >50 nonsynonymous deleterious mutations in the 11,416 whole exome cancer cohort samples. Performing evolutionary profile betokened no conservancy for the observed mutations.

Discussion: Integrating the mutations and expression status of *GCLC*, *RAC1* and *NQO1*, revealed the up-regulation of *NQO1* due to the activation of the PI3 kinase, and *HMOX1*, while inactivating of BET and KEAP1 concurrently. Up-regulation of *GCLC* designates NF-KB and *HMOX1* to be activated, while *CYB5R4* and BET are negatively regulated. The dysregulation of these genes disrupts the free radical scavenging pathway, cell death and survival pathways, and anti-apoptotic pathways. These genes are majorly expressed in the detoxifying organs like liver and kidney. This study shows that the NRF2 and its upstream molecules are found to be efficacious biomarkers in the future and early detection of cancer additionally will come true with these efficient biomarkers.

Speaker Biography

Mantri Dharaneeswar Reddy has completed his MSc in Genetics (2017) from University of Mysore, India. His Master's research focused on the role of NRF2 in ROS and RNS dependent cancer formation and early detection of cancer. His interest lies in the continuation of his research on biomarkers for early detection of cancer. He did his Bachelor's in Biochemistry at Sri Krishnadevaraya University, India.

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Accepted Abstracts

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Reactivation of herpesvirus in patients with hepatitis C treated with direct-acting antiviral agents

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Introduction: Advances in hepatitis C virus (HCV) drug development in the last few years have taken a new turn and the evolution of antiviral therapy for HCV has rapidly progressed from interferon (IFN) up to the development of direct-acting antivirals (DAAs) (Lutchman et al., 2015). HCV infection can now be treated in almost all patients with these tolerable and effective combinations of oral DAAs. Now even those patients who due to advanced liver disease or with co-morbidities were not eligible for treatment by PEG-IFN-based regimens, or those who had previous treatment failure, now have excellent choice of treatment modalities (EASL, 2014). Perelló et al., reported Herpesvirus (HV) reactivation in patients with HCV infection treated with direct acting antiviral therapy (DAA) (Perelló et al., 2016). Changes in the immune system after initiation of DAAs could play a role in HV reactivation. However, the exact mechanisms involved in HV reactivation in the early phases of HCV clearance in patients treated with DAAs are not clear (European Medicines Agency, 2016).

Patients and methods: This is a follow-up study including 100 chronic hepatitis C (CHC) patients attending the outpatient clinics of the Tropical Medicine & Gastroenterology and the Internal Medicine Departments-Qena University Hospital. All eligible patients were included according to inclusion criteria approved by the national committee for control of viral hepatitis (NCCVH): Age 18-75 years, HCV RNA positivity, any BMI (weight in kilograms/squared height in meters), Treatment-naïve patients only were included

in this study. Exclusion criteria included HBV co-infection, HIV, decompensated liver cirrhosis, inadequately controlled diabetes mellitus (HbA1c >9%), hepatocellular carcinoma or extra-hepatic malignancy. Diagnosis of Liver cirrhosis was on clinical basis involving laboratory tests and ultrasonography findings of liver cirrhosis and/or liver stiffness measurement ≥ 12.5 kPa (Castera et al., 2008). Patients were subjected to history taking, clinical examination and routine laboratory work up. All patients were treated with Sofosbuvir-based treatment regimens according to the approved treatment recommendations. The study was approved by ethical committee of Qena Faculty of Medicine-South Valley University. Written informed consent was obtained from all patients before treatment.

Results: Our study included 100 patients with mean age 45 ± 12 years. Males were predominant presenting 69% of our cases. 80% of cases were noncirrhotic at the start of treatment and 20% of patients had evidence of liver cirrhosis. Sustained virological response (SVR) was found in 94% of treated patients while 6% of the treated patients relapsed. Table 1 In the first two months after starting DAAs, we encountered 4 noncirrhotic cases with vesicular eruptions varying in distribution with 2 patients had vesicles over right side of the chest and 2 patients had the vesicles extending to the upper back. A diagnosis of Herpes Zoster (HZ) was made after consultation of dermatology consultant who prescribed antiviral and analgesics. All patients achieved SVR.

