death in women (RR = 1.17, 95% CI 1.06–1.29, 2p = 0.003; attributable fraction 3%), but fewer women (17%) than men (62%) were smokers, and their cigarette consumption per smoker was lower.
**Conclusion:** This study goes to show that even though liver cancer from tobacco use kills about 200,000 people yearly in these three developing countries, the deaths from lung cancer (1.5 million yearly worldwide) is still higher than liver cancer deaths.

**736**

## POLYMORPHIC CYP GENES AND ABC-TRANSPORTER GENES IN HEPATOCELLULAR CARCINOMA

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**Background:** Detoxication and biliary secretion of endogenous and exogenous substances (e.g. drug, xenobiotics) in the liver are important to prevent accumulation of mutagens/carcinogens in hepatocytes. This serial process is maintained by drug metabolizing enzymes (mainly cytochrome P450) and drug transporters (ABC-TP). Genetic mutation(s) of these proteins may impair the protective system against accumulation of hazardous compounds leading to hepatocellular carcinoma (HCC).
**Methods:** We analyzed the genetic polymorphisms of (1) major CYP proteins and (2) ABC efflux-TP using DNA samples of hepatitis C-seropositive HCC Japanese patients, and compared with healthy Japanese.

1. We identified seven mutant alleles and related CYP genotypes in HCC patients (n = 44): *1C heterozygous, *1C homozygous and *1F homozygous for CYP1A2; *4A homozygous for CYP2A6, *2A/*3 heterozygous, *2A/*3 homozygous and *2A and *3 heterozygous for CYP2C19; and *10/*5 homozygous for CYP2D6, and compared the frequencies with those reported for healthy Japanese.
2. We searched for 11 single nucleotide polymorphisms (SNPs) in efflux ABC-TP (MRP2, BSEP, BCRP and MDR1) to identify HCC susceptibility genes in HCC patients (n = 58), and compared the frequencies with healthy subjects.

**Results:**

1. There were no significant differences in genetic mutant alleles between two groups, except for CYP2A6*4A homozygous genotype. The frequency of this genotype was significantly higher in HCC patients than in healthy Japanese (0.144 vs. 0.034; $P < 0.05$; odds ratio 3.36).
2. No significant association was found in all SNPs when single genes were tested. SNP combinations of 3435C>T in MDR1 and 825T>C in MRP1, 3435C>T in MDR1 and (CTCT) deletion in BSEP, and 825T>C in MRP1 and (CTCT) deletion in BSEP increased the risk of HCC, with morbidity odds ratios 3.8–4.5.

**Conclusions:** Some genotypes of CYP or combinations of SNPS of ABC efflux-TP may increase the risk of hepatocarcinogenesis leading to HCC in HCV(+) chronic hepatitis patients. Further studies of the precise mechanism are warranted.

**737**

## INTRAOPERATIVE APPLICATION OF REAL-TIME TISSUE ELASTOGRAPHY FOR FOCAL LIVER LESIONS. THE INITIAL EXPERIENCE USING MINI PROBE FOR INTRAOPERATIVE USE

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**Background and Aims:** Intraoperative Ultrasonography (IOUS) is regarded as an essential diagnostic tool to make the precise intraoperative diagnosis and perform the adequate resection. Real-time tissue elastography (RTE) visualizes the information of tissue elasticity applicating the principle of ultrasonography. The aim of this study is to investigate the feasibility and efficacy of intra-operative RTE (IORTE) in clinical setting.
**Methods:** Between October 2010 and August 2011, IORTE was performed for 70 hepatocellular carcinomas (HCCs), 54 adenocarcinomas, 19 other malignant tumors (ex. neuroendocrine tumor), 13 benign solid tumors (ex. hemangioma), and 15 liver cysts, after routine B-mode IOUS during hepatectomy. Elasticity images were classified into six types, from type1 (even strain) to type6 (no strain), according to the degree of strain contrast with the surrounding liver [modified elasticity type of liver tumor (mod.ETLT)]. Then, we examined the compliance of mod.ETLT with the pathological diagnosis or diagnostic imaging. We also compared the diagnostic performance of IORTE with B-mode IOUS.
**Results:** Elasticity images were obtained for all malignant tumors. With mini-linear probe, 55 of the 66 HCCs were classified as type 3 or type 4 or type 5, with a sensitivity of 83%, a specificity of 60%, and an accuracy of 70%. Meanwhile, 36 of the 53 adenocarcinomas were classified as type 6, with a sensitivity of 68%, a specificity of 96%, and an accuracy of 86%. Additionally, 11 of the 12 benign solid tumors were classified as type 1 or type 2, with a sensitivity of 92%, a specificity of 92%, and an accuracy of 94%.IORTE was performed for 59 lesions within 1.5 cm in diameter. Among 59 lesions, IORTE clearly depicted 11 lesions with obscure contour on B-mode (19%) and 6 undetectable lesions on B-mode (10%) successfully with sufficient contrast.
**Conclusions:** Using a new criteria, Mod. ETLT, IORTE was useful in the differential diagnosis of liver tumors, especially, IORTE was most helpful in distinguishing adenocarcinomas from benign tumors. IORTE could assume a large role in future intra-operative diagnosis.

