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Immunohistochemical and molecular profile of Epithelial Mesenchymal Transition Markers in Hepatocellular carcinoma patients in Egypt

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Statement of the Problem: The currently used clinical and pathologic prognostic parameters are not fully valid in all hepatocellular carcinoma (HCC) cases since HCC is highly heterogeneous and tumors with similar clinical and pathological features may behave differently. The achievement of comprehensive molecular classification of HCC may hopefully help in identifying valuable therapeutic targets. The role of epithelial-mesenchymal transition (EMT) markers have been investigated in various cancers with few studies on HCC and no reports are available from Egyptian HCC patients. The purpose of this study is to identify novel tissue biomarkers that can be used as reliable prognostic factors to predict recurrence and metastasis in HCC patients.

Methodology & Theoretical Orientation: HCC liver tissue specimens from 100 patients, who underwent hepatectomy with available follow-up data, were immunostained with E-Cadherin, Keratin, Vimentin, N-Cadherin, Integrins, CDX2, Stat-3, SNAIL, Slug, Zeb1 and Twist. Real-time PCR was performed to analyze the molecular profile of EMT. Results of immunostaining were correlated with the clinicopathological features, molecular profile as well as the follow-up data.

Findings: Upregulation of Keratin, Vimentin, and E-Cadherin expression profile were significantly correlated with extrahepatic recurrence after 12 months following curative surgery ($p < 0.001$, $p = 0.001$, $p < 0.001$) and after 24 months ($p < 0.001$, $p < 0.001$, $p < 0.001$) respectively. Moreover, Keratin, Vimentin and E-Cadherin expression profile were significantly correlated with microvascular invasion ($p = 0.015$, $p = 0.015$, $p = 0.11$) respectively. None of N-Cadherin, Integrin, CDX2, STAT3, Zeb1, Twist, SNAIL and Slug were correlated with extrahepatic recurrence following curative surgery or microvascular invasion. No correlation was detected between any of the 11 EMT markers and AFP level, advanced AJCC tumor stage or tumor histological grade.

Conclusion & Significance: EMT expression profiles are useful prognostic markers for recurrence in HCC patients. High Keratin, Vimentin, and E-Cadherin expression profile are closely associated with advanced tumor stage, microvascular invasion, and metastasis indicating poor tumor behavior.

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