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Is it diabetic neuropathy if the pancreas transplantation fails?

Aims: Pancreas transplantation (PT), either simultaneous pancreas-kidney (SPK) or pancreas after kidney (PAK) transplantation, has shown to improve the overall prognosis of individuals with type 1 diabetes (T1D) and end-stage kidney disease (ESKD). Data on the association of diabetic neuropathy (DN) improvement with outcomes after PT are lacking. This study aimed to assess the impact of DN on outcomes after PT, specifically graft survival and incident cardiovascular disease (CVD), and to explore whether the changes in neuropathy parameters after PT could affect these outcomes during follow-up.
Methods: This is a cohort study on individuals with T1D and ESKD who underwent PT between 1999 and 2015. DN was evaluated using vibration perception thresholds (VPTs) and orthostatic hypotension measurements before transplantation and after 6 months, 2-3, 5-6, and 8-10 y transplantation. The study examined the independent association between DN markers and PT outcomes, including graft failure/dysfunction and incident CVD, i.e., ischemic cardiac disease (clinical or subclinical), cerebrovascular events, and peripheral vascular events.
Results: The study included 187 participants (70% men, age 39.9±7.1 y, diabetes duration 27.1 y, n = 176 with SPK and n = 11 with PAK), with a median follow-up of 11.3 y. Before PT, 15.6% of participants had orthostatic hypotension and 53% abnormal VPTs. After transplantation, VPTs improved (22.4±8.4 pretransplant versus 16.1±6.1 V at 8-10 y post-PT; P<0.001) and the prevalence of abnormal VPTs decreased (53% pretransplant versus 24.4% at 8-10 y; P<0.001). No changes in orthostatic hypotension were observed during follow-up.
After adjusting for age, sex, diabetes duration, blood pressure, body mass index, and previous CVD, pretransplant VPTs ≥25 V were independently associated with pancreas graft failure/dysfunction (hazard ratio [HR], 2.01 [1.01-4.00]) and incident CVD (HR, 2.57 [1.17-5.64]). Persistent abnormal VPTs after 6 months post-transplantation were also linked to worse outcomes for graft failure/dysfunction (HR, 2.80 [1.25-6.23]) and incident CVD (HR, 3.19 [1.14-8.96]). No relationship was observed between orthostatic hypotension and PT outcomes or incident CVD during follow-up.
Conclusions: These results confirmed the effectiveness of PT in ameliorating DN manifestations in patients with T1D and ESKD. Baseline neuropathy, as assessed by VPTs, was an independent predictor of CVD and poorer pancreas graft outcomes.

Comments. This is the first study to examine both the beneficial effects of PT on DN and the potential role of DN, including its changes after transplantation, in identifying individuals with poorer pancreas graft and CVD outcomes. The beneficial effects of PT on DN had already been observed by the same Authors, demonstrating improvements in nerve conduction parameters, in both the short (Agudo R et al. Med Clin (Barc). 2002 Apr 20;118(14):534-8) and long term (Recasens M et al. Transplant Proc. 2002 Feb;34(1):200-3) after PT. Moreover, the study highlights the independent association between DN, specifically VPTs, and both pancreas graft function and CVD events after transplantation. The lack of association with cardiovascular autonomic neuropathy parameters is likely due to using only orthostatic hypotension as an index of autonomic dysfunction. These findings emphasize the importance of assessing DN to identify individuals at a higher risk of developing CVD or poorer pancreas graft outcomes. Therefore, pending further studies to confirm these findings, implementing VPTs in clinical practice could help tailor the management of this complex population.

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Reference. Boswell L, Ventura-Aguiar P, Alejaldre A, Navarro-Otano J, Cofan F, Serés-Noriega T, Pané A, Montagud-Marrahi E, Molina-Andújar A, Ruiz M, Cucchiari D, Musquera M, Ferrer-Fàbrega J, Diekmann F, Esmatjes E, Amor AJ. Diabetic Neuropathy Is Independently Associated With Worse Graft Outcomes and Incident Cardiovascular Disease After Pancreas Transplantation: A Retrospective Cohort Study in Type 1 Diabetes. Transplantation. 2023 Feb 1;107(2):475-484. doi: 10.1097/TP.0000000000004275. Epub 2022 Aug 15. PMID: 35969040.
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