**738**

## THE IDENTIFICATION OF POSSIBLE GENETIC PROFILE OF BIOMARKER IN THE EARLY DIAGNOSIS OF HEPATOCELLULAR CARCINOMA AMONG EGYPTIAN PATIENTS WITH CHRONIC HEPATITIS C

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**Background:** Hepatocellular carcinoma (HCC) is a multi-step process associated with changes in gene expression. Gene expression of biomarkers could be used for early diagnose of HCC.
**Aim:** Determine a possible genetic profile for early detection of HCC in Egyptian patients with chronic hepatitis C by assessment of tissue expression of Glypican-3 (GPC-3), Paternally expressed gene 10 (PEG-10), Midkine (MDK), Serpin peptidase inhibitor (SERPINI1), and Ubiquinol-cytochrome (QP-C).
**Patients and Methods:** Prospective study was conducted on 70 patients with hepatitis C related chronic liver disease and HCC patients, they were categorized into four groups; chronic hepatitis C group (n = 25), post-hepatitis C compensated cirrhosis group (n = 24), HCC group (n = 21) in addition to 7 healthy individuals who were candidates for living donor related transplantation. All patients were subjected to clinical assessment and routine laboratory investigations, imaging procedure in addition to liver biopsy. HCC patients were diagnosed according to AASLD guidelines 2005. Liver tissue obtained from all patients was subjected to total RNA extraction, reverse transcription of extracted RNA into cDNA and finally tissue expression of GPC-3, MDK, PEG-10, SERPINI1 and QP-C by qRT-PCR.
The ROC curves were performed to determine the best cutoff, sensitivity and specificity values for the candidate genes that could differentiate HCC from non-cancerous patients.

**Results:** A significant increase in the tissue expression of GPC-3, MDK, SERPINI1, and QP-C was detected in HCC tissue compared to non-cancerous liver tissue, in contrast to PEG-10 which was significantly expressed in chronic hepatitis C patients. The ROC curves was able to identify best cutoff values, sensitivity and specificity for GPC-3 (7.26, 81%, 58%), SERPINI1 (0.16, 80%, 70%), MDK (3.8, 60%, 70%) and QP-C (0.45, 65%, 79%) respectively. There was no significant correlation between the level of any of markers expression and the size of hepatic focal lesion.

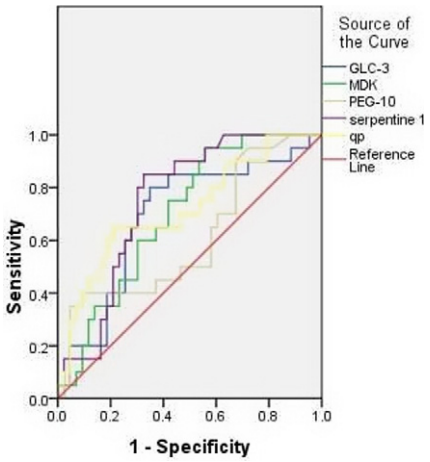


Figure 1. ROC curve. Diagonal segments are produced by ties.

**Conclusion:** Tissue expression of GPC-3, MDK, SERPINI1, and QP-C was highly expressed among HCC patients. This could highlight the importance of these biomarkers as a potential genetic profile for the early detection of HCC.