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Perioperative liver function after hepatectomy in a tertiary university hospital in Damascus

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Background: Liver resection is the only viable therapeutic treatment option for several neoplastic entities of the liver. Although, the number of resectable patients is increasing in Syria, liver failure is still a major complication affecting mortality and morbidity rates. **Methods:** Between 2009 and 2016, 104 patients undergoing liver resection in Damascus University Faculty of Medicine were retrospectively analyzed. Liver function tests were conducted before surgery (ps) and in the perioperative period (po) and comparisons were performed with division into anatomic VS non-anatomic or malignant VS non-malignant groups. **Results:** Liver synthetic, excretory and detoxifying functions deteriorated after liver resection (INR ps 'presurgery'=1.129 po 'perioperative'=1.426 P<0.001, TP ps=7.426 po=5.581

P<0.001, ALB ps=4.204 po=3.242 P<0.001, T-Bill ps=0.061 po=0.136 P<0.001) and liver cell necrosis increased after resection (ALT ps=27.597 po=200.221 P<0.001, AST ps=33.395 po=190.553 P<0.001). There was no significant difference in liver functions when we compared anatomic VS non-anatomic groups or malignant VS non-malignant groups, but liver cell necrosis was higher with malignancies (ALT malignant group=236.475 non-malignant group=89.5 P=0.002, AST malignant group=222.644 non-malignant group=101.125 P=0.001). **Conclusion:** Although liver resection affects liver function significantly, no differences in outcomes were found between anatomic VS non-anatomic or malignant VS non-malignant groups.

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Clinical evaluation of hepatoprotective effect of *Bhumyamalki (Phyllanthus amarus)* and *Phaltrikadi* decoction (an ayurvedic herbal composition) in patients of acute viral hepatitis

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Background: Hepatitis infection has become a major worldwide health problem because the potential nature of course of the disease to cirrhosis and the hepatocellular carcinoma (HCC). Acute viral infection is the most common cause of all forms of hepatitis. The viral hepatitis have been thought to be self-limiting in nature but sometimes majority of patients of viral hepatitis have been observed ending up with a serious complications like hepatic failure, etc. So, the clinical study was planned to evaluate the hepatoprotective effect of *Bhumyamalki (Phyllanthus amarus)* and *Phaltrikadi* decoction (an Ayurvedic herbal composition) on scientific parameters.

Aim and objectives: To clinically evaluate the hepatoprotective effect of *Bhumyamalki (Phyllanthus amarus)* and *Phaltrikadi* decoction in patients of acute viral hepatitis.

Materials and Methods: This prospective, clinical trial was conducted at Department of Medicine, Desh Bhagat Ayurvedic College & Hospital, Mandi Gobindgarh, Punjab. Only those patients were selected for clinical trial, who presented themselves with anorexia, nausea, vomiting, low grade fever, weakness, dark urine, jaundice and tender hepatomegaly with abnormal liver function test (LFTs). Each

patient was subjected to series of laboratory tests such as serum bilirubin, AST, ALT, serum alkaline phosphatase, HbSAg, HCV and liver ultrasound before treatment, after 15 days of treatment and after one month of treatment to know the extent of liver damage as well as the rate of response to trial drugs. In the clinical trial, three groups of patients of viral hepatitis have been studied to evaluate the hepatoprotective effect of *Bhumyamalki and Phaltrikadi* decoction. The first group was given 50 ml of freshly prepared *Bhumyamalki* decoction, made from 10 gm of crude drug, twice daily. The second group was given a standardized decoction of herbal composition *Phaltrikadi* decoction, in a dosage of 50 ml made from 10 gm of crude drug, twice daily. The third group was given 100 gm of glucose powder daily.

