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Identification of factors associated with sural nerve regeneration and degeneration in diabetic neuropathy.

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Abstract

OBJECTIVE: Patients with diabetic neuropathy (DN) demonstrate variable degrees of nerve regeneration and degeneration. Our aim was to identify risk factors associated with sural nerve degeneration in patients with DN. **RESEARCH DESIGN AND METHODS:** Demographic, anthropometric, biochemical, and anatomical data of subjects with DN from a 52-week trial of acetyl-L-carnitine were retrospectively examined. Based on the change in sural nerve myelinated fiber density (ΔMFD%), subjects were divided into three groups: regenerator (top 16 percentiles, n = 67), degenerator (bottom 16 percentiles, n = 67), and intermediate (n = 290), with dramatically increased, decreased, and steady ΔMFD%, respectively. ANOVA, Fisher exact test, and multifactorial logistic regression were used to evaluate statistical significance. **RESULTS:** ΔMFD%s were 35.6 ± 17.4 (regenerator), -4.8 ± 12.1 (intermediate), and -39.8 ± 11.0 (degenerator). HbA1c at baseline was the only factor significantly different across the three groups (P = 0.01). In multifactorial logistic regression, HbA1c at baseline was also the only risk factor significantly different between regenerator (8.3 ± 1.6%) and degenerator (9.2 ± 1.8%) (odds ratio 0.68 [95% CI 0.54-0.85]; P < 0.01). Support Vector Machine classifier using HbA1c demonstrated 62.4% accuracy of classifying subjects into regenerator or degenerator. A preliminary microarray experiment revealed that upregulated genes in the regenerator group are enriched with cell cycle and myelin sheath functions, while downregulated genes are enriched in immune/inflammatory responses. **CONCLUSIONS:** These data, based on the largest cohort with ΔMFD% information, suggest that HbA1c levels predict myelinated nerve fiber regeneration and

degeneration in patients with DN. Therefore, maintaining optimal blood glucose control is likely essential in patients with DN to prevent continued nerve injury.

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