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Circulating microRNAs as promising non-invasive molecular biomarkers of HCC

A. Salvi [1], M. Manganelli [1], I.Grossi [1], G. Baiocchi [2], N. Portolani [2], G. De Petro [1]

[1] *Department of Molecular and Translational Medicine, Division of Biology and Genetics, University of Brescia, Italy*
[2] *Department of Clinical and Experimental Sciences, Surgical Clinic, University of Brescia, Italy*

Introduction: Human hepatocellular carcinoma (HCC) is the most frequent primary tumor of the liver and is the third cause of cancer-related deaths. The prognosis of HCC is poor and thus the identification of novel molecular biomarkers for the early diagnosis in at-high risk patients is needed. Circulating microRNAs (miRs) have been detected in different human body fluids, including serum, plasma and urine.

The main aim: of our study was the identification of given miRs as circulating molecular biomarkers of HCC. To accomplish this task we measured the levels of microRNA–23b and –126–3p in the plasma from HCC patients.

Materials and methods, results and conclusions: We studied the circulating expression levels of these miRs by Real-Time PCR and digital drop PCR (ddPCR), because we had previously found their downregulation in HCC tissues respect to their matched peri-tumoral (PT) counterparts. Here, we found that the levels of circulating miR–23b–3p measured by ddPCR were significantly lower in HCC patients ($n = 25$) respect to healthy subjects ($n = 37$) and the ROC analysis displayed a discrete capability of miR–23b–3p to discriminate HCC from controls individuals (AUC = 0.67; $p = 0.019$). The same trend of dysregulation was observed for plasma circulating miR-126–3p. The ROC curve analysis performed on 25 controls and 25 HCC patients supported the diagnostic potential of circulating miR–126–3p (AUC = 0.78; *P*–value = 0.0007). In the same cohort, the expression levels of the tumor suppressor lncRNA GAS5 were significantly lower in HCC patients compared to healthy subjects. The ROC curve analysis evidenced a good diagnostic potential of GAS5 (AUC = 0.72; *P*–value = 0.007). In conclusion, our results contribute to identify potential novel non-invasive biomarkers of diagnosis of HCC and prone us to study the dynamic changes of these non-coding transcripts in the liquid biopsy of HCC patients in response to therapy.

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SCCA-IgM in hepatocellular carcinoma patients treated with transarterial chemoembolization: gender-related differences

F. Pelizzaro [1], F. Soldà [1], R. Cardin [1], A. Imondi [1], A. Sartori [1], B. Penzo [1], A. Sammarco [1], C. Aliberti [2], A. Vitale [3], U. Cillo [3], F. Farinati [1]

[1] *Department of Surgery, Oncology and Gastroenterology, Gastroenterology Unit, University of Padova, Padova, Italy*
[2] *Department of Radiology, AOP-University of Padova, Padova, Italy*
[3] *Department of Surgery, Oncology and Gastroenterology, Hepatobiliary Surgery and Liver Transplant Unit, University of Padova, Padova, Italy*

Background: Squamous Cell Carcinoma Antigen (SCCA)-IgM proved to be useful in defining hepatocellular carcinoma (HCC) patients' prognosis. Gender has an impact on SCCA-modulated p53 and mTOR activity, but no studies evaluated its predictive capacity according to sex.

Aims: Aim of our study was to investigate gender-related differences in SCCA-IgM determination, in particular regarding its prognostic role, in hepatocellular carcinoma (HCC) patients treated with transarterial chemoembolization (TACE).

Materials and methods: SCCA-IgM levels where determined in a group of 208 consecutive patients treated with TACE. In a subgroup of 149 a second determination was obtained 4 weeks after the treatment, when the control CT was performed. Associations with clinical and tumor characteristics, response to treatment and survival were evaluated.

Results: The male and female subgroups differed in sample size (80 % males and 20 % females), age, etiology, MELD, MELD-Na, number of nodules, presence of metastases and AFP levels. There was no difference in SCCA-IgM levels according to gender. Higher SCCA-IgM levels were detected in males with advanced ITALICA prognostic score (> 3) and in females with earlier stage tumors ($\leq$ 3). SCCA-IgM levels and their variation after TACE were not associated with radiological response. At the established cut-off (130 AU/mL), in the overall population SCCA-IgM was not efficient in predicting the prognosis. However, when males and females were separately considered, an opposite behavior was observed: males with SCCA-IgM levels below the cut-off had a longer overall survival (35.7 vs. 20.8 months; $p = 0.007$); in contrast, females with marker levels below it had a worse prognosis (15.7 months vs. 36.4 months; $p = 0.01$).

Conclusion: SCCA-IgM predicts survival differently according to gender. More studies are needed to confirm our data, clarify the prognostic role of SCCA-IgM according to gender and identify the mechanisms underlying this different, gender-specific, behavior.

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[1] giuseppina.depetro@unibs.it.