CALCIFICATION MEDICINE
CPP/T50 NEWSLETTER
MAY 2023

T50 is an independent predictor of all-cause mortality in hemodialysis patients

A prospective observational study investigated whether the T50 calcification propensity test predicts all-cause mortality in unselected incident and prevalent hemodialysis patients in a real-world setting.

Researchers from Fresenius Medical Care determined T50 once at baseline from 776 hemodialysis patients (mean age 72 years, 64% males).*

Mean T50 in the cohort was 283 minutes, 24% of patients died during the 2-year follow-up.

A cross-validated model consistently **identified T50 as independent and linear predictor of all-cause mortality**. T50 remained in the model after addition of known predictors (c-statistics final model 0.69). Every 10 minutes higher T50 was associated with 4.3% longer survival.

Interestingly, phosphate, magnesium and bicarbonate were not identified as significant linear predictors of all-cause mortality in additional analysis.

The authors state that *novel approaches are clearly needed to reduce the high morbidity and mortality burden of dialysis patients* and that *T50 has previously been shown to be therapeutically modifiable in patients with kidney disease.*

Commentary by Prof. Andreas Pasch:
Prediction of all-cause mortality of hemodialysis patients is challenging. The predictive value (c-statistics) of the model presented here, is in the range of much more elaborate models.

T50 was identified as an independent *linear* predictor of all-cause mortality. Unlike the other model variables like age or medical history, T50 was the only modifiable variable, and thus the only potential target for therapeutic intervention.

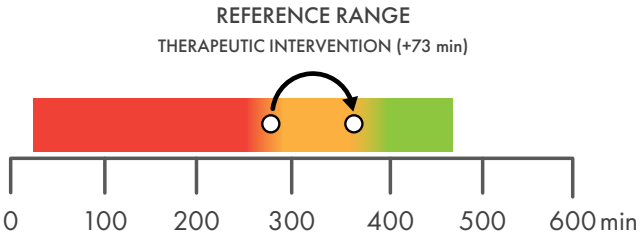
Based on the numbers presented, therapeutically improving T50 might translate into considerably improved survival, as e.g. 50-100 minutes higher T50 was associated with a 22-44% reduction in the risk of death.

T50 may in the future replace phosphate as *primary* treatment target in dialysis patients.

*Assessment of a serum calcification propensity test for the prediction of all-cause mortailty among hemodialysis patients.** Zawada AM, Wolf M, Rincon Bello A, Ramos-Sanchez R, Hurtado Munoz S, Ribera Tello L et al. BMC Nephrol. 2023 Feb 15;24(1):35.

A recent randomized, double-blinded interventional trial with a hemodialysis cohort demonstrated a 73-minute increase in T50.† Such a single intervention would bring the cohort studied by Zawada et al. to an estimated 360 minutes, that is well into the normal range of 270-470 (as defined in a group of Swiss blood donors). Individualization of the intervention(s) can further improve T50. The colors in the scale bar do not represent biological cut-off values but are for illustration purposes only. T50 is linearly related with prognosis.

†: Bressendorff et al., CJASN, 2018



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SHORT OVERVIEW:
T50, CALCIPROTEIN PARTICLES (CPP) AND MINERAL BUFFER SYSTEM

Calciprotein particles (CPP, Fig. 1) are naturally occurring circulating nanoparticles. They consist of calcium, phosphate and specific proteins, mainly fetuin-A, and other bioactive molecules. CPP are a part of the body's recently discovered **mineral buffer system**, i.e. the physiological system to control precipitation and to facilitate the transportation and excretion of calcium phosphate mineral. The mineral buffer system is fundamental for cardiovascular health and healthy aging.

CPP2 induce *oxidative stress, inflammation and calcification*. In contrast, CPP1 are regarded as relatively non-toxic. This dichotomous CPP system resembles the cholesterol system of LDL ("bad cholesterol") and HDL ("good cholesterol").