**739**

**PSYCOLOGICAL PROFILE AND HEALTH RELATED QUALITY OF LIFE (HRQOL) IN PATIENTS WITH HEPATOCELLULAR CARCINOMA (HCC)**

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**Background and Aims:** It is well known that in some tumors (e.g. lung or breast) psychosocial interventions may reduce negative feelings and enhance HRQOL. The effects of psychological variables on HRQOL of patients with HCC have been rarely evaluated as well as the interaction between physical and psychological variables in relation to HRQOL. The aim of this work is to evaluate the behavioral and psychological profile of a group of patients with HCC and to correlate it with the HRQOL and prognostic features.
**Methods:** We enrolled 32 consecutive patients with HCC (median age 71 yrs, range 56–82; BCLC stage: A 17, B 4, D 3; Child A 29, B 3; male 23). On outpatient setting and before having information on his own clinical condition, each subject underwent administration of the following questionnaires: SF 36 for the evaluation of the HRQOL; Hamilton-D (quantitative evaluation of depression; positive for scores ≥8); Symptom Check List SCL 90 for the evaluation of general psycopathologic profile (nine items, each positive for score >1); Toronto alexithimia scale (TAS) (positive if score ≥60).
**Results:** 25% of patients exhibited significant values for hostility and paranoid ideation of the SCL 90 test; TAS: 53.8% of patients is positive for alexithimia and 12.5% borderline; Hamilton D: 48% is positive for depression. Pearson correlation test showed: a positive significant association between Hamilton D and the following SCL 90 items: somatization, obsession, interpersonal sensitivity, depression, anxiety, fobic anxiety; a positive association between alexithimic features and emotional reactions (somatization and hostility). SCL 90, Hamilton D and TAS scores increase in Child and BCLC stage higher values. SF 36 questionnaire showed low values for physical role (M±DS: 49±45, C.I. 15.6) and emotional role (43±42, C.I. 14.5); for Child A HCC patients these values were significantly lower than those reported for normal subjects and Child A cirrhotic patients.
**Conclusions:** To our knowledge this is the first report on the psychological profile patients with HCC; the results open questions on the role and the directions of psychological interventions that may improve the quality of life of patients before treatment and in the long term follow up.

**740**

**COFFEE REDUCES OXIDATIVE DNA DAMAGE IN PATIENTS WITH HCV-RELATED CHRONIC HEPATITIS BOTH AFTER ACUTE AND CHRONIC EXPOSURE**

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**Background and Aims:** Coffee is a complex mixture of chemical species containing many different types of antioxidant molecules. Many epidemiological and experimental studies demonstrated the protective properties of coffee against the risk of hepatocellular carcinoma (HCC). The aim of this study, divided into a randomized prospective and a retrospective part, was to assess the extent of genomic oxidative damage in relation to liver inflammation and viral load in HCV-related chronic hepatitis. The molecular mechanisms of HCV pathogenesis are not yet fully known, but oxidative stress seems to have a key role in the progression of liver damage.
**Methods:** We recruited 37 patients with HCV-related chronic hepatitis for the prospective part of the study. Patients, before entering to the study, were randomized in two groups, respectively, or to take 4 coffee/day or to remain abstinent from drinking it. After 30 days, the two groups were reversed for intake/withdrawal. In the retrospective part of the study 69 patients with HCV-related chronic hepatitis, who performed a liver biopsy between 2000 and 2011, were contacted. The patients were sub-divided into 2 groups according to their routine coffee consumption: 0–2 and 3–5 coffees/day.
In this study we evaluated, both in blood and in tissues samples, the following parameters: liver function tests by routine clinical procedures, viral load by nested PCR and 8-hydroxydeoxyguanosine (8-OHdG) through HPLC-ED.
**Results:** Both in the randomized prospective and retrospective part of the study, liver function tests (in particular GGT) were lower in relation to higher coffee consumption; viral load was significantly higher ($p = 0.05$), although increases higher than one logarithm were never documented, and 8-OHdG levels were significantly lower ($p = 0.05$), in patients with higher coffee consumption or during acute exposure.
**Conclusions:** In this study, we demonstrated that the coffee intake acts positively on liver function indices and reduces the 8-OHdG levels, marker of DNA oxidative damage, probably mediating the protection with respect to progression to HCC. The meaning of the increased in viral load in patients who consume more coffee or after acute exposure remains to be elucidated.