T50 NEWSLETTER
AUGUST 2022

T50 Associates with Disease Severity in *Pseudoxanthoma Elasticum*

Lower T50 values are associated with a more severe phenotype in PXE patients

Pseudoxanthoma elasticum (PXE) is a rare genetic disease (prevalence about 1:100.000), caused by mutations in the ABCC6-Gen. PXE is characterized by severely reduced plasma levels of pyrophosphate, a calcification inhibitor, and the pathological calcification of elastic connective tissue manifested in skin, eyes and cardiovascular system.

T50 calcification propensity measures the functional capacity of the mineral buffer system in blood. As therapeutic trials in PXE are severely hampered by the lack of reliable biomarkers, this study investigated T50's suitability as a potential biomarker for PXE disease severity.

Professor Olivier M. Vanakker and his team from Ghent University, Ghent, Belgium, studied the association between T50 and calcification severity at various body sites (n = 57 patients, mean age 45.2 years, 68.4% female).*

Multivariate regression analysis identified serum fetuin-A ($p < 0.001$), phosphorus ($p = 0.007$) and magnesium levels ($p = 0.034$) as significant determinants of T50. After correction for covariates, T50 was found to be an independent determinant of ocular ($p = 0.013$), vascular ($p = 0.013$) and overall disease severity ($p = 0.016$).

According to the authors, «T50 might be a clinically relevant biomarker in PXE and may thus be of importance to future therapeutic trials.»

*Serum Calcification Propensity T50 Associates with Disease Severity in Patients with Pseudoxanthoma Elasticum. Nollet, L, Van Gils, M, Fischer, S, Campens. L, Karthik, S, Pasch, A, De Zaeytijd, J, Leroy, BP, Devos, D, De Backer, T, Coucke, PJ, Vanakker, OM. J. Clin. Med. 2022, 11(13),3727

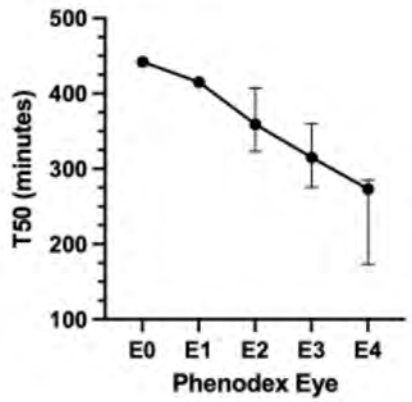

Figure 2B: Associations of Phenodex disease severity score with T50 in PXE. Serum T50 inversely correlated with Phenodex eye ($p < 0.001$).

Commentary by Prof. Andreas Pasch:
This is the first study demonstrating an association between T50 and disease severity in PXE. I interpret the findings as indicative of synergistic effects generated by a lack of the local calcification inhibitor pyrophosphate in PXE, and an augmentation effect mediated by the performance of the systemic humoral calcification (inhibition) system, as measured by T50. Therapeutically, the clinical course of PXE may be modifiable by improving the T50 value in the future.

The *T50 Newsletter* presents News concerning T50, CPP and Calciscon to the interested medical, scientific and business community.

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