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High-sensitivity troponin T and C-reactive protein have different prognostic values in Hemo- and peritoneal dialysis populations: A cohort study

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Abstract

Background--Dialysis patients have an exceedingly high mortality rate. Biomarkers may be useful tools in risk stratification of this population. We evaluated the prognostic value of high-sensitivity cardiac troponin T (hs-cTnT) and CRP (C-reactive protein) in predicting adverse outcomes in stable hemodialysis and peritoneal dialysis (PD) patients. Variability in hs-cTnT was also examined. Methods and Results--A retrospective cohort study included 574 dialysis patients (hemodialysis 347, PD 227). Outcomes examined included mortality and major adverse cardiovascular events, with median follow-up of 3.5 years. hs-cTnT was an independent predictor of both outcomes in hemodialysis and PD patients. Increased risk only became significant when hs-cTnT reached quintile 3 (> 49 ng/L). Area under the receiver operating curve analysis showed that the addition of hs-cTnT to clinical parameters significantly improved its prognostic performance for mortality in PD patients (P=0.002). CRP was an independent predictor of both outcomes in PD patients only. Only CRP in the highest quintile (> 16.8 mg/L) was associated with increased risk. hs-cTnT remained relatively stable for the whole follow-up period for hemodialysis patients, whereas for PD patients, hs-cTnT increased by 23.63% in year 2 and 29.13% in year 3 compared with baseline (P < 0.001). Conclusions--hs-cTnT and CRP are useful tools in predicting mortality and major adverse cardiovascular events in hemodialysis and PD patients. Given that hs-cTnT levels increase over time in PD patients, interval monitoring may be valuable for risk assessment. In contrast, hs-cTnT in hemodialysis patients has little interval change and progress monitoring is not indicated.

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ORIGINAL RESEARCH

High-Sensitivity Troponin T and C-Reactive Protein Have Different Prognostic Values in Hemo- and Peritoneal Dialysis Populations: A Cohort Study

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***Background*—**Dialysis patients have an exceedingly high mortality rate. Biomarkers may be useful tools in risk stratification of this population. We evaluated the prognostic value of high-sensitivity cardiac troponin T (hs-cTnT) and CRP (C-reactive protein) in predicting adverse outcomes in stable hemodialysis and peritoneal dialysis (PD) patients. Variability in hs-cTnT was also examined.

***Methods and Results*—**A retrospective cohort study included 574 dialysis patients (hemodialysis 347, PD 227). Outcomes examined included mortality and major adverse cardiovascular events, with median follow-up of 3.5 years. hs-cTnT was an independent predictor of both outcomes in hemodialysis and PD patients. Increased risk only became significant when hs-cTnT reached quintile 3 (>49 ng/L). Area under the receiver operating curve analysis showed that the addition of hs-cTnT to clinical parameters significantly improved its prognostic performance for mortality in PD patients (P=0.002). CRP was an independent predictor of both outcomes in PD patients only. Only CRP in the highest quintile (>16.8 mg/L) was associated with increased risk. hs-cTnT remained relatively stable for the whole follow-up period for hemodialysis patients, whereas for PD patients, hs-cTnT increased by 23.63% in year 2 and 29.13% in year 3 compared with baseline (P<0.001).

***Conclusions*—**hs-cTnT and CRP are useful tools in predicting mortality and major adverse cardiovascular events in hemodialysis and PD patients. Given that hs-cTnT levels increase over time in PD patients, interval monitoring may be valuable for risk assessment. In contrast, hs-cTnT in hemodialysis patients has little interval change and progress monitoring is not indicated. **(*J Am Heart Assoc*. 2018;7:e007876. DOI: 10.1161/JAHA.117.007876.)**

Key Words: biomarker • end-stage renal disease • major adverse cardiac event • mortality • risk stratification

The mortality rate of the dialysis population far exceeds that of the general population.[1] Traditional cardiovascular disease risk factors are common in end-stage kidney disease patients, but do not fully explain the high mortality rate.[2] Nontraditional factors, such as chronic low-grade inflammation, are important characteristics of end-stage kidney disease patients and have contributed to the high mortality rate.[2,3] Given that traditional risk factors are inadequate at predicting adverse outcome in the dialysis population, serum biomarkers can be a useful tool in risk stratifying these patients.

Troponin is a powerful predictor of cardiovascular and all-cause mortality.[4] Most of the studies investigating troponin were performed using traditional troponin assay and on hemodialysis patients.[4,5] Information on peritoneal (PD) patients is lacking. The high-sensitivity cardiac troponin T (hs-cTnT) assay introduced in recent years has a greater sensitivity for cardiac myocyte necrosis.[6,7] There is a paucity

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Accompanying Tables S1 and S2 are available at http://jaha.ahajournals.org/content/7/5/e007876/DC1/embed/inline-supplementary-material-1.pdf

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Clinical Perspective

What Is New?

- Increased level of high-sensitivity cardiac troponin T (hs-cTnT) was an independent predictor for mortality and major adverse cardiovascular events in both hemodialysis and peritoneal dialysis patients.
- CRP (C-reactive protein) was an independent predictor for mortality and major adverse cardiovascular events in peritoneal dialysis patients only.
- Increased risk of adverse outcome was not linearly related to increased hs-cTnT and CRP.
- For hs-cTnT, risk did not become significant until hs-cTnT reached quintile 3 (>49 ng/L), whereas for CRP, only quintile 5 (>16.8 mg/L) was associated with increased risk.
- There was a significant increase in hs-cTnT level in peritoneal dialysis patients over time, wheras for hemodialysis patients, hs-cTnT level remained relatively stable.

What Are the Clinical Implications?

- hs-cTnT and CRP are useful tools in predicting mortality and major adverse cardiovascular events in the dialysis population at 3.5 years.
- The prognostic value of hs-cTnT is better than CRP.
- The frequency of hs-cTnT measurement should be at least yearly for peritoneal dialysis patients to establish baseline given the level increases significantly.
- For hemodialysis patients, a less-frequent measurement may be acceptable as the change over time is minimal.

of information regarding the prognostic value of hs-cTnT in the dialysis population.

CRP (C-reactive protein) is also a powerful predictor of clinical outcomes in the general population[8,9] and patients on dialysis.[10–12] As with the studies for troponins, most of these studies were performed on hemodialysis patients, with information on PD patients lacking.

Previously, we conducted a 1-year prospective study investigating the prognostic values of hs-cTnT in predicting adverse outcomes. In the current study, we investigated a larger sample size with a longer follow-up of 3.5 years to evaluate the prognostic value of hs-cTnT and CRP in predicting major adverse cardiovascular events (MACE) or death. Furthermore, we also compared the prognostic value of hs-cTNT with CRP and traditional clinical parameters and studied the variability of hs-cTnT over time.

Methods

The data, analytical methods, and study materials are available from the corresponding author on reasonable request.

Study Cohort

The study was approved by the South Western Sydney Local Health District Human Research Ethics Committee, and the requirement for informed consent was waived. We included 574 patients receiving dialysis in a tertiary metropolitan hospital network (Sydney, NSW, Australia) between July 2011 and January 2015. All of them were followed up until January 2015. Of these patients, 347 of them started dialysis before July 2011, and 227 started dialysis after July 2011. Inclusion criteria were: aged ≥18 years and had been undergoing dialysis for >2 weeks. Patients were excluded if there was no blood test performed or if they were hospitalized in the week before baseline blood tests, were pregnant, or had a known acute systemic inflammatory disorder or active infection.

