no association was found between stent forces and the occurrence of pain, perforation or hematemesis, except for the stricture fokalata format. The study included 95 patients with benign esophageal stricture.

Conclusion: Both SAEs and recurrence of dysphagia following esophageal stent placement were not associated with RF, AF or degree of elongation. It can be speculated that their occurrence is a multifactorial process determined by a combination of patient- and tumor-related characteristics.

Disclosure of Interest: None declared

OP330 CLINICAL OUTCOMES FOLLOWING STENT PLACEMENT IN REFRACTORY BENIGN ESOPHAGEAL STRICATURE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: The management of benign esophageal strictures is challenging. Common causes are represented by peptic injury, caustic ingestion, radiation treatment and anastomotic anomaly after esophageal resection. The first management strategy includes endoscopic dilation using bougies or balloons. Although the success rates and recurrence rates are low to moderate, about 30% to 40% of patients experience recurrent dysphagia within the first year of follow-up. The management of such relapsing refractory cases consists of repeat dilations. To provide alternative and more definitive treatment option, self-expandable stents have been used. Three different types of stents have been used: metallic (SEMS), plastic (SEPS) and biodegradable stents (BD).

Aims & Methods: We performed a systematic review and meta-analysis to examine the efficacy of stent placement in the long-term resolution of dysphagia in patients with refractory benign esophageal stricture (RBES). PubMed, SCOPUS, Google Scholar were searched (up to January 2015). Studies recruiting adults with RBES treated with stent placement were eligible. The success, complication and migration rates were pooled by means of a random effect model and compared with a 95% confidence interval (CI). Statistical heterogeneity was tested using the Q test (significance level: 0.05) and I^2 statistic. If high levels of heterogeneity among the trials occurred (I^2 > 50% or P < 0.05), the sources of heterogeneity were explored by sensitivity analysis and meta-regression analysis.

Results: Eighty studies (444 patients) were eligible for inclusion. The pooled clinical success rate was 40.5% (95%CI, 31.5-49.5%), yielding an odds of 0.68 (95%CI 0.46-0.98) with high heterogeneity (I^2 = 65.0%). The meta-regressions and meta-regression analysis of the target levels and Fisher's exact test for independence of the target level and factor variables.

Disclosure of Interest: None declared

OP332 PERORAL ENDOSCOPIC REMYOTOMY (RE-POEM): A SALVAGE OPTION FOR PERSISTENT/RECURRENT SYMPTOMS AFTER PREVIOUS POEM

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Introduction: Peroral endoscopic myotomy (POEM) has been described with high success rates for the treatment of achalasia. However, persistence/recurrent symptoms occur after POEM.

Aims & Methods: Our purpose was to evaluate the feasibility, safety and efficacy of salvage peroral endoscopic remyotomy (Re-POEM) for patients after failed POEM. Fifteen patients with persistence/recurrence of symptoms (Eckardt symptom score ≥4) after previous POEM were identified from a prospectively maintained database that included a total of 1454 consecutive achalasia patients. The primary outcome was symptom relief during follow-up, defined as an Eckardt score of ≤3. Secondary outcomes were procedure-related adverse events, lower esophageal sphincter (LES) pressure on manometry, and reflux symptoms before and after Re-POEM.

Results: All patients underwent successful Re-POEM after a mean of 13.5 months (range 4-37 months) from the time of the primary POEM. The mean operation time was 41.5 minutes (range 28-62 minutes). Submucosal tunnel infection occurred in one case and was successfully managed with conservative treatments. During a mean follow-up period of 11.3 months (range 3-18 months), treatment success was achieved in all patients. The mean Eckardt score pre-treatment was 5.6 (range 4-8) and post-treatment was 2.1 (range 0-3). The mean treatment was 33.5% (range 0-100%) with a significant difference in the mean post-treatment score of 1.2 (range 0-3; P < 0.001). Mean LES pressure also decreased from a mean of 25.0 mmHg to 9.5 mmHg after Re-POEM (P < 0.001). The overall clinical reflux complication rate of Re-POEM was 33.33%.

