Abstract

Background & Objectives

Patients with stage II CRC have a varying survival outcomes, Therefore, it is critical to identify new prognostic and predictive biomarkers that can help to identify more aggressive disease forms among stage II patients and to individualize therapy accordingly. MicroRNAs (miRNAs) are small, noncoding, single stranded RNAs that regulate gene expression post-transcriptionally. Present findings have indicated that miRNAs are differently expressed in normal and neoplastic colon tissues and they can distinguish CRC tumors according to histopathologic, prognostic, and predictive characteristics. The aim of this prospective study was to identify the potential prognostic value of five suggested miRNAs, namely; miR-21, miR-498, miR-137, miR-145 & miR-320, in patients with stage II CRC. Also, this study assessed the concordance between tissue and blood miRNAs.

Patients and Methods:

This study included 124 patients with stage II CRC who attended the NCI - Medical Oncology clinics during the period from January 2004 to December 2014. All patients included in the study received treatment and were followed-up in the NCI during the last 10 years. The expression levels of the five studied miRNAs were examined by qRT-PCR analysis. Additionally, blood samples were drawn from 41 patients recruited in the study in the last 3 years of recruitment to assess the level of miRNAs in blood.

Results:

Assessment of miRNAs in tumor tissues of 124 patients showed that miR-137, miR-145 and miR-320 were significantly under-expressed in 39.5%, 38.4% and 52.4% of cases, respectively while miR-21 and miR-498 were significantly over-expressed in 48.4% and 40.3%, respectively. On the other hand, assessment of these miRNAs in the blood of 41 cases revealed that miR-137, miR-145 and miR-320 were significantly under-expressed in 46.3%, 46.3% and 51.2% of cases, respectively while miR-21 and miR-498 were significantly over-expressed in 46.3% and 43.9%, respectively. After a median follow up period of 27 months ranging from 3 to 152 months. The 5 & 10 year DFS were 60.2% & 45.6%, respectively. The 5 & 10 year OS were 69.1& 56.5%, respectively. The significant correlations with survival were found only in tissue but not with blood miRNAs. The concordance between tissue and blood was weak with miR-320 and miR-145 (kappa 40-65%) and it was considered intermediate with miR-498 and miR-137 (kappa 65-75%) while strong concordance has been achieved with miR-21 (kappa 75-85%). Performance status, over-expression of miR-21 and miR-498 and under-expression of miR-137, miR-145, and miR-320 were associated with inferior DFS and OS in a univariate analysis. In a multivariate analysis, deregulated miR-498 and miR-320 were independent prognostic factors for worse DFS, while over-expressed miR-498 and miR-21 were found to be independent prognostic factors for inferior OS.

Conclusion & Recommendations:

MiRNAs play an important role as prognostic markers in resected stage II CRC patients. Assessing the concordance between tissue and blood miRNAs has had a potential ability to give an idea about prognosis of CRC tumors via a non-

invasive method, when the tissue blocks are unavailable or lost. However, drawing a definitive conclusion about the concordance needs a larger number of studied patients and a longer period of F/U. Large-scale collaborative efforts are still absolutely essential to aid in determining the clinical potential of miRNAs as diagnostic, prognostic, and predictive biomarkers in CRC, and also to help in tailoring the chemotherapy regimens according to the molecular markers in order to achieve better survival rates.

Keywords: Stage II CRC, MicroRNAs, Prognosis.