Blood Sampling and Analysis

hs-cTnT and CRP were measured as part of the protocol at patients' routine yearly blood tests. For hemodialysis patients, blood was taken before the start of the second dialysis session of the week through the patient's dialysis access. PD patients' blood samples were taken by a BD Vacutainer system (BD Biosystems, San Jose, CA) during their monthly outpatient visits. hs-cTnT level was repeated on a yearly basis. Assays were performed using a fifth-generation electrochemiluminescence assay (Elecsys, Cobas 8000, e602 analyzer; Roche Diagnostics, Indianapolis, IN) in an accredited laboratory (National Association of Testing Authorities, Australia).[13] According to the manufacturer of the assay, limit of detection was 5 ng/L, the 99th percentile upper reference limit was 14 ng/L in the normal population, the analytical range was 3 to 10 000 ng/L, and the coefficient of variation was <10% at the lowest concentration of 13 ng/L. CRP was measured using Roche Cobas 8000 c702 (Roche Diagnostics), with a detection range of 0.3 to 350 mg/L. Laboratory personnel were blinded to patients outcome data or history at the time of assay.

Data Collection, Outcomes, and Definitions

Baseline characteristics and outcome data were obtained from electronic medical records and hospital databases. Personnel who collected such data were blinded to patients' blood test results. Outcomes analyzed were all-cause mortality and MACE, and the change in hs-cTnT over the 3.5-year follow-up was also examined. Patients were censored for further follow-up if they underwent kidney transplantation, were transferred to another dialysis unit, or changed dialysis modality.

The definition of MACE was cardiac death, nonfatal myocardial infarction, or target lesion revascularization. Myocardial infarction was defined by a rise in hs-cTnT (>20% increase from a previous baseline) in addition to ischemic symptoms, new ECG changes, or identification of an intracoronary thrombus by angiography.[14] Cardiac mortality was defined as any death with a demonstrable cardiovascular cause or sudden cardiac death. Coronary heart disease (CHD) included diagnosis of myocardial infarction, angina pectoris, and silent myocardial ischemia. Combined clinical parameters used in the analysis included age, sex, dialysis vintage, history of diabetes mellitus, CHD, and peripheral vascular disease.

Statistical Analysis

Continuous variables are presented as mean with SD or median with interquartile range (IQR). Distributions between groups were compared using the Student *t* test or Mann–Whitney *U* test, ANOVA, or Kruskal–Wallis tests, as appropriate. Categorical variables are presented as frequency (%), and the association between categorical variables was assessed using the chi-square test. Strength of association between hs-cTnT and CRP was quantified using Spearman rank correlation. Kaplan–Meier time-to-event curves with log-rank test were used to compare outcomes across hs-cTnT and CRP quintiles. Univariable and multivariable Cox proportional hazard models were used to estimate time to all-cause mortality or MACE and hazard ratio (HR) with 95% confidence interval (CI) were calculated. Step-wise backward regression analysis was used to identify variables that were independent predictors of outcomes. Variables shown to be significant in the univariable analysis were included in the backward regression model. Probabilities for entry or removal from the model were 0.050 and 0.100, respectively.

For analysis of the prognostic performance of hs-cTnT and CRP using receiver operating characteristics (ROC) curves at 3.5 years and variability in hs-cTnT over this period of time, we only included 347 patients who were already on dialysis in July 2017. ROC curves were calculated for the prognostic performance of hs-cTnT, CRP, and combined clinical parameters. Area under the ROC curve (AUC) was used to quantify the global prognostic performance of each of these variables. We also investigated whether adding hs-cTnT to clinical parameters improved the prognostic performance of clinical parameters. AUC was compared using the method described by Delong et al.[15]

We fitted a linear mixed-effects model to investigate the variability of hs-cTnT level over time. hs-cTnT levels were log transformed to approximate normality and stabilize the variance before analysis. Patient identifier was considered as a random effect, type of dialysis as a fixed effect, and year since baseline troponin as both a fixed effect and as a random effect with a general positive definite covariance structure. Parameter estimates and their 95% CIs were back-transformed to present results as percentage change from baseline.

IBM SPSS (version 23; IBM Corp, Armonk, NY) and R software (version 3.3.1; R Foundation for Statistical Computing, Vienna, Austria) were used to analyze the data. A *P* value of <0.05 was considered statistically significant.

Results

Clinical Characteristics and Outcomes

A total 574 patients were included, of whom 347 were on hemodialysis and 227 were on PD (Figure 1). Of the patients assessed for eligibility, 158 were excluded. No patient was lost to follow-up.

Baseline characteristics of these patients were summarized in Table 1. Median age was 66.0 (IQR, 55.0–73.5) years, with 342 (59.6%) of these patients being male. Median duration of dialysis was 1.3 (IQR 0.3–3.6) years, and 228 (39.7%) had a history of CHD. During a median follow-up of 3.5 years, there were 176 (30.6%) deaths, of which 60 were attributed to cardiac causes. One hundred eleven (19.3%) patients experienced MACE.

Baseline hs-cTnT and CRP Levels

Median hs-cTnT for the total cohort was 59 ng/L (IQR, 3,6–97). Only 17 patients (3%) had hs-cTnT below the upper reference limit for the normal population (14 ng/L). In the subpopulation of patient without CHD, 15 (6.6%) had hs-cTnT below the upper reference limit. Hemodialysis patients had higher hs-cTnT than PD patients (63 versus 55 ng/L; *P*=0.011).

Patients were divided into quintiles based on their hs-cTnT level. Clinical characteristics associated with higher hs-cTnT quintiles were older age (*P*<0.001), male sex (*P*<0.001), history of diabetes mellitus (*P*<0.001), respiratory disease (*P*=0.041), and CHD (*P*<0.001; Table S1).

Median CRP for the total cohort was 4.9 mg/L (IQR, 2.0–2.7). Two hundred ninety-three patients (52%) had a CRP below the upper reference limit of 5 mg/L. Hemodialysis patients had a higher CRP than PD patients (6.1 versus 3.5 mg/L; *P*<0.001). Clinical characteristics associated with higher CRP quintiles were CHD (*P*<0.001) and longer dialysis vintage (*P*=0.009; Table S2).

There was no significant association between hs-cTnT and CRP level (total cohort Spearman rank correlation, 0.080; *P*=0.060; hemodialysis Spearman rank correlation, 0.068; *P*=0.209; PD Spearman rank correlation, 0.037; *P*=0.574).