Conclusion: Re-POEM seems to be a safe and effective salvage option for failed POEM, resulting in short-term symptom relief in all patients and without serious complications.

Disclosure of Interest: None declared

TUESDAY, OCTOBER 27, 2015

15:45–17:15

BASIC ASPECTS OF HEPATOCARCINOGENESIS AND REGENERATION – ROOM ES

OP331 PREDICTORS OF PARTIAL VS. COMPLETE SYMPTOMATIC RESPONSE IN PATIENTS WITH ESOPHAGEAL ACHALASIA TREATED BY PER ORAL ENDOSCOPIC MYOTOMY (POEM)

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Introduction: POEM results in treatment success in more than 90% of operated patients. Treatment failure is usually defined as an Eckardt score of ≤2 (ES=0 or 1) or ≥3 (ES=2 or 3) and completed at least 6 months follow up (27 female, 32 male, mean age 48 years). We performed multivariate logistic regression with stepwise selection of predictors and tested equality of means for continuous variables for the two target levels and Fisher's exact test for independence of the target level and factor variables.

Results: Among 59 analyzed patients, 36 (61%) had a complete symptomatic response (post-POEM ES=0-2 patients (39%) had partial symptomatic response (post-POEM ES 1 or 2). The mean age of patients with a complete response was lower(51 vs. 42 years) as well as the frequency of pre-POEM treatments (botulinum toxin injection or pneumatic dilatation; 11% vs. 35%). The patients with a complete symptomatic response had higher both the pre-POEM IRP (mean 30.1 vs. 23 mmHg) and the mean basal LES tonus (44 vs. 32 mmHg). The frequency of type II achalasia was higher in patients with a complete symptomatic response (83% vs. 61%). Both groups did not differ regarding to the procedure related data length of the procedure, length of myotomy, etc. The stage of the disease (duration of symptoms, esophageal width) and the frequency of partial recovery of esophageal peristalsis after POEM (33% vs. 30%) were similar in both groups. Post-POEM esophagitis was more frequent in patients with a complete symptomatic response (36% vs. 26%). In multivariate logistic regression analysis, only age (under 40, p=0.03), pre-POEM basal LES-tonus (under 40 mmHg, p=0.04) and any prior treat-ment for achalasia (p=0.04) have been found as independent predictors of partial symptomatic response.

Conclusion: Among the patients with treatment success, approx. 40% do not have a complete symptomatic response. Younger age, lower pre-POEM basal LES tonus and previous treatment attempts with botulinum toxin or balloon dilatation are independently associated, despite the overall treatment success, with an incomplete symptomatic response.

Disclosure of Interest: None declared

OP333 CONTRIBUTION OF NATIVE AND ACTIVATED HEPATIC STELLATE CELLS IN LIVER REGENERATION AFTER PARTIAL HEPATECTOMY AND 2-ACETYLAMINOFLUOREN INJECTION

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Introduction: Actual problem of modern hepatology is to find new and atho-genetic treatment of liver diseases. One of these methods could be cell therapy with using hepatic stellate cells (HSC), that are thought to be regional stem cell of liver. Experiments on fully isolated rat HSC transplantation confirmed their participation in liver regeneration after partial hepatectomy (PH). However, the role of freshly isolated and activated in vivo HSC transplantation to rats undergoing PH and the injection of 2-acetylaminofluen (AAF) is still unknown.

Aims & Methods: To study the influence of transplanted HSC on activity of liver regeneration after PH and AAF injection.

