T-02

Impact of multidisciplinary team approach to liver tumors: 5-Years experience

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Background: Multidisciplinary team (MDT) approach is a major requirement to guarantee a fair access to treatment to heterogeneous patients with liver neoplasms and to improve the quality of care provided. This work retrospectively analyzes the impact of MDT experience at our tertiary center.

Methods: Between 2011 and 2016, 490 consecutive patients with a liver mass were discussed at standardized meetings involving hepatologists, radiologists, surgeons, pathologists, oncologists. Patients with HCC were assigned a BCLC stage, treated accordingly BCLC recommendation whenever possible and followed-up as per AASLD/EASL guidelines (median f-up: 26 months).

Results: Out of 490 patients, 70% had a HCC diagnosis, 5% cholangiocarcinoma or metastasis and 25% benign liver nodules. Among 341 HCC patients, 55% were BCLC 0/A, 29% BCLC B and 15% BCLC C. Of them, 80% received treatment after the first MDT discussion. Patients with BCLC B stage had significantly more treatments (2.5 ± 0.9 treatments per patient), compared to BCLC 0/A (1.3 ± 0.1) and to BCLC C (1.2 ± 0.5, both $p < 0.05$). First-line BCLC recommendations for therapy were followed in 67%, 59%, 32% of cases for BCLC 0/A, B, C respectively. In 274 HCC patients managed until February 2015 (median f-up: 30 months), median survival from first MDT discussion was 37 months. Main predictors of outcomes were BCLC stage (5-years survival in BCLC 0/A 54%, B 21%, C 23%, $p < 0.0001$), CHILD score (5-years survival CHILD A 42%, B 20%, C 0%, $p < 0.0001$) and first treatment applied (survival at 5 years from OLT 90%, resection 49%, ablation 40%, TACE 28%, sorafenib 15%, $p < 0.0001$)

Conclusions: A MDT approach to HCC patients allowed a rational revision of treatments suggested by BCLC recommendations in 30% to 70% of cases; this discrepancy did not affect survival outcomes, indicating that the difficulties related to the applicability of the current guidelines in the clinical practice could be overcome by a MDT approach.

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T-03

In experimental liver cirrhosis impaired secretion of renalase into blood may lead to organ damage and sympathetic overactivity

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Introduction: Sympathetic overactivity and generation of pro-oxidant molecules are crucial in liver fibrogenesis and functional renal failure of advanced cirrhosis. Renalase (REN), 38 kDa amine oxidase with just 13% aminoacid identity with monoamine oxidase A, is secreted into the blood and clears plasma from excess catecholamines. Isomers of β-NAD(P)H are also substrates for tissue REN, a reaction leading to H_2O_2 and β-NAD(P)$^+$ production in liver and kidney.

Aims: To study plasma and tissue content and function of REN in experimental preascitic and ascitic cirrhosis.

Methods: In normal rats (group G1), rats with CCl_4-dependent liver cirrhosis without ascites (G2) and with ascites (G3) we evaluated: REN levels and activity in plasma, liver and kidney; REN gene transcription and immunohistochemical localization in both organs; liver histology and matrix deposition, hormonal status and kidney function.

Results: In plasma, mature (38 kDa) REN and REN activity, well detected in normal rats, were virtually absent in rats with compensated or ascitic cirrhosis ($P < 0.01$ vs. G1). In G2 and G3 rats, but not in G1, we found large amount of enzymatically active high-molecular weight (78 kDa) REN and very little 38 kDa protein in hepatocytes of regenerative nodules of the cirrhotic liver and in kidney tubules. RT-PCR confirmed higher levels of REN gene transcription in both liver and kidney of G2-3 ($P < 0.03$ vs. G1). Rats with preascitic liver damage showed increased plasma catecholamines, normal renin-angiotensin system activation and subtle sodium retention, while ascitic rats had both secondary aldosteronism and increased adrenergic activation.

Conclusions: Active 78 kDa REN accumulates in diseased liver and kidney and generates H_2O_2 and other pro-oxidant molecules, but release of mature (38 kDa) REN into the circulation is almost absent, leading to increased levels of catecholamines and early sodium retention in preascites.

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T-04

A novel role for heparanase in the onset of liver fibrosis

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Introduction: Activation of both Kupffer cells and hepatic stellate cells (HSCs) plays a fundamental role in fibrosis process. Heparanase (HPSE) is the only mammalian endoglucuronidase capable of cleaving heparan sulfate (HS) chains of HS proteoglycans. The involvement of HPSE in chronic liver disease has not been demonstrated so far.