Observations and Results: The trial was conducted for one month and liver functions test were periodically evaluated to assess the hepatoprotective effect of drugs under trial. At the end of the trial, group first and second exhibited hepatoprotective efficiency over the control.

Conclusion: Thus it can be concluded that *Bhumyamalki and Phaltrikadi* decoction drugs are effective in the management of acute viral hepatitis.

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A subtle increase in wild-type RTK levels provides a permissive context allowing multiple signaling cooperators to initiate liver cancer

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Aberrant receptor tyrosine kinase (RTK) signaling is essential during liver cancer evolution and resistance to therapies. Using mouse genetics, we recently demonstrated that a subtle increase of wild-type RTK levels leads to cancer in sensitive tissues, illustrating how the shift towards cancerogenesis can stem from a slight perturbation of signaling dosage. In particular, when the Met RTK is slightly enhanced in liver, mice (namely Alb-R26^{Met}) spontaneously develop hepatocellular carcinoma (HCC), which belong to the so called “proliferative progenitors” subclass (*Fan et al. Hepatology* 2017 Nov;66(5):1644-1661). To uncover new genes that cooperate with RTKs during tumor initiation, we combined the clinically-relevant Alb-R26^{Met} mice with the *Sleeping Beauty* (SB) transposon (*T2/ONC*) mutagenesis system. Whereas neither Alb-R26^{Met} nor *T2/onc-Alb-R26SB/+* mice developed tumors at 30 weeks of age, *T2/onc-Alb-R26SB^{Met}* mice (with enhanced Met in liver in addition to active SB-driven mutagenesis) developed multiple liver

tumors, each carrying distinct genomic insertions. Analysis of 251 independent tumors led to the identification of 285 putative cancer-related genes: some of them correspond to known proto-oncogenes or tumor suppressors, thus validating the overall strategy we employed for cancer gene discovery; other genes have not previously linked to cancer. Integrative analysis with human data revealed that a large proportion of identified genes are also altered in HCC patients. Moreover, we compared our screen outcomes with those performed in other tumor-sensitizing contexts and found 71 genes that emerged specifically in our RTK-sensitized background. *In vivo* assays established the functional relevance of several new putative tumor suppressors. Overall, our screen strategy identifies new functional mechanisms destabilizing liver homeostasis and illustrates how a subtle increase in wild-type RTK levels provides a permissive context for several types of cooperative mechanisms leading to liver tumor initiation.

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Is ERCP the best treatment for choledocholithiasis? Laparoscopic and robotic management in choledocholithiasis

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Cholelithiasis and choledocholithiasis is a disease where incidence increases with age and can have serious complications such as pancreatitis, cholangitis and liver abscesses, but its management is controversial, because there are minimally invasive laparoscopic and endoscopic surgical procedures. The best method for the diagnosis of choledocholithiasis is magnetic resonance cholangiopancreatography, which shows a sensitivity of 95%, is not invasive, does not use ionizing radiation, and is of low risk to the patient. Its accuracy for the diagnosis of choledocholithiasis is similar to that of endoscopic retrograde cholangiopancreatography (ERCP) or transparietohepatic cholangiography, without the risks associated with these invasive procedures. Endoscopic treatment is indicated during the perioperative period or during cholecystectomy, while surgical treatment consists of exploration of the cystic duct or classical choledochotomy, and also during laparoscopic or robotic cholecystectomy. The time of diagnosis of choledocholithiasis is important to establish

the type of treatment. Bile duct exploration through the laparoscopic access has been suggested as the gold standard for the treatment of choledocholithiasis, including robotic surgery, by some authors. The access to the biliary tract can be obtained through the cystic or common bile duct. In our service, patients with few stones in the bile duct, in a distal position, colecystectomized, with high anesthetic or surgical risk, with sickle cell anemia, severe obese and with suppurative acute cholangitis are submitted to ERCP. And the other hand, patients submitted to Gastric Bypass or Gastrectomy with BII or Y-Roux reconstruction, with a disproportionate caliber of the distal choledochus in relation to the stones, with multiple or proximal choledocholithiasis and when ERCP fault or is not available, are submitted to biliary whitening through choledochotomy. Therefore, I would like to reveal our protocol to approach choledocholithiasis as well as demonstrate our step-by-step procedure for the main biliary tract in these cases, presenting our results.