Before transplantation HSC were labeled by the gene of Enhanced Green Fluorescent Protein (GFP). We selected the classical model of acute liver damage – partial hepatectomy. In one case, we transplanted native HSC, in another – in vivo activated HSC. Activation was carried out by lead nitrate injection into the tail vein of rats donor, HSC were isolated 2 days thereafter.
To inhibit hepatocyte proliferation in the recipient rats, animals were adminis-
tered AAF 5 days before the liver surgery. The cases were sacrificed after 1, 2, 3, 5, 7 and 14 days after the transplantation of HSC. Paraffin slices were stained by immunohistochemistry with antibodies to desmin – marker of HSC and e-SMA- myofibroblast marker.

Regarding desmin-positive hepatocytes were detected (found, stained) in liver parenchyma even at the first days after transplantation. All groups showed an increase in the number of desmin- positive cells in the parenchyma. After transplantation of freshly isolated and activated HSC to rats after PH and AAF administration, the number of desmin-positive cells was found gradually decreased. Desmin-positive HSC in animals after PH without AAF injection retained in the liver longer: in case of freshly isolated HSC transplantation – till the 5th day, after in vivo activated HSC transplantation - till the 7th day. In all groups e-SMA positive myofibroblasts were not detected.

**Conclusion:** Transplantation of native and activated HSC stimulates liver regeneration and contributes to hepatocytes repopulation without the risk of liver fibrosis.

**Disclosure of Interest:** None declared

**OP334**

G-glcNac transferase promotes fatty liver-associated liver cancer through activating JNK and NF-kB pathways

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Immunohistochemical stain of TAA + octreotide group (0.5 mg/kg) for 14 days, a unique glycosyltransferase, is involved in metabolic reprogramming. Using transcriptome sequencing, OGT was identified to be highly expressed in non-alcoholic steatohepatitis (NASH)-associated hepatocellular carcinoma (NASH-HCC) compared to their adjacent non-tumor tissues of 18 patients. However, the role of OGT in NASH-HCC is still unclear.

**Aims & Methods:** We aim to investigate the functional role of OGT in NASH-HCC and its potential clinical implication. The biological function of OGT was determined by proliferation, colonyogenicity, migration and invasion experiments through gain- or loss-of OGT functional assays in vitro and in nude mice. OGT target factors and pathways were identified by promoter luciferase assay, DNA binding activity assay and Western blot. The effects of OGT on oxidative stress, reactive oxygen species (ROS), lipid peroxide and endoplasmic reticulum (ER) stress and ER stress-related cascades were also investigated. The clinical impact of OGT was evaluated in 209 serum samples of 137 NAFLD patients and 72 control subjects by ELISA.

**Results:** OGT upregulated in 12 out of 18 (66.7%) NASH-HCC tumor tissues compared with their adjacent non-tumor tissues by transcriptome sequencing. Enhanced OGT expression was further confirmed in an independent set of 9 pairs of human NASH-HCC tissues (66.7%) by Western blot and in six HCC cell lines and two NASH-HCC cell lines, but silenced in normal livers and weak in immortalized normal hepatocyte cell lines MIHA and LO2. OGT production was significantly induced in MIHA cells treated with insulin (P<0.01) or cholesterol (P<0.01). Ectopic expression of OGT in MIHA and LO2 cells promoted cell growth, cell proliferation and migration, and invasion ability whereas knockdown of endogenous OGT in two NASH-HCC cell lines had opposite effects. Moreover, subcutaneous tumor xenografts of LO2 cells with stable OGT expression in nude mice exhibited an increased tumor growth compared with the control group. Immunohistochemically, OGT induced ROS production, increased lipid peroxide levels and enhanced the protein expression of ER stress markers GRP78 and IRE1α in LO2 and MIHA cells. In this connection, OGT significantly increased endoplasmic reticulum stress (ER stress) and consequently activated JNK and NF-kB pathways. Western blot for p-JNK and p-NF-kB was dramatically reduced when compared with control group.

**Conclusion:** OGT plays an oncogenic role in NASH-associated HCC through activating JNK and NF-kB pathways. OGT production was significantly induced in MIHA cells treated with insulin or cholesterol. The overexpression of OGT could promote proliferation and migration of hepatocytes whereas knockdown of OGT could inhibit the proliferation and migration of hepatocytes.

