

UNIVERSITY OF MEDICINE AND PHARMACY OF TÂRGU MUREȘ

DOCTORAL SCHOOL

**HEPATIC TUMORS: STAGE-SPECIFIC INCIDENS AND COMPLEX METHODS USED
FOR THEIR DIAGNOSIS**

DOCTORAL THESIS

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ABSTRACT

In this doctoral thesis we intended to perform a complex statistical study focussed upon the classical clinicopathological parameters of primary and secondary hepatic tumors. In case of primary tumors, these parameters were correlated with a prognostic immunohistochemical panel, in hepatocellular carcinoma (HCC) respectively intrahepatic cholangiocarcinoma (IHCC). The last goal of the thesis was to examine the particularities of angiogenesis in primary hepatic tumors.

To reach the previously named objectives, an eight-year retrospective study (2004-2011) of primary and secondary hepatic tumors diagnosed at Department of Pathology of Emergency County Hospital of Tîrgu-Mureș, Romania, was performed. In this period of time a number of 748 hepatic tumors were diagnosed; 264 of them were primary tumors (35,29%), the other 484 being liver metastases (64,71%).

For the immunohistochemical study on tissue microarray, five antibodies (p53 protein, COX-2, VEGF, CD31 and CD105) were used to process the cases of HCC and IHCC. The CD31 and CD105 were used to study the intensity of tumor angiogenesis, respectively the endothelial area (EA). For its quantification, a semi-automatic method was applied (ImageJ NIH's software).

The conclusive results drawn from our study are as follows:

o in case of primary hepatic tumors

- HCC was predominated, followed by IHCC
- Male predominance was characteristic, in both HCC and IHCC
- A significant proportion of HCC presented associated-cirrhosis or other alcohol-related injuries
- Most of the primary benign tumors were cavernous hemangioma, followed by simple serous liver cyst, both of them being especially diagnosed in females

o in case of secondary hepatic tumors

- Most of the cases were metastatic carcinomas, the commonest origin of the primary tumor being the gastrointestinal tract (colorectal, pancreatic and gastric carcinomas)
- Males were predominantly affected in the seventh decade of their life; the only exception was the metastasis provided from gallbladder that presented a female preponderance

O results of the immunohistochemical study

- An overexpression of COX-2 was revealed by well differentiated tumors (HCC and IHCC), compared to the poorly differentiated ones, and also by HCC that do not presented associated-cirrhosis and/or Mallory bodies
- A lower p53 positivity was identified in the well differentiated tumors (HCC and IHCC) compared to the poorly differentiated ones
- Well differentiated tumors (IHCC and HCC) presented a higher VEGF (Vascular Endothelial Growth Factor) intensity, compared to the poorly differentiated ones
- In case of HCC, EA decreased at the same time with increasing of tumor stage
- EA was higher in HCC associated with cirrhosis, steatosis and/or Mallory bodies compared to the cases that showed associated-hepatitis and/or cholestasis
- EA was directly correlated with VEGF intensity, in both HCC and IHCC and reversly correlated with COX-2 expression, in case of IHCC

ORIGINAL CONTRIBUTIONS

- Performing of a complex statistical and immunohistochemical study, identifying the specific parameters that could have a prognostic and/or predictive role in primary malignant tumors of the liver
- Elaborating of a standard model of histological report to be used in the daily diagnosis of primary malignant hepatic tumors