A Prognostic Tool for Hypertrophic Scar Formation based on Fundamental Differences in Systemic Immunity; A Prospective Observational Cohort Study by

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Introduction: Unpredictable hypertrophic scarring (HS) occurs after approximately 35% of all surgical procedures and causes significant physical and psychological complaints. Parallel to the need to understanding the mechanisms underlying HS formation, a prognostic tool is needed. To determine whether (systemic) immunological differences exist between patients who develop HS and those who develop normotrophic scars (NS) and to assess whether those differences can be used to identify patients prone to developing HS.

Methods: Prospective cohort study with NS (n=15) and HS (n=16) groups in which i) cytokine release by peripheral blood mononuclear cells (PBMC) and ii) the irritation threshold (IT) after an irritant (sodium lauryl sulphate) patch test were evaluated.

Results: Univariate regression analysis of PBMC-cytokine secretion shows that low MCP-1, IL-8, IL-18 and IL-23 levels have a strong correlation with HS (p<0.010-0.004; AUC=0.790-0.883). Notably, combinations of 2 cytokines (MCP-1 and IL-23; AUC: 0.921, Nagelkerke R²: 0.703) or 3 cytokines (TNF-a, MCP-1 and IL-23; AUC: 0.942, Nagelkerke R²: 0.727) showed an improved AUC indicating better correlation with HS than single cytokine analysis. These combination models produce excellent prognostic results over a broad probability range (sensitivity: 93.8%, specificity 86.7%, accuracy 90.25% between probability 0.3 and 0.7). The HS group had a lower IT than the NS group and an accuracy of 68%.

Discussion: The systemic immune system seems to play a larger role than previously suspected in HS formation, with a reduced inflammatory response found in HS patients, conflicting with current beliefs. The measurement of the irritation threshold and HS formation have not been linked before.

Conclusions: Whereas the cytokine assay forms the basis of an extremely predictive prognostic test for HS formation, the less-invasive and easily performed irritant skin patch test provides a more accessible option for daily practice. These findings offer new insights
into pathophysiological mechanisms and enable future research into prevention and treatment.