Variability in hs-cTnT Over Time

We investigated the variability in hs-cTnT level over time. For hemodialysis patients, hs-cTnT remained relatively

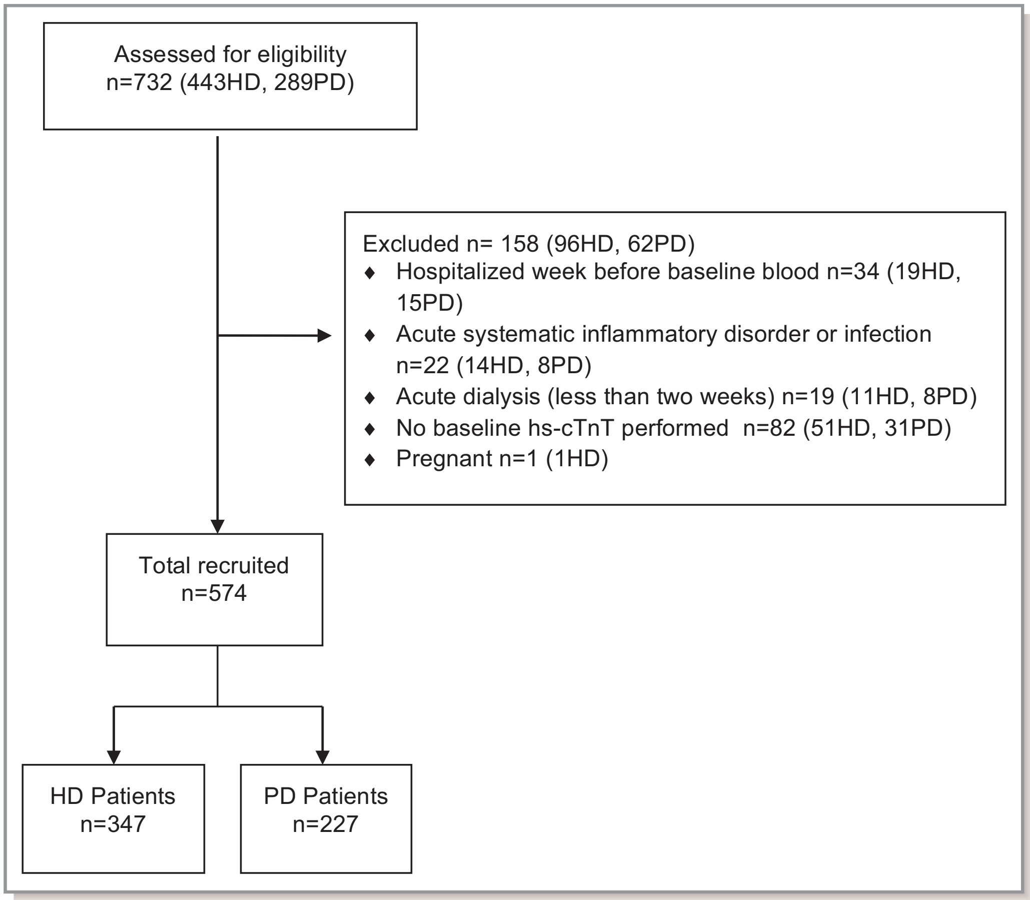

Figure 1. Flow diagram for patients included in the study. HD indicates hemodialysis; PD, peritoneal dialysis.

stable for the whole follow-up period compared with baseline. For PD patients, hs-cTnT increased by 23.63% in year 2 (P<0.001) and 29.13% in year 3 (P<0.001) compared with baseline.

Hs-cTnT and CRP as Predictors of Outcomes

Survival analysis

Figure 2 illustrated the Kaplan–Meier curves of outcomes based on hs-cTnT. hs-cTnT in the first quintile (<32 ng/L) was associated with the best outcome whereas hs-cTnT in the fifth quintile (>108 ng/L) was associated with the worst outcome for both mortality (log-rank P<0.001) and MACE (log-rank P<0.001). PD and hemodialysis subgroup analysis results were similar (mortality P<0.001 for both PD and hemodialysis, MACE P=0.004 for PD, 0.006 for hemodialysis).

Kaplan–Meier curves based on CRP quintiles showed that higher CRP quintiles were associated with increased risk of mortality in both PD (P<0.001) and hemodialysis (P=0.042) patients. With regard to MACE, higher CRP quintiles were associated with increased risk in PD patients (P=0.002) only, but not in hemodialysis patients.

Univariable analysis

Table 2 presented the HR with associated CI for mortality and MACE from univariable analysis. Higher hs-cTnT quintiles predicted increased risk of mortality and MACE compared with the lowest quintile. The highest risk was in the fifth quintile (>108 ng/L), with mortality HR of 3.67 and MACE HR of 3.90. With regard to CRP, only the highest quintile (>16.8 mg/L) was predictive of both mortality (P<0.001) and MACE (P=0.008). Subgroup analysis of hemodialysis and PD patients showed a similar result for hs-cTnT. However, for CRP, it was not a predictor for MACE in hemodialysis patients.

Multivariable analysis

When analyzing mortality as the outcome (Table 2), in the total cohort, older age (P<0.001), malignancy (P=0.046), longer dialysis vintage (P=0.020), lower albumin (P=0.002), and higher hs-cTnT and CRP remained statistically significant independent predictors. In hemodialysis patients (Table 3),

Table 1. Baseline Characteristics and Outcomes of the Study Population

Variables	All Group (N=574)	Hemodialysis (N=347)	PD (N=227)	*P* Value
Age, y	66.0 (55.0–73.5)	65.8 (55.0–73.5)	66.0 (56.0–73.8)	0.707
Sex, male	342 (59.6)	203 (58.5)	139 (61.2)	0.514
Comorbidities (N=570)				
Diabetes mellitus	310 (54.0)	198 (57.6)	112 (49.3)	0.061
CHD	228 (39.7)	141 (40.6)	87 (38.3)	0.552
Hepatitis B or C	31 (5.4)	24 (6.9)	7 (3.1)	0.046
DVT/PE	33 (5.7)	21 (6.1)	12 (5.3)	0.691
Malignancy	69 (12.1)	45 (13.0)	24 (10.6)	0.378
Respiratory	85 (14.8)	58 (16.7)	27 (11.9)	0.107
Neurological	76 (13.2)	41 (11.8)	35 (15.4)	0.220
PVD	42 (7.3)	34 (9.8)	8 (3.5)	0.005
Laboratory values				
hs-cTnT, ng/L (N=574)	59 (36–97)	63 (38–103)	55 (32–86)	0.011
Albumin, g/L	39 (36–42)	40 (37–43)	38 (34–41)	<0.001
Calcium, mmol/L	2.28 (2.16–2.38)	2.25 (2.14–2.37)	2.31 (2.21–2.42)	0.001
Phosphate, mmol/L	1.65 (1.32–2.07)	1.63 (1.25–1.98)	1.72 (1.40–2.15)	0.006
Magnesium, mmol/L	0.90 (0.81–1.00)	0.93 (0.84–1.04)	0.88 (0.76–0.95)	<0.001
Hemoglobin, g/L	113 (103–124)	114 (104–124)	112 (102–123)	0.467
CRP, mg/L (N=565)	4.9 (2.0–12.7)	6.1 (2.6–16.5)	3.5 (1.6–9.2)	<0.001
PTH, pmol/L	32.5 (14.5–57.2)	35.4 (13.7–69.1)	31.6 (15.6–48.4)	0.240
Dialysis vintage, y	1.3 (0.3–3.6)	2.16 (0.51–5.11)	0.75 (0.08–2.09)	<0.001
Outcomes				
Mortality	176 (30.6)	119 (34.3)	57 (25.1)	0.020
MACE	111 (19.3)	80 (23.1)	31 (13.7)	0.005

Data are expressed as n (%), median (interquartile range), or mean (SD) depending on normality tests. Statistical significance was assessed between hemodialysis and PD groups. CHD indicates coronary heart disease; CRP, C-reactive protein; DVT, deep vein thrombosis; hs-cTnT, high-sensitivity cardiac troponin T; MACE, major adverse cardiovascular events; PD, peritoneal dialysis; PE, pulmonary embolism; PTH, parathyroid hormone; PVD, peripheral vascular disease.

older age (*P*<0.001), CHD (*P*=0.008), longer dialysis vintage (*P*=0.045), lower albumin (*P*=0.007), and higher hs-cTnT were independent predictors, whereas in PD patients, older age (*P*=0.004), lower albumin (*P*=0.031), and higher hs-cTnT and CRP were independent predictors.

