

## EPIDERMAL NERVE FIBRE DEPLETION IN SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANT PATIENTS: NO CHANGE AT FOLLOW-UP AFTER 18 MONTHS OF NORMOGLYCEMIA

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**Objectives:** Skin biopsy with epidermal nerve fibre (ENF) counts may be used to analyze possible nerve regeneration in patients with type 1 diabetes mellitus (DM) following simultaneous pancreas and kidney transplantation (SPK). We report on the results of lower limb ENF counts in normoglycemic SPK patients at 18 months follow-up.

**Methods:** Skin biopsies were performed using a 3-mm punch from lower thigh and upper calf areas of 16 SPK recipients (of mean  $\pm$ SD age  $46\pm 8$  years; DM duration  $28\pm 10$  years) at the time of SPK and at  $18\pm 4$  months post-transplant. Fourteen healthy sex- and age-matched controls (C) were also examined. After fixation and freezing, 40  $\mu$ m sections were stained using rabbit polyclonal antibody to the panaxonal marker PGP 9.5 followed by mouse anti-rabbit IgG antibody conjugated with rhodamine. Samples were imaged with a digital camera, mounted on a microscope, equipped for fluorescence. The average number of ENF per mm length of epidermis was derived.

**Results:** Excellent metabolic control (HbA<sub>1c</sub> IFCC values: SPK  $3.8\pm 0.4$  vs. C  $3.8\pm 0.4$  %;  $p>0.05$ ) and adequate kidney graft function (P-creatinine  $111\pm 24$   $\mu$ mol/l) were achieved in SPK recipients. Severe depletion of ENF was present in baseline skin biopsies from SPK recipients (SPK vs. C thigh:  $1.6\pm 3.1$  vs.  $11.4\pm 4.2$ ; calf:  $0.8\pm 1.9$  vs.  $8.0\pm 3.0$  ENF/mm;  $p<0.001$ ) with total ENF absence in thigh and calf samples of 8 and 12 SPK recipients, respectively. No significant change was seen at follow-up (thigh:  $0.9\pm 2.1$ ; calf:  $0.4\pm 1.1$  ENF/mm;  $p>0.05$  vs. baseline) with absence of ENF fibres in 11 thigh and 10 calf biopsies.

**Conclusions:** Lower limb epidermal nerve fibre depletion was not improved following establishment of normoglycemia in pancreas and kidney transplant recipients. Although prolonged follow-up is clearly needed, these preliminary results confirm the presence of structural, poorly reversible changes in advanced diabetic neuropathy.

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