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Acute-on-chronic liver failure (ACLF)

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Acute on chronic liver failure (ACLF) is a distinct clinical syndrome characterized by liver failure due to an acute hepatic injury on an underlying chronic liver disease with high 28-day mortality. Acute insults include alcohol, hepatotropic viruses, and drugs whereas the underlying chronic liver disease is cirrhosis due to alcohol, hepatitis B or C, or NASH. After an acute insult, persistent inflammation, systemic inflammatory response syndrome and the cytokine storm have a central role in the pathogenesis of liver failure and subsequent organ failure. Abstinence, antiviral therapy,

and withdrawal of harmful drug are specific therapies that could help ameliorate or reverse the liver failure. Liver transplantation is the definitive treatment, and a good outcome is achieved with early transplantation in carefully selected patients; liver dialysis and plasmapheresis can help as 'bridge therapies.' What about the magnitude of the problem in the Middle East and Africa? Is there any difference between the definitions of ACLF, risk factors, and presentations in different parts of the world?

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Right lobe live liver donation-safe approach

Sanjay Goja

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Introduction: Right lobe graft providing adequate functional liver mass to recipient without compromising donor safety, is well-established surgical treatment for end stage liver disease in adult.

Material and Methods: We adopted tailored approach for MHV retrieval in 665 RL-LDLTs (Jan2013-Aug2015) based primarily on three factors volumes, anatomy and metabolic demand. Donor parameters included were remanant volume, age, sex, BMI, segment IV venous drainage, MHV anatomy, Middle vein dominance, size of segment V and VIII veins. Recipient factors were GRWR, MELD score (disease MELD) and severity of portal hypertension

Results: 347 patients received graft with MHV, 318 without MHV. Outcomes in donors and recipients were comparable.

RLG without MHV was retrieved in 15 out of 18 donors with steatosis more than 10%. GRWR, cold ischemia time (CIT) was significantly more and remnant volume less in non MHV group. 29.3% of donors had complication (26% Clavien-Dindo grade I, II) with no statistically significant difference among groups. MELD score was higher in MERLG group. One and three year patient survival was similar among different GRWR and type of RLG groups.

Conclusion: Selective and tailored approach for right lobe donor hepatectomy based on optimal functional volume and metabolic demands of both recipient and donor addresses both key issues in LDLT, optimal recipient outcomes and donor safety.

WORLD LIVER CONFERENCE 2018

May 25-26, 2018 | New York, USA

Robotic liver resections –My experience

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Background: The authors present their experience of robotic liver resections in comparison with open surgery.

Methods: Retrospective review of liver resections done robotically from February 2015 to October 2017 compared to cohort of open cases from January 2012 to December 2016.

Results: Nineteen patients in the study group were compared with matched control of 38 open cases. Mean operative duration was 442 ± 135 minutes in the robotic compared to 357 ± 127 minutes in control group ($p = 0.03$). Mean

blood loss was 270 ± 311 ml in the robotic compared to 451 ± 330 ml in control group ($p = 0.06$). Minor complications developed in 17% of robotic cases compared to 41% in open surgery ($p = 0.5$), while major complications occurred in 5.8% of robotic cases compared to 8.8% of open ($p = 0.3$). Mean hospital stay was 5.35 ± 0.8 days for the robotic group and 7.7 ± 4.2 days for open group ($p = 0.02$).

