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Impact of Factor-XIII val34leu-polymorphism on healing of diabetic foot ulcers

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Introduction: Factor-XIII plays a central role in the coagulation cascade by polymerizing fibrin chains and stabilizing fibrin clots. The aim of this study was to test the hypothesis whether there is a link between factor-XIII gene polymorphism, Factor-XIII activity and the healing of diabetic foot ulcers. **Material and Methods:** Consecutive diabetic patients with active foot ulcers were included. Follow-up was performed for 365 days or until healing or amputation if earlier. Healing was defined as complete epitheliazation. Amputation was categorized as major or minor amputation. Patients undergoing revascularisation during follow-up were excluded from the analysis. Plasma Factor-XIII activity was assessed by ELISA. Genetic polymorphism was detected using the ABI PRISM® SNaPshot™ Multiplex Kit followed by capillary electrophoresis on an ABI 3100 Genetic Analyzer. Results are expressed as median [min-max]. Differences between groups were calculated by Kruskal-Wallis or CHI^2-test when appropriate. A $p<0.05$ was considered significant. **Results:** 92 consecutive patients were enrolled in the study. Val34Leu-polymorphism (VLP) was found in 50 subjects (54%) with 42 (46%) being heterocygot (val/leu) and 8 (9%) being homocygot (leu/leu). Plasma Factor-XIII activity was increased in patients with VLP (val/val: 102% [33-282]; val/leu: 146% [55-282]; leu/leu: 187% [122-269]; $p<0.0001$). The three groups were highly comparable for baseline characteristics. Healing rates were similar between the groups (val/val: 67%; val/leu: 60%; leu/leu: 63%; $p=0.794$) whereas amputation rates were higher in the VLP groups (val/val: 2.4%; val/leu: 17%; leu/leu: 25%; $p=0.044$). Initial $tcpO_2$-readings were lower in the VLP-groups (val/val: 35 [1-65]; val/leu: 16 [0-58]; leu/leu: 28 [1-38] mmHg; $p=0.029$). Similarly, plasma factor-XIII activity negatively correlated with $tcpO_2$-readings ($r^2=-0.314$; $p=0.014$). **Conclusions:** These data suggest that VLP is common in diabetic foot ulcer patients. Increased plasma Factor-XIII activity might induce microvascular hypercoagulability with consecutive microthromboses resulting in decreased tissue oxygenation.