Similar analysis was performed for MACE. In the combined population, CHD (*P*=0.046), respiratory disease (*P*=0.019), peripheral vascular disease (*P*=0.001), and higher hs-cTnT were shown to be independent predictors for MACE. In hemodialysis patients (Table 3), CHD (*P*=0.045), respiratory disease (*P*=0.031), peripheral vascular disease (*P*=0.024), lower albumin (*P*=0.040), and higher hs-cTnT were independent predictors, whereas in PD patients, higher hs-cTnT and CRP were independent predictors.

We also analyzed the subgroup of patients without CHD (n=346; Table 4) and found that higher hs-cTnT was an independent predictor for both mortality and MACE.

Area under the receiver operating curve analysis

ROC curve was used to compare the prognostic performance of hs-cTnT, CRP, and combined clinical parameters and to investigate whether adding hs-cTnT to clinical parameters further improves risk stratification for prediction of mortality and MACE (Table 5). AUC for CRP, hs-cTnT, and combined clinical parameters were 0.59 (95% CI, 0.54–0.64), 0.71 (95% CI, 0.66–0.75), and 0.70 (95% CI, 0.65–0.75), respectively, for mortality and 0.52 (95% CI, 0.47–0.58), 0.62 (95% CI, 0.57–0.67), and 0.63 (95% CI, 0.58–0.69) for MACE. Both hs-cTnT and clinical parameters have larger AUC than CRP for mortality and MACE. There was no significant difference between AUC for hs-cTnT and clinical parameters. In the combined population, adding hs-cTnT to clinical parameters significantly increased AUC for mortality (*P*=0.012), but not MACE. In the subgroup analysis of hemodialysis and PD

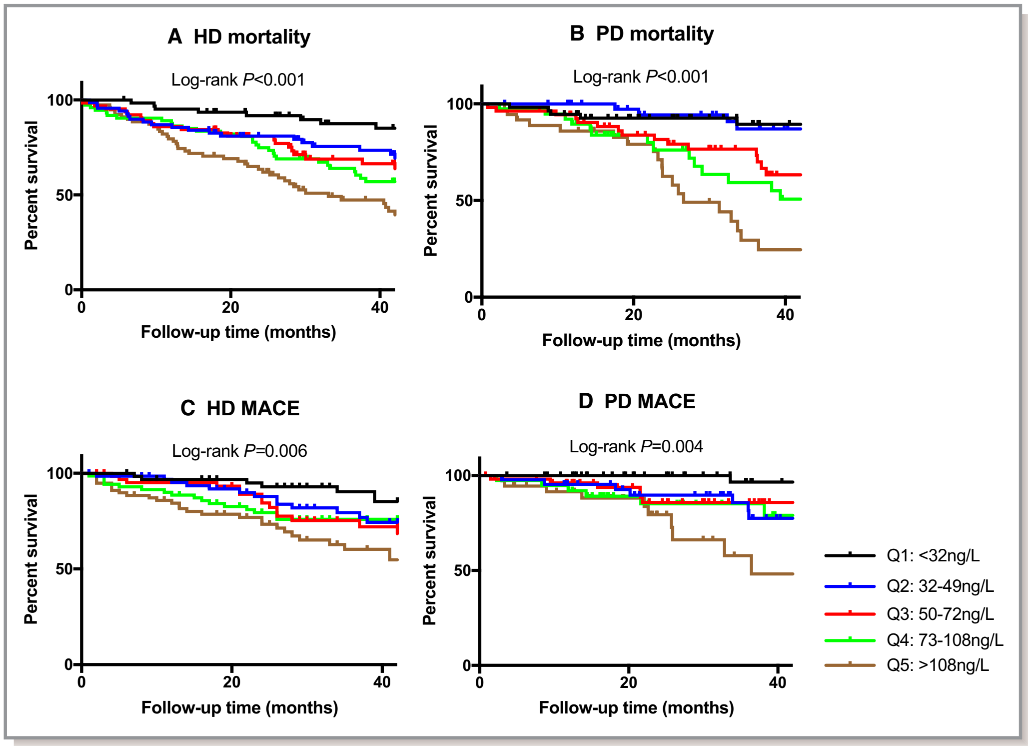

Figure 2. Kaplan–Meier curves based on quintiles of hs-cTnT for mortality (A and B) and MACE (C and D). HD indicates hemodialysis; hs-cTnT, high-sensitivity cardiac troponin T; MACE, major adverse cardiovascular events; PD, peritoneal dialysis; Q, troponin quintile.

patients, adding hs-cTnT to clinical parameters increased AUC for mortality in PD patients (*P*=0.002), but not hemodialysis patients. Adding CRP to clinical parameters did not increase AUC.

Discussion

We reported several important findings in this study. First, hs-cTnT and CRP levels and their prognostic performance were significantly different in PD compared with hemodialysis patients. PD patients had lower hs-cTnT and CRP than hemodialysis patients. In PD patients, both hs-cTnT and CRP were independent predictors for mortality and MACE whereas for HD patients, only hs-cTnT was an independent predictor. There was a significant increase in hs-cTnT level in PD patients over time. However, for hemodialysis patients, hs-cTnT level remained relatively stable. Second, the increased risk of adverse outcome was not linearly related to increased hs-cTnT and CRP. For hs-cTnT, the risk did not become significant until hs-cTnT reached quintile 3 (>49 ng/L) whereas for CRP, only quintile 5 (>16.8 mg/L) was associated with increased risk.

hs-cTnT as a Predictor of Outcomes

We established that increased level of hs-cTnT was associated with a higher risk of mortality and MACE. Troponin has been extensively studied in patients with chronic kidney disease prompting 2 meta-analyses.[4,5] However, very few studies were performed with hs-cTnT. The studies that were performed with hs-cTnT, including the 1 we previously conducted, were limited by smaller sample size or shorter follow-up period.[16–20] In addition, information on PD patients is lacking. There have not been any studies assessing the association between hs-cTnT and MACE, and there is also a lack of information regarding the variability in hs-cTnT over time. Our current study has addressed all of these issues and shown that hs-cTnT is an independent predictor for mortality and MACE in both HD and PD patients at 3.5-year follow-up.

Compared with older troponin T assays that were reported to be elevated in up to 82% of the dialysis population,[21] we found an even higher proportion with elevated hs-cTnT (97%), which is consistent with other studies performed on hs-cTnT.[16,18,22] Previous studies on hs-cTnT analyzed it as a continuous variable.[16,17] We have shown that the increased risk of adverse outcomes with increased hs-cTnT quintiles did not follow a linear relationship. The increased risk only became significant when hs-cTnT reached quintile 3 (>49 ng/L), and there was a significant step up in HR when hs-cTnT increased from quintile 4 (73–108 ng/L) to quintile 5 (>109 ng/L).