Conclusion: This study highlights the utility of robotics for liver resections with better outcomes and decreased length of stay compared to open surgery albeit at a higher cost at present.

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MiRNA199a-3p controls liver Tumor Microenvironment (TME)

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Increasing significance of tumor–stromal interaction in development and progression of cancer implies that signaling molecules in the tumor microenvironment (TME) might be the effective therapeutic targets for hepatocellular carcinoma (HCC). Here, the role of microRNA miR-199a-3p in the regulation of TME and development of HCC has been investigated by several *in vitro* and *in vivo* assays. Expression of miR-199a-3p was observed significantly low in HCC tissues and its overexpression remarkably inhibited *in vivo* tumor growth and metastasis to lung in NOD-SCID mice. *In vitro* restoration of miR-199a-3p expression either in endothelial cells (ECs) or in cancer cells (CACs) significantly diminished migration of ECs in co-culture assay. Again incubation of miR-199a-3p transfected ECs with either conditioned media (CM) of CACs or recombinant VEGF has reduced tube formation, in ECs and it was also dropped upon growth in CM of either anti-VEGF antibody-treated or miR-199a-3p-

transfected CACs. In addition, bioinformatics and luciferase-reporter assays revealed that miR-199a-3p inhibited VEGF secretion from CACs and VEGFR1 and VEGFR2 expression on ECs and thus restricted cross talk between CACs and ECs. Again, restoration of miR-199a-3p in hepatic stellate cells (HSCs) reduced migration and invasion of CACs in co-culture assay, while it was enhanced by the overexpression of HGF suggesting miR-199a-3p has hindered HSC-CACs cross talk probably by inhibiting HGF and regulating matrix metalloproteinase MMP2, which were found as targets of miR-199a-3p subsequently by luciferase-reporter assay and gelatin zymography, respectively. Thus, these findings collectively highlight that miR-199a-3p restricts metastasis, invasion and angiogenesis in HCC and hence it may be considered as one of the powerful effective therapeutics for management of HCC patients.

WORLD LIVER CONFERENCE 2018

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Transabdominal sonography of the gall bladder & its hepatic & peritoneal perforations

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TransAbdominal Sonography of the Gall Bladder can reveal Hepatic & ExtraHepatic & Peritoneal Perforations of the Gall Bladder, whether it is impending perforations, frank perforations, sealed perforations, concealed perforations & its complications. It can also demonstrate adhesions in the Gall Bladder Fossa at the Right Upper Quadrant. All these cases are compared & proved with gold standards

like Laparoscopic & Open surgery & endoscopy. Some extra efforts taken during all routine or emergent ultrasonography examinations can be an effective non-invasive method to diagnose primarily hitherto unsuspected Gall Bladder impending perforations, frank perforations, sealed perforations, concealed perforations & its complications, so should be the investigation of choice.

WORLD LIVER CONFERENCE 2018

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HGF/R-spondin1 rescues liver dysfunction through the induction of Lgr5+ liver stem cells

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The induction of endogenous adult stem cells by administering soluble molecules provides an advantageous approach for tissue damage repair, which could be a clinically applicable and cost-effective alternative to transplantation of embryonic or pluripotent stem cell-derived tissues for the treatment of acute organ failures. Here we show that HGF/Rspo1 induce liver stem cells to rescue liver dysfunction. Carbon tetrachloride treatment causes both fibrosis and Lgr5+ liver stem cell proliferation,

whereas Lgr5 knockdown worsens fibrosis. The Injection of HGF in combination with Rspo1 increases the number Lgr5+ liver stem cells and improves liver function by attenuating fibrosis. We observed Lgr5+ liver stem cells in human liver fibrosis tissues, and once isolated these cells were able to form organoids, treatment with HGF/Rspo1 promoted their expansion. We suggest that Lgr5+ liver stem cells represent a valuable target for liver damage treatment and that HGF/Rspo1 can be used to promote liver stem cell expansion.