IMPAIRED BONE METABOLISM IN MULTIPLE MYELOMA ASSESSED BY THE BONE MARKERS SCLEROSTIN AND DICKKOPF-1

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Objective: Multiple Myeloma (MM) is one of the most frequent hematological malignancies leading to bone destruction with serious consequences on morbidity and mortality. We aimed to evaluate serum levels of sclerostin and Dickkopf-1 (DKK1) as bone destruction markers in newly diagnosed patients with MM.

Design: Thirty-two newly diagnosed patients (28 with MM and 4 with monoclonal gammopathy of undetermined significance (MGUS)) and 33 age matched healthy controls were enrolled in this study. Serum levels of sclerostin and DKK-1 were measured by ELISA. All symptomatic patients were divided into two groups (G) in respect to their whole-body low dose CT evaluation: G1 – 9 patients with 0-3 osteolytic lesions and G2 – 19 patients with >3 osteolytic lesions and/or pathologic fractures. Descriptive analysis, Mann-Whitney test for assessment of differences between groups and non-parametric correlation analysis were performed using GraphPad Prism v8.01.

Results: The median serum levels of sclerostin and DKK-1 from MM patients were higher compared to controls (513.7 ng/ml vs 74.76 ng/ml, $p<0.001$ and 62.49 pg/ml vs 46.62 pg/ml, $p<0.001$, respectively). Higher levels of both markers were found in G2 patients compared to G1 and controls (G2 vs G1, $p=0.082$ and G2 vs controls, $p<0.001$ for sclerostin; G2 vs G1, $p=0.022$ and G2 vs controls, $p<0.0001$ for DKK1). No statistical difference was found for both markers between MGUS patients and controls. A moderate correlation between sclerostin and β2-microglobulin (Spearman $r=0.546$, $p=0.05$) and between DKK and β2-microglobulin (Spearman $r=0.637$, $p=0.04$) was also observed.

Conclusion: Serum levels of sclerostin and DKK-1, inhibitors of the canonical Wnt pathway, responsible for osteoblast differentiation, reflect the severity of bone disease in MM and may be used as a potential tool for disease monitoring.