Troponin T in hemodialysis patients: Unraveling the challenges of interpretation and diagnosis

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Patients with chronic kidney disease (CKD) undergo early vascular aging that increases the risk of coronary artery disease (CAD) [1]. Several studies have reported associations between elevated cardiac troponin T (cTnT) and age-related conditions, such as hypertension, type-2 diabetes, and CKD. The use of cTnT as a marker for detection of CAD in hemodialysis (HD) patients is a topic of ongoing research and debate within the nephrology community. Whereas cTnT is a valid and commonly used biomarker for the diagnosis of acute myocardial infarction in the general population cTnT can be elevated in the absence of acute coronary events due to persistent inflammation, underlying myocardial injury related to hemodynamics and structural uremic heart disease in HD patients. In a study by Szramowska et al. [2] high-sensitivity cTnT (hs-cTnT) was analyzed in HD patients who underwent coronary angiography. Their study indicates that patients below 52 years of age and plasma hs-cTnT <69 ng/l may not need to be submitted for diagnostic workup for obstructive coronary artery disease. It is of clinical importance to identify dialysis patients at increased cardiovascular risk after kidney transplantation (KTx). These patients need further diagnostic workup and sometimes coronary artery revascularization. The results of this study must be considered in relation to what has been previously reported about the use of cTnT in HD-patients.

In a Swedish cohort study [3] on adult dialysis patients, where high-sensitivity cardiac troponin I (hs-cTnI) and T (hs-cTnT) levels were monitored in prevalent patients monthly for 3 months, a correlation was observed between variability in troponin levels and outcome [4]. 198 HD patients and 78 peritoneal dialysis patients were monitored with high-sensitivity troponin levels measured monthly, for a total of 4 times. Comorbidities were registered in detail including nutritional status based on subjective global assessment. The patients did not have any ongoing cardiac events during the period. Troponin levels were overall higher in patients with congestive heart failure (HF), coronary and peripheral vascular disease, but only hs-cTnT was related to protein energy wasting, and diabetes mellitus (DM). The troponin variation over three months was significantly increased with protein energy wasting and congestive HF. However, patients with ischemic heart disease, peripheral vascular disease or DM did not show increased variability of troponin levels. Importantly the greatest variation was seen between patients rather than within patients. This may signify that serial regular measurements could be used to determine an individual patient's levels in a stable setting and compared to dynamic changes during, for example, suspected acute coronary syndrome. Still there is no clinical standard or reference for using troponins in diagnosing CAD in dialysis patients. An important factor is the relation of cTnT to poorer nutritional status and congestive HF. An ongoing challenge in caring for dialysis patients is estimating their

dry weight and higher troponins add to the insight that fluid overload puts strain on the patient's cardiac function. For the purpose of relating variability to outcome, patients were divided into tertile groups of troponin levels at baseline and analyzed based on staying in one group during the study period or having levels vary between tertiles. Most patients remained in their respective groups. Follow-up for survival was 36 months, and patients with the highest mortality were observed in the group of patients with persistently high cTn levels. However, after adjusting for standard variables, cardiovascular diseases, DM and nutritional status, cTnT but not cTnI predicted mortality. The main findings of the study were the large variability of hs-cTnI and hs-cTnT in dialysis patients, differences in variability between different troponins, clinical factors predicting variability and the predictive value of hs-cTnT but not hs-cTnI for survival.

Clinicians should also consider other clinical, laboratory and imaging findings to make an accurate CAD diagnosis and guide appropriate management. Recent data suggest that there are several novel opportunities. Since inflammation is a major driver of residual cardiovascular risk in this patient group [5], it is important to study whether adding IL-6 (or C-reactive protein) in an algorithm for cardiological qualification will help clinicians to better identify HD-patients at risk after KTx. Clinicians should also use the opportunity to score medial arterial calcification after KTx. A recent study by Erlandsson et al. [6] showed that the medial calcification score is a reliable method to identify patients with high and low risk of cardiovascular events and mortality following KTx. Furthermore, since biological vascular age estimated by aortic pulse wave components is a better predictor of composite cardiovascular endpoints than chronological age [7], studies need to test the predictive value of surrogate markers of biological age in dialysis patients undergoing KTx. Chronic kidney disease is a condition associated with premature biological aging [8], and investigations of DNA methylation biomarkers may be used for prognostic or risk stratification in CKD. A recent study evaluating epigenetic clocks through DNA methylation suggests that end-stage kidney failure patients have an epigenetic age of about 5 years older than their chronological age [9]. In the future, the extent of vascular aging in the toxic uremic milieu needs to replace chronological age as a more accurate measure. Further research is needed to elucidate the mechanisms underlying the association between cTnT levels and biological aging and to determine the clinical implications for risk stratification and management of cardiovascular disease in older adults.

Taken together, the study by Szramowska et al. [2] indicates that an hs-cTnT cut-off at approximately 50–100 ng/l could be useful for detecting CAD in HD patients. Since the intraindividual variation of hs-cTnT is large and there are lot-to-lot variations of the immunoassay, larger studies are needed to establish robust decision limits for cardiac assessment in HD patients.

Article information

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