PhD Thesis - ABSTRACT

Clinicopathological and histogenetic features of patients with hepatocellular carcinoma, after liver transplantation or surgical resection

PhD student: Decebal FODOR
PhD supervisors
Prof. Ioan Jung, MD, PhD –"G.E. Palade" UMPhST Târgu-Mureş - Romania
Prof. László Kóbori, MD, PhD – Semmelweis University, Budapest - Hungary

Introduction: Understanding of hepatocellular carcinoma (HCC), from experimental to oncologic steps, is far to be elucidated. Despite improving the therapeutic approach, it still represents the sixth cancer-related incidence and fourth place in cancer-related deaths. Most of the patients died in their first 12 months after diagnosis. A significant increasing incidence was reported from 1990 to 2015. For this reason, liver transplantation was considered as a gold standard for saving lives. It is still difficult to do a proper selection of patients for whom transplantation might be the best therapeutic decision. One of the criteria used for patients' selection is known as the" Milano criteria". It was proved that the best overal survival rate can be obtained in aptients with a single tumor ≤ 5 cm or maximum three tumors ≤ 3 cm, without vascular invasion. In the present PhD thesis, the PhD student, under coordination of two professor from two countries, aimed to present a transdisciplinary approach of HCC, from basic to clinical examination of the cases.

In ***first study*** it was hypothesized that the overall survival is mainly based on the selection criteria of patients who can benefit by liver transplantation. It was considered a long-term examination of the results and it was proved that, for patients from eastern Europe, the "Milano criteria" are the most suitable parameters used to improve the 3-year overall survival rate. Moreover, the survival rate of these patients was similar with those obtained after transplantation for cirrhosis.

The second study was focused on patients with HCC from the" waiting list". If transplantation is not possible, it was proved that Transarterial Chemoembolization with Lipiodol (TACE) might pe a short-term solution for tumor shrinkage. It was even proved that the extension of post-TACE tumor necrosis area does not depend on the histological grade of differentiation.

The third study of the PhD thesis considered the pathologist point of view about HCC. As the AJCC staging system is frequently modified, it was aimed to examine the clinical impact of the eight edition of AJCC which was compared with the seventh edition. It was observed that the T2 stage was sub-divided and down-staged, without prognostic impact. However, the proposed division is very useful for the pathologist, who should classify the tumors, based on AJCC rules.

The last study included in the PhD thesis was focused on angiogenesis of HCC. The authors performed an immunohistochemical (IHC) approach of HCC and examined the angiogenic profile of tumor cells in correlation with the type and density of the intra- and peri-tumoral vessels. It was concluded that, although an oscillating character is proved for the angiogenic immunophenotype, some characteristics might have prognostic impact. In patients with HCC and cirrhosis, angiogenesis seems to be mediated via VEGF. In contrast, the non-cirrhotic patients, rather developed a COX-2 mediated angiogenesis. If this fact are experimentally proved, the newest clinical trials might have superior results if are based on the angiogenic pathways.

This complex approach of HCC open new gates for understanding genesis, evolution and therapeutic management of patients with such tumors.

Final conclusions: 1. If serious criteria of selection, such Milano criteria, are used to identify those patients with HCC who can benefit by transplantation, the results can be amazing, with even curative role; 2. In patients with HCC who cannot benefit by transplantation, TACE might be the intermediary gate between chemotherapy and transplant and can induce tumor downstaging and necrosis, independently from the histological grade of differentiation; 3. The newest AJCC system is friendly to be used by pathologist but does not add prognostic impact; 4. The antiangiogenic therapy can be sued as a therapeutic option, for patients with HCC, but its implementation needs to be based on the angiogenic pathway of tumor cell, being based on anti-VEGF or anti-COX-2 medications.