Patients in the highest quintile of hs-cTnT may require special attention. This group of patients had the highest HR,

Table 2. Univariable and Multivariable Analysis With Cox Proportional Hazard Model to Examine Variables Influencing Outcomes in Total Cohort

Variables	Mortality						MACE					
	Univariable			Multivariable			Univariable			Multivariable		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Age, y (per decade)	1.57	1.38 to 1.80	<0.001	1.45	1.26 to 1.66	<0.001	1.24	1.06 to 1.44	0.006	1.15	0.98 to 1.36	0.081
Sex, male	1.39	1.02 to 1.89	0.039				1.20	0.82 to 1.76	0.349			
Comorbidities												
Diabetes mellitus	1.08	0.80 to 1.45	0.634				1.63	1.10 to 2.40	0.014			
CHD	1.82	1.36 to 2.45	<0.001	1.37	1.00 to 1.87	0.051	2.04	1.40 to 2.96	<0.001	1.49	1.01 to 2.20	0.046
Hepatitis B/C	0.69	0.33 to 1.47	0.339				1.80	0.94 to 3.46	0.075			
DVT/PE	0.78	0.38 to 1.58	0.488				0.45	0.14 to 1.42	0.172			
Malignancy	1.86	1.27 to 2.72	0.001	1.51	1.01 to 2.25	0.046	0.77	0.40 to 1.47	0.424			
Respiratory	1.34	0.91 to 1.98	0.136				1.83	1.17 to 2.88	0.009	1.74	1.10 to 2.76	0.019
Neurological	1.02	0.67 to 1.56	0.928				0.96	0.56 to 1.65	0.875			
PVD	1.68	1.05 to 2.67	0.030				2.81	1.71 to 4.6	<0.001	2.40	1.43 to 4.03	0.001
Laboratory values												
hs-cTnT quintile												
1 (≤31 ng/L)	Reference						Reference					
2 (32–49 ng/L)	1.93	0.98 to 3.81	0.059	1.24	0.62 to 2.50	0.544	2.81	1.29 to 6.10	0.009	2.31	1.05 to 5.09	0.037
3 (50–72 ng/L)	3.17	1.68 to 5.97	<0.001	2.29	1.20 to 4.34	0.011	2.82	1.29 to 6.16	0.009	2.54	1.15 to 5.59	0.021
4 (73–108 ng/L)	3.93	2.12 to 7.31	<0.001	2.75	1.47 to 5.16	0.002	2.97	1.37 to 6.44	0.006	2.47	1.13 to 5.41	0.024
5 (≥109 ng/L)	6.54	3.59 to 11.92	<0.001	3.67	1.98 to 6.82	<0.001	5.86	2.82 to 12.15	<0.001	3.90	1.85 to 8.22	<0.001
Albumin (per 10 g/L)	0.50	0.38 to 0.66	<0.001	0.60	0.43 to 0.82	0.002	0.61	0.42 to 0.88	0.009	0.68	0.45 to 1.01	0.058
Calcium (per 1 mmol/L)	0.92	0.42 to 1.98	0.824				1.54	0.59 to 4.01	0.381			
Phosphate (per 1 mmol/L)	1.13	0.86 to 1.47	0.377				1.37	0.99 to 1.89	0.058			
Magnesium (per 1 mmol/L)	0.51	0.22 to 1.18	0.116				1.13	0.44 to 2.95	0.797			
Hemoglobin (per 10 g/L)	0.97	0.87 to 1.07	0.509				0.95	0.83 to 1.08	0.396			
CRP quintile												
1 (≤1.6 mg/L)	Reference						Reference					
2 (1.7–3.6 mg/L)	1.56	0.89 to 2.72	0.119	1.31	0.75 to 2.32	0.345	1.30	0.67 to 2.49	0.437			
3 (3.7–7.3 mg/L)	1.73	1.01 to 2.98	0.046	1.38	0.80 to 2.39	0.248	1.76	0.96 to 3.21	0.067			
4 (7.4–16.8 mg/L)	1.74	0.99 to 2.96	0.053	1.41	0.81 to 2.45	0.230	1.18	0.61 to 2.30	0.619			
5 (≥16.9 mg/L)	3.02	1.82 to 5.00	<0.001	2.30	1.37 to 3.87	0.002	2.26	1.24 to 4.13	0.008			

Continued

Table 2. Continued

Variables	Mortality						MACE					
	Univariable			Multivariable			Univariable			Multivariable		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
PTH (per 1 pmol/L)	1.00	0.99 to 1.00	0.564				1.00	0.98 to 1.02	0.571			
Dialysis vintage, y	1.05	1.02 to 1.09	0.004	1.05	1.01 to 1.09	0.020	1.02	0.97 to 1.07	0.396			
Types of dialysis (hemodialysis compared with PD)	1.28	0.93 to 1.75	0.131				1.60	1.06 to 2.43	0.026	1.49	0.96 to 2.32	0.079

CHD indicates coronary heart disease; CI, confidence interval; CRP, C-reactive protein; DVT, deep vein thrombosis; HR, hazard ratio; hs-cTnT, high-sensitivity cardiac troponin T; MACE, major adverse cardiovascular events; PD, peritoneal dialysis; PE, pulmonary embolism; PTH, parathyroid hormone; PVD, peripheral vascular disease.

which almost doubled that of the fourth quintile. They had an extremely high mortality (53.5%) and MACE (32.5%) rate at 3.5 years. Interestingly, their age was not particularly advanced, with a median age of 65. Therefore, selectively targeting this group of patients for prevention or more-intensive intervention may be particularly beneficial.

We also investigated the variability in hs-cTnT level over the 3.5-year period. The pattern of change in hs-cTnT level was different in hemodialysis and PD patients. Surprisingly, hs-cTnT did not change in hemodialysis patients, whereas in PD patients, it increased significantly from year 2. There has only been 1 study investigating the variability in hs-cTnT in hemodialysis only over 1 month and showed no change.[16] This has implications on the frequency of hs-cTnT monitoring. For PD patients, yearly measurements at least are necessary to establish baseline. For hemodialysis patients, a less-frequent measurement may be acceptable. Further study is needed to determine whether variation in hs-cTnT over time can provide additional prognostic information.

CRP as a Predictor of Outcomes

Inflammation has been recognized as an essential component of chronic kidney disease attributed to a variety of reasons.[3] Low-grade inflammation is associated with increased atherosclerotic risk and mortality.[11,23,24] Despite novel inflammatory markers being described in recent years, CRP remains the most measured of inflammatory markers. Use of CRP has increased significantly over the last decade, and dialysis units measuring CRP in more than 50% of their dialysis patients had lower cardiovascular-related mortality.[25]

We evaluated the prognostic value of CRP and compared it with hs-cTnT. Consistent with other studies, we found that CRP was an independent predictor in PD patients only. We are the first study to analyze CRP in quintiles because it was not normally distributed, and found that the increased risk of adverse outcomes with increased CRP quintiles only became statistically significant when CRP reached quintile 5 (>16.8 mg/L). Prognostic performance of CRP was inferior to hs-cTnT. Adding CRP to clinical parameters did not improve its prognostic value.

