ous. Aim was to determine whether coding variants in hTERT and TERT RNA template (hTERC) are enriched in NASH-related HCC.

**Patients and methods:** In 14 consecutive unrelated patients with HCC in NASH-related disease or cirrhosis, or cryptogenic cirrhosis likely resulting from NASH, we re-sequenced hTERT/hTERC coding regions and intron–exon boundaries.

**Results:** We detected novel rare coding variants of hTERT in three patients: Ala67Val in homozygosity, and Pro193Leu and Glu668Asp in heterozygosity (prevalence 21.5%, \( p = 0.013 \) vs. expected rare coding alleles frequency). No mutations were detected in hTERC. Of patients positive for TERT mutations, two were men and one female, mean age was 70 ± 8 years. All presented with a single HCC lesion (p = 0.05 vs. negative patients) of 3.5 ± 1.4 cm (vs. 3.8 ± 1.2) in previously undiagnosed liver disease with compensated cirrhosis (p = 0.06), all had diabetes and were positive for the I148M PNPLA3 variant predisposing to HCC. Mortality was 100% (vs. 65% in negative) at 24 months.

**Conclusions:** hTERT mutations are enriched in patients with NASH-related HCC, may be associated with peculiar clinical features and a poor outcome, and may have implications for family screening in relatives.

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OC-30

**DYSREGULATION OF MICRNORNA EXPRESSION IN PBMCs FROM PATIENTS WITH HCV-RELATED MALIGNANCIES**

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**Introduction:** Hepatocellular carcinoma (HCC) is a major cause of death for malignancy worldwide, and its association with HCV infection has been definitively established. Besides HCC, HCV is of death for malignancy worldwide, and its association with HCV was limited to NHL patients.

**Aim:** We previously showed a down-regulation of miR-26b in peripheral blood mononuclear cells (PBMCs) from patients with HCV-related mixed cryoglobulinemia (MC) or NHL, and an up-regulation of miR-16, miR-21 and miR-155 in NHL patients.

In this study, we analyzed the expression of the same panel of malignancy-associated microRNAs also in PBMCs from HCV patients with or without HCC.

The comparative analysis of miRNA expression between hepatic and lymphatic malignancies could provide some hints on the issue of a differential evolution of HCV infection to HCC or NHL, suggesting the existence of common or distinct pathogenetic pathways and identify new useful biomarkers.

**Methods:** The expression of miR-16, miR-21 miR-26b, miR-146a and miR-155 was analyzed by Real-Time PCR, using miR-let-7b as endogenous control.

**Results:** Data obtained showed the up-regulation of miR-21 and down-regulation of miR-26b in HCC patients compared to controls (p < 0.001). MiR-146a levels were comparable in patients and controls. The expression of miR-16 and miR-155 did not differ in HCC patients and controls, indicating that their deregulated expression was limited to NHL patients.

**Conclusion:** This study shows that some microRNAs are differently expressed in PBMCs from HCV patients who developed HCC or NHL, while others share a common behavior. Thus, the analysis of the expression of microRNAs could represent a non-invasive markers of HCV-related cancerogenesis; this could be suitable both to identify the existence of a malignancy and to discriminate between the two major HCV-related cancers.

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OC-31

**BARCELONA CLINIC LIVER CANCER STAGING AND THE NET BENEFIT OF LIVER RESSECTION FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA: A MULTICENTRE, COHORT STUDY**

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**Background:** The role of hepatic resection for patients with hepatocellular carcinoma (HCC) in different Barcelona Clinic Liver Cancer (BCLC) stages remains controversial due to the scarcity of randomized controlled trials and the intrinsic prognostic heterogeneity within each BCLC stage. Two large prospective databases were merged to measure the net survival benefit of hepatic resection over non-surgical-therapies in each BCLC stage.

**Methods:** Using BCLC stage D, extra-hepatic metastases, and liver transplantation as exclusion criteria, we selected 4713 consecutive HCC patients from one Eastern (n = 2266) and one Western (n = 2447) database. We performed three independent multivariate Cox survival analyses including patient-, liver function-, and tumor-related covariates within subgroups who underwent resection (n = 1340), loco-regional (n = 2406), or supportive care (n = 967). The obtained models were then used to predict individual 5-year life expectancy (LE) with resection compared to loco-regional therapy (LRT) or best supportive care (BSC), in each enrolled patient independently from therapy actually received. The results were expressed as net benefit of resection (proportion of LE variation due to resection over LRT weighted for BSC) using the formula:

\[ \text{LE-resection} - \text{LE-LRT}/\text{LE-BSC}. \]

**Results:** Multivariate Cox survival analysis included the following variables: patient-related (age, nationality), liver function-related (child class and portal hypertension), tumor-related (nodule size, number, and alpha-fetoprotein), and BCLC staging, while treatment (resection, LRT, or BSC) was included as stratifying covariate.

Mean net benefit (95% confidence interval) of resection over LRT significantly increased according to BCLC stage: BCLC 0 = 9.75% (6.04–13.47), A = 13.82% (11.99–15.66), B = 31.46% (28.93–33.98), C = 46.02% (44.39–47.65). Diameter of the largest nodule was the main contributor to this model.
Conclusion: Hepatic resection may result in net survival benefit for HCC patients regardless BCLC stage, provided that technical feasibility and oncological radicality are guaranteed.

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OC-32

A REGRET-BASED APPROACH TO CHOOSE BETWEEN TRANS-CATHETER ARTERIAL EMBOLIZATION AND HEPATIC RESECTION FOR INTERMEDIATE HEPATOCELLULAR CARCINOMA

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Introduction: Trans-catheter arterial chemo-embolization (TACE) is the first-line therapy recommended by western guidelines for intermediate hepatocellular carcinoma (HCC); however, in clinical practice, such patients are often referred to surgical teams for evaluation and treatment. After making a decision under uncertainty, physicians may discover that the alternative approach would have been preferable, imparting a sense of regret. Regret theory postulates that the optimal choice would be the one associated with the least amount of regret, in the case it is proven wrong.

Aim: To apply regret theory to the decision-making of treatment of intermediate HCC.

Methods: Data from 247 cirrhotic patients, resected for intermediate HCC, were used to build a prognostic model and to compute a regret decision-curve analysis (DCA) integrating physician’s preferences expressed in terms of regret associated with surgery and TACE choices. Physician’s treatment preferences were indicated by a threshold probability (Pt) at which the physician is uncertain whether or not perform surgery. A survey among 40 hepatologists and surgeons regarding three hypothetical clinical cases was performed to assess if the physicians’ preferences cluster within relatively narrow domains.

Results: The 3- and 5-year overall survival rates after surgery were 48.7% and 33.8%, respectively. Child–Pugh score, tumor number and presence of oesophageal varices were independent predictors of overall survival after hepatectomy (P<0.05). Regret DCA showed that the use of the prediction model was associated with the least amount of regret until Pt=70%, above which TACE of all patients was the least regretful strategy. The survey pointed to, on average, a significant separation among physicians’ preferences, pointing to the need for separate elicitation of individual preferences of each decision-maker. However, the use of regret DCA uniformed final decisions.

Conclusions: Regret theory provides a new perspective for treatment-related decisions and can be applied in the setting of treatment of intermediate HCC.