**Disclosure of Interest:** None declared

**OP336**

Genomic mutations and pathways identified by whole-exome sequencing in NAFLD-associated hepatocellular carcinoma

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Introduction: Epidemiological studies have shown that obesity and its related non-alcoholic fatty liver disease (NAFLD) promotes the development of hepato-
cellular carcinoma (HCC). However, the underlying genetic mechanism of obesity-related HCC is still largely unknown.

**Aims & Methods:** We aimed to uncover the genetic alterations of obesity-asso-
ciated HCC using cross-species oncogenomics and whole-exome sequencing. We performed a comprehensive genome-wide sequencing in genetic obese (db/db) mice and dietary obese mouse keep on high-fat diet was monitored in comparison with wild-type lean mice kept on normal diet treated with diet-induced (DEN). Pair fed HCC tumor and adjacent normal samples from mice were sequenced by whole-exome sequencing and cross-species oncogenomics to reveal genetic alterations.

Candidate mutation genes were further validated in HCC tumor and adjacent normal samples from 16 genetic and 13 dietary obese mice and 16 control lean mice by PCR Sanger sequencing. The bio-functional significance and molecular pathways of the candidate mutation genes was evaluated.

**Results:** Significantly higher tumor incidence, multiplicity and larger tumor size of NAFLD-HCCs were found in both genetic and dietary obese mice compared with those of lean HCCs in wild-type mice. Totally 272 and 388 genes were found to be mutated in liver tumors from obese mice and control lean mice, respectively, with only 8 genes overlapped by whole-exome sequencing. Eight important metabolic or cancer-related pathways were significantly enriched in mutated genes found in obese HCC, whereas only two pathways were enriched in mutated genes found in lean HCC. Mutation frequency of Cel was significantly higher in obese HCC than in lean HCC (34.5% vs. 6.3%, P<0.05). Mutations in hRas were detected in 10.3% of obese HCCs, all located at codon 61, but not in lean HCCs. CEL, activating mutation and hras activating mutation promote liver cell growth. Inactivating mutation in CEL (D645F and D555N) led to the accumulation of cholesteryl ester, which activated ER stress and consequent IRE1α/JNK/i-Jun/AP-1 signaling cascade; while activating mutations in hRas (Q61R and Q61L) activated MAPK and PI3K/Akt signaling cascades to promote cell growth.

**Conclusion:** The genetic alterations of NAFLD-associated HCC are distinguished from that of lean HCC. Mutations in CEL and hRas play important roles in NAFLD-associated hepatocarcinogenesis.

**Disclosure of Interest:** None declared

**OP335**

Antiangiogenic treatment with octreotide attenuates portal hypertension of the cirrhotic rats through somatostatin receptor 2

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Introduction: Angiogenesis is pivotal for the development of portal hypertension in cirrhosis. Somatostatin (SST) and its analogue octreotide are widely used for the management of gastrointestinal varices bleeding. However, the molecular and cellular mechanism of SST and octreotide on portal hypertension remains unclear.

**Aims & Methods:** To investigate the mechanism of octreotide on regulation of portal hypertension.

**Results:** Peritoneal injection of thiacetamide (TAA) was employed to induce liver cirrhosis (200 mg/kg every 3 days for 16 weeks). 36 male Sprague-Dawley rats were randomized into control, TAA and TAA + octreotide with 12 animals in each group. TAA + octreotide group received TAA plus octreotide (50 mg/kg/ day) by i.p. injection 5 days before and after surgery. The animals were sacrificed after 1, 2, 3, 5, 7 and 14 days after the transplantation of HSC. Paraffin slices were stained by immunohistochemistry with antibodies to desmin – marker of HSC and e-SMA- myofibroblast marker.

**Conclusion:** Transplantation of native and activated HSC stimulates liver regeneration and contributes to hepatocytes repopulation without the risk of liver fibrosis.

**Disclosure of Interest:** None declared