Hemodialysis Patients

For hemodialysis patients, hs-cTnT level was an independent predictor of mortality and MACE, together with known clinical factors like CHD. This result is consistent with previous studies, which found hs-cTnT to be predictive of mortality in a combined PD and hemodialysis population at 3 years,[17] cardiovascular mortality for hemodialysis at 6 months,[16] and all-cause mortality for hemodialysis at 2 years.[18] We have shown this to be true for both hemodialysis and PD patients at

Table 3. Multivariable Analysis With Cox Proportional Hazard Model to Examine Variables Influencing Mortality and MACE in Hemodialysis and PD Patients

Variables	Hemodialysis						PD					
	Mortality			MACE			Mortality			MACE		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Age, y (per decade)	1.49	1.26 to 1.76	<0.001				1.44	1.13 to 1.83	0.004			
Comorbidities												
CHD	1.67	1.15 to 2.44	0.008	1.60	1.01 to 2.54	0.045						
Respiratory	1.56	0.99 to 2.48	0.057	1.82	1.06 to 3.12	0.031						
PVD				1.94	1.09 to 3.45	0.024						
Laboratory values												
hs-cTnT quintile												
1 (≤31 ng/L)	Reference						Reference					
2 (32–49 ng/L)	1.73	0.74 to 4.05	0.206	2.18	0.88 to 5.39	0.092	0.55	0.14 to 2.10	0.383	3.81	0.78 to 18.53	0.097
3 (50–72 ng/L)	2.36	1.03 to 5.44	0.043	2.61	1.06 to 6.45	0.038	2.49	0.89 to 6.93	0.081	3.53	0.71 to 17.52	0.124
4 (73–108 ng/L)	2.46	1.11 to 5.47	0.027	2.19	0.90 to 5.37	0.086	3.54	1.25 to 10.05	0.017	5.55	1.11 to 27.63	0.037
5 (≥109 ng/L)	3.55	1.64 to 7.70	0.001	3.27	1.40 to 7.62	0.006	5.63	2.02 to 15.67	0.001	10.66	2.27 to 50.14	0.003
Albumin (per 10 g/L)	0.56	0.36 to 0.85	0.007	0.61	0.38 to 0.98	0.040	0.56	0.33 to 0.95	0.031			
CRP quintile												
1 (≤1.6 mg/L)	Reference						Reference					
2 (1.7–3.6 mg/L)							1.34	0.57 to 3.14	0.497	0.77	0.24 to 2.55	0.672
3 (3.7–7.3 mg/L)							2.06	0.86 to 4.94	0.107	1.91	0.63 to 5.84	0.255
4 (7.4–16.8 mg/L)							1.24	0.49 to 3.16	0.654	0.82	0.20 to 3.31	0.783
5 (≥16.9 mg/L)							3.62	1.62 to 8.07	0.002	3.60	1.29 to 10.03	0.014
Dialysis vintage, y	1.05	1.00 to 1.10	0.045									

Nonsignificant factors not shown in the table included hepatitis B/C, DVT/PE, malignancy, neurological disease, calcium, phosphate, magnesium, hemoglobin, and PTH. CHD indicates coronary heart disease; CI, confidence interval; CRP, C-reactive protein; DVT, deep vein thrombosis; HR, hazard ratio; hs-cTnT, high-sensitivity cardiac troponin T; MACE, major adverse cardiovascular events; PD, peritoneal dialysis; PE, pulmonary embolism; PTH, parathyroid hormone; PVD, peripheral vascular disease.

3.5-year follow-up. This is the first study to show that hs-cTnT is also an independent predictor of MACE. These findings are inconsistent with Voroneanu et al, who found that hs-cTnT was not an independent predictor for all-cause mortality in hemodialysis patients at 24 months.[20] This inconsistency could be attributed to the difference in sample size, follow-up period, and analysis method.

For hemodialysis patients, we found that CRP was not an independent predictor for mortality or MACE. Our result is consistent with 1 other study with follow-up of 10 years, which showed that CRP was not a significant predictor for mortality.[26] However, this is contrary to other studies, which showed that CRP was predictive of mortality at 1[24] and 2 years.[11,25,27] The difference may be attributed to the longer follow-up period in our study, and level of CRP may be influenced by many processes and fluctuate significantly over time. It has been shown that CRP is only a good predictor of risk in the short term (1 year of follow-up).[28] Over longer periods, given that other factors influence a patient's prognosis, the association between CRP and mortality weakens.[29] Therefore, it has been proposed that repeated measurement of CRP may be more useful than a single measurement.[29]

PD Patients

There is a paucity of evidence regarding the use of biomarkers in risk stratification of PD patients. We have previously demonstrated that hs-cTnT is an independent predictor of cardiac events and mortality at 1 year.[30] The current study has shown this to be true at 3.5 years. There has been only 1 previous study assessing CRP for prediction of mortality in PD patients,[31] which showed it to be a significant predictor at 2-year follow-up. We confirmed this result at 3.5-year follow-up, and, in addition, it is also a predictor for MACE. We demonstrated the prognostic value of hs-cTnT, and CRP was

Table 4. Univariable and Multivariable Analysis With Cox Proportional Hazard Model to Examine Variables Influencing Outcomes in Patients Without CHD

Variables	Mortality						MACE					
	Univariable			Multivariable			Univariable			Multivariable		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Age, y (per decade)	1.46	1.22 to 1.75	<0.001	1.35	1.11 to 1.64	0.002	1.30	1.05 to 1.61	0.018	1.22	0.97 to 1.55	0.091
Sex, male	1.46	0.94 to 2.28	0.094				0.94	0.54 to 1.62	0.814			
Comorbidities												
Diabetes mellitus	1.11	0.73 to 1.70	0.625				1.42	0.82 to 2.46	0.214			
Hepatitis B/C	0.78	0.29 to 2.12	0.623				1.31	0.47 to 3.63	0.606			
DVT/PE	1.00	0.37 to 2.74	0.995				1.29	0.40 to 4.13	0.672			
Malignancy	2.39	1.45 to 3.95	0.001	1.71	1.00 to 2.94	0.051	1.20	0.54 to 2.67	0.651			
Respiratory	0.98	0.53 to 1.81	0.952				1.43	7.15 to 2.84	0.313			
Neurological	1.07	0.57 to 2.01	0.831				1.10	0.49 to 2.43	0.822			
PVD	2.07	0.95 to 4.48	0.066				3.08	1.31 to 7.22	0.010			
Laboratory values												
hs-cTnT quintile												
1 (≤31 ng/L)	Reference						Reference					
2 (32–49 ng/L)	1.82	0.81 to 4.10	0.148	1.78	0.77 to 4.13	0.176	1.55	0.52 to 4.61	0.432	1.41	0.48 to 4.22	0.534
3 (50–72 ng/L)	1.72	0.75 to 3.92	0.197	1.68	0.73 to 3.86	0.223	2.08	0.74 to 5.85	0.164	1.91	0.68 to 5.38	0.221
4 (73–108 ng/L)	3.05	1.45 to 6.48	0.004	2.75	1.27 to 5.96	0.01	2.97	1.12 to 7.92	0.029	2.49	0.93 to 6.68	0.069
5 (≥109 ng/L)	5.50	2.66 to 11.38	<0.001	4.76	2.27 to 9.96	<0.001	6.34	2.51 to 15.99	<0.001	5.54	2.19 to 14.02	<0.001
Albumin (per 10 g/L)	0.44	0.30 to 0.64	<0.001	0.67	0.44 to 1.02	0.064	0.46	0.28 to 0.75	0.002	0.56	0.34 to 0.93	0.024
Calcium (per 1 mmol/L)	0.95	0.29 to 3.12	0.937				2.02	0.42 to 9.64	0.379			
Phosphate (per 1 mmol/L)	1.22	0.84 to 1.78	0.304				1.37	0.85 to 2.19	0.197			
Magnesium (per 1 mmol/L)	0.19	0.05 to 0.71	0.015	0.26	0.06 to 1.05	0.058	1.81	0.51 to 6.46	0.363			
Hemoglobin (per 10 g/L)	0.96	0.83 to 1.11	0.572				0.94	0.78 to 1.13	0.487			
CRP quintile												
1 (≤1.6 mg/L)	Reference						Reference					
2 (1.7–3.6 mg/L)	1.18	0.56 to 2.51	0.665				1.28	0.48 to 3.41	0.623			
3 (3.7–7.3 mg/L)	1.37	0.67 to 2.80	0.395				2.24	0.95 to 5.29	0.065			
4 (7.4–16.8 mg/L)	1.83	0.93 to 3.60	0.080				1.36	0.53 to 3.53	0.527			
5 (≥16.9 mg/L)	2.19	1.10 to 4.36	0.026				2.53	1.03 to 6.10	0.042			
PTH (per 1 pmol/L)	1.00	1.00 to 1.00	0.769				1.00	1.00 to 1.00	0.963			