T50 is a unique diagnostic blood test that measures the transformation from CPP1 to CPP2 *in vitro* (Fig. 1). The result is given in minutes (Fig. 2). A rapid transformation time (low T50) is associated with poor prognosis (all-cause mortality, cardiovascular mortality, calcification progression and others) (Fig. 3). Consequently, T50-guided treatments are expected to considerably improve patient prognosis.

Research interest in CPP and T50 continues to grow, indicating the establishment of the new and highly relevant medical field of *Calcification Medicine* (Fig. 4). Given their close association with prognosis, T50 and CPP may also become important novel targets for drug development.

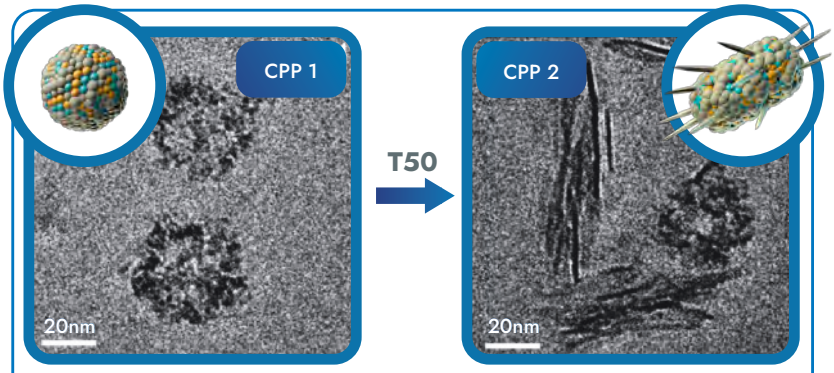

Figure 1: Electron microscopy of CPP 1 and CPP 2. T50 measures the transformation from CPP 1 to CPP 2 *in vitro*.

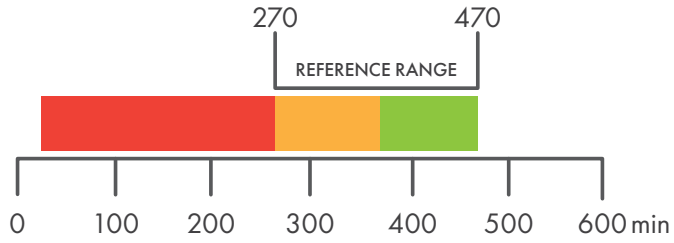

Figure 2: T50 reference range. Colors are for illustration purposes only.

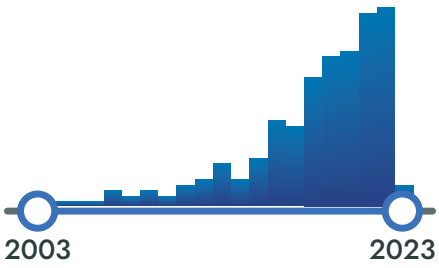

Figure 4: Pubmed listed publications on "calcification propensity" and/or "calciprotein particles" as of early 2023 (202 results).

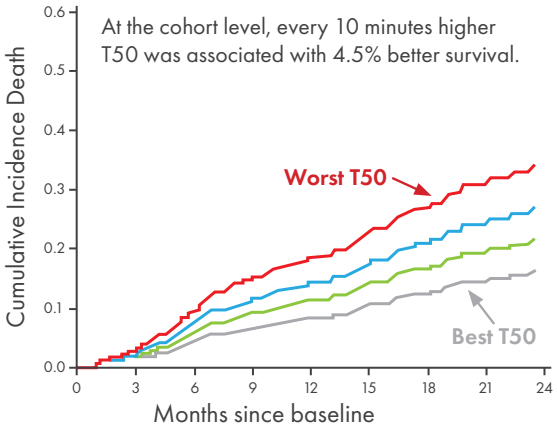

Figure 3: Kaplan-Meier survival plot of ~800 prevalent dialysis patients by T50 value. Lowest (= worst) T50 is associated with highest mortality rate.

References for the statements made here are provided upon request.

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If you want to know more, or want to have T50 or CPP measured in your research samples, please contact:
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