Continued

Table 4. Continued

Variables	Mortality						MACE					
	Univariable			Multivariable			Univariable			Multivariable		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Dialysis vintage, y	1.04	0.98 to 1.09	0.177				1.01	0.94 to 1.09	0.720			
Types of dialysis (hemodialysis compared with PD)	1.10	0.71 to 1.71	0.671				1.60	0.89 to 2.92	0.125			

CHD indicates coronary heart disease; CI, confidence interval; CRP, C-reactive protein; DVT, deep vein thrombosis; HR, hazard ratio; hs-cTnT, high-sensitivity cardiac troponin T; MACE, major adverse cardiovascular events; PD, peritoneal dialysis; PE, pulmonary embolism; PTH, parathyroid hormone; PVD, peripheral vascular disease.

greater than that of other known clinical risk factors, such as sex, history of diabetes mellitus, and CHD, in the multivariable analysis. When adding hs-cTnT to clinical parameters in the ROC analysis, it improved the prognostic performance of clinical parameters significantly.

hs-cTnT and CRP Levels Are Different in Hemodialysis Patients Compared With PD Patients

There are a few differences between hemodialysis and PD patients that are worthwhile noting. First, hemodialysis patients had a higher baseline hs-cTnT and CRP level than PD patients, even though prevalence of CHD in the 2 cohorts is similar. It is well established that hemodialysis patients have high baseline troponin levels, without acute myocardial infarction or coronary artery disease.[32–34] The reason for this is controversial, but there is emerging evidence suggesting that hemodialysis-induced myocardial stunning may be the cause of high troponin levels in these patients, and it may contribute to the increased adverse outcomes.[35,36] On the other hands, PD is not associated with myocardial stunning.[37] However, PD is not completely benign. It may still induce subclinical myocardial injury and hence result in their higher-than-normal baseline value.[38] Second, we found that CRP was a predictor in PD patients, but not hemodialysis patients. One possible reason may be that hemodialysis patients are subject to more factors such as dialysis membrane incompatibility and dialysate backflow, which can cause larger CRP fluctuations than PD patients. Third, there is less hs-cTnT variability in hemodialysis patients than PD patients. It would be interesting to see whether variation in hs-cTnT level can also predict outcome. However, this analysis is beyond the scope of this study.

hs-cTnT as a Risk Predictor in Patients Without Known CHD

In the subgroup of patients without CHD, even though they had lower hs-cTnT than patients with CHD, the majority still had elevated hs-cTnT. This group of asymptomatic patients still had poor survival, and the higher their hs-cTnT, the higher the risk of mortality or MACE. There has been 1 study showing similar results in PD patients with traditional troponin assay.[39] The mechanism for this is unclear. However, there is emerging evidence that elevated hs-cTnT may indicate subclinical myocardial stunning in hemodialysis patients rather than coronary artery disease.[36] In PD patients, it has also been proposed that the elevated troponin could be attributed to subclinical myocardial injury.[38] Given that this population is not usually under stringent cardiac monitoring, they may benefit the most from biomarker risk stratification and subsequent referral to a cardiologist.

Table 5. AUC for hs-cTnT, CRP, and Combined Clinical Parameters as Predictors of Outcomes at 3.5 Years

		hs-cTnT		CRP		Clinical Parameters			Clinical Parameters+hs-cTnT	
	Outcomes	AUC	95% CI	AUC	95% CI	AUC	95% CI	*P* Value*	AUC	95% CI
All group	Mortality	0.71	0.66 to 0.75	0.59	0.54 to 0.64	0.70	0.65 to 0.75	0.012	0.74	0.69 to 0.79
	MACE	0.62	0.57 to 0.67	0.52	0.47 to 0.58	0.63	0.58 to 0.69	0.066	0.65	0.60 to 0.70
PD	Mortality	0.77	0.67 to 0.85	0.58	0.48 to 0.68	0.69	0.59 to 0.78	0.002	0.84	0.75 to 0.90
	MACE	0.66	0.57 to 0.75	0.55	0.45 to 0.64	0.69	0.59 to 0.78	0.332	0.71	0.61 to 0.79
Hemodialysis	Mortality	0.67	0.61 to 0.73	0.60	0.53 to 0.66	0.72	0.66 to 0.78	0.251	0.74	0.67 to 0.79
	MACE	0.60	0.53 to 0.66	0.50	0.44 to 0.57	0.63	0.57 to 0.69	0.570	0.64	0.57 to 0.70

AUC indicates area under the receiver operating curve; CI, confidence interval; CRP, C-reactive protein; Hs-cTnT, high-sensitivity cardiac troponin T; MACE, major adverse cardiovascular events; PD, peritoneal dialysis.

**P* values presented here are for comparison between clinical parameters and clinical parameters+hs-cTnT. Clinical parameters used in the analysis included age, sex, dialysis vintage, history of diabetes mellitus, coronary heart disease, and peripheral vascular disease.

Limitations

This is a single-center observational study, which may limit the generalizability of our findings. The outcome data were based on clinical records, and sudden death was considered a cardiac death if no other cause was recognized. Cause of death was not confirmed by postmortem examination, but based on clinical assessment. In addition, the focus of this study was not to understand the underlying pathophysiology for elevated troponin; as such, echocardiographic and coronary angiographic results or hemodynamic data during hemodialysis sessions was not collected nor factored into the analysis.

Clinical Implications

Our study has several important clinical implications. First, we confirmed that increased level of hs-cTnT is an independent predictor for mortality and MACE in both hemodialysis and PD patients. Its prognostic value is better than CRP. The increased risk of adverse outcomes with increased hs-cTnT quintiles did not follow a linear relationship. The increased risk only became significant when hs-cTnT reached quintile 3 (50–72 ng/L), and the HR peaked at quintile 5 (>108 ng/L). Second, CRP is an independent predictor for mortality and MACE in PD patients only. The increased risk was only associated with patients with CRP in quintile 5 (>16.8 mg/L), but not lower quintiles. Third, in PD patients, where there is a paucity of information, we have shown that both CRP and hs-cTnT are independent predictors for both mortality and MACE. Adding hs-cTnT to clinical parameters significantly improved the risk prediction of clinical parameters. Fourth, the frequency of hs-cTnT measurement should be at least yearly for PD patients to establish baseline given the level increases significantly. For hemodialysis patients, a less-frequent measurement may be acceptable given that the change over time is minimal.

Future work should assess the cost-effectiveness of routine measures of these biomarkers in clinical practice, and how they can be used to improve clinical management and therapeutic intervention.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. Baseline characteristics and outcomes across quintiles based on hs-cTnT.

	Q1 (N=118) Hs-cTnT<=31ng/L	Q2 (N=113) 32-49ng/L	Q3 (N=118) 50-72ng/L	Q4 (N=111) 73-108ng/L	Q5 (N=114) 109+ng/L	*P* Value
Age, years	57.7 (48-68.8)	67.2 (56.8-75.1)	68.0 (56.3-75.0)	68.3 (61.0-75.4)	65.0 (57.5-73.5)	<0.001
Sex, male	49 (41.5)	57 (50.2)	75 (63.6)	74 (66.7)	87 (76.3)	<0.001
Comorbidities						
Diabetes	38 (32.2)	56 (49.6)	62 (52.5)	70 (63.1)	84 (73.7)	<0.001
CHD	27 (22.9)	46 (40.7)	50 (42.4)	45 (40.5)	60 (52.6)	<0.001
Hepatitis B/C	10 (8.5)	6 (5.3)	5 (4.2)	6 (5.4)	4 (3.5)	0.486
DVT/PE	8 (6.8)	6 (5.3)	7 (5.9)	7 (6.3)	5 (4.4)	0.938
Malignancy	15(12.7)	8 (7.1)	16 (13.6)	11 (9.9)	19 (16.7)	0.229
Respiratory	13 (11.0)	10 (8.8)	23 (19.5)	15 (13.5)	24 (21.1)	0.041
Neurological	13 (11.0)	16 (14.2)	14 (11.9)	20 (18.0)	13 (11.4)	0.481
PVD	7 (5.9)	7 (6.2)	6 (5.1)	9 (8.1)	13 (11.4)	0.37
Laboratory values						
Albumin, g/L	40 (37-42)	39 (35-42)	40 (36-42)	39 (36-42)	39 (35-42)	0.092
Calcium, mmol/L	2.27 (2.17-2.37)	2.27 (2.14-2.36)	2.30 (2.16-2.42)	2.27 (2.15-2.39)	2.28 (2.21-2.38)	0.348
Phosphate, mmol/L	1.53 (1.26-1.99)	1.67 (1.31-2.11)	1.71 (1.38-2.06)	1.64 (1.35-1.98)	1.72 (1.31-2.11)	0.347
Magnesium, mmol/L	0.88 (0.81-0.97)	0.91 (0.81-1.05)	0.89 (0.81-0.99)	0.93 (0.83-1.04)	0.91 (0.81-0.99)	0.360
Hemoglobin, g/L	115 (102-122)	112 (98-123)	116 (106-126)	113 (104-125)	114 (101-125)	0.280
CRP, mg/L	4.2 (2.4-11.1)	4.8 (1.6-13.7)	5.3 (1.9-11.3)	5.1 (1.9-13.4)	5.0 (2.7-17.1)	0.420
PTH, pmol/L	35.7 (20.5-75.2)	29.5 (11.8-49.9)	34.3 (18.6-56.8)	35.6 (15.1-58.2)	24.3 (12.5-55.7)	0.043
Dialysis Vintage, years	0.8 (0.1-2.4)	1.2 (0.4-3.2)	1.3 (0.2-4.3)	2.1 (0.4-5.5)	1.6 (0.4-3.8)	0.011
Outcomes						

Mortality	13 (11.0)	23 (20.4)	36 (30.5)	43 (38.7)	61 (53.5)
MACE	9 (7.6)	22 (19.5)	21 (17.8)	22 (19.8)	37 (32.5)

DVT indicates deep vein thrombosis; PE, pulmonary embolism; CHD, coronary heart disease; PVD, peripheral vascular disease; hs-cTnT, high sensitivity cardiac troponin T; CRP, C-reactive protein; PTH, parathyroid hormone; MACE, major adverse cardiovascular events.

Table S2. Baseline characteristics and outcomes across quintiles based on CRP.

	Q1 (N=114) CRP<=1.6mg/L	Q2 (N=115) 1.7-3.6mg/L	Q3 (N=114) 3.7-7.3mg/L	Q4 (N=109) 7.4-16.8mg/L	Q5 (N=113) 16.9+mg/L	*P* Value
Age, years	65.0 (56.6-71.6)	66.0 (53.7-73.6)	67.1 (53.8-75)	66.1 (53-73.4)	66.3 (57.2-75.7)	0.958
Sex, male	70 (61.4)	66 (57.4)	64 (56.1)	68 (62.4)	69 (61.1)	0.843
Comorbidities						
Diabetes	61 (53.5)	69 (60.0)	71 (62.3)	51 (46.8)	56 (49.6)	0.111
CHD	30 (26.3)	47 (40.9)	47 (41.2)	40 (36.7)	62 (54.9)	<0.001
Hepatitis B/C	12 (10.5)	5 (4.3)	3 (2.6)	6 (5.5)	5 (4.4)	0.092
DVT/PE	5 (4.4)	4 (3.5)	8 (7.0)	12 (11.0)	4 (3.5)	0.087
Malignancy	8 (7.0)	15 (13.0)	13 (11.4)	20 (18.3)	11 (9.7)	0.116
Respiratory	10 (8.8)	18 (15.7)	15 (13.2)	20 (18.3)	21 (18.6)	0.199
Neurological	12 (10.5)	17 (14.8)	16 (14.0)	15 (13.8)	16 (14.2)	0.898
PVD	3 (2.6)	10 (8.7)	8 (7.0)	6 (5.5)	14 (12.4)	0.059
Laboratory values						
Hs-cTnT, ng/L	56 (34-91)	62 (37-105)	60 (35-108)	52 (31-77)	74 (44-121)	<0.001
Albumin, g/L	40 (36-42)	40 (37-43)	40 (37-42)	39 (36-42.5)	38 (43-41)	0.010
Calcium, mmol/L	2.26 (2.13-2.38)	2.29 (2.16-2.39)	2.30 (2.21-2.42)	2.28 (2.13-2.365)	2.26 (2.16-2.36)	0.148
Phosphate, mmol/L	1.64 (1.33-1.94)	1.68 (1.4-2.12)	1.61 (1.32-2.08)	1.60 (1.24-2.01)	1.72 (1.41-2.10)	0.253
Magnesium, mmol/L	0.91 (0.82-1.01)	0.92 (0.85-1.00)	0.92 (0.81-1.04)	0.86 (0.80-1.00)	0.89 (0.80-0.98)	0.189
Hemoglobin, g/L	113 (105-123)	116(104-125)	114 (103-123)	113 (106-125)	110 (99-122)	0.363
PTH, pmol/L	24.1 (13.0-44.9)	35.4 (13.9-62.7)	37.4 (16.7-74.5)	33.5 (13.3-65.2)	33.0 (15.3-51.9)	0.104
Dialysis Vintage, years	1.0 (0.2-3.1)	0.9 (0.2-2.9)	1.5 (0.2-3.5)	1.6 (0.5-3.9)	2.3 (0.5-5.9)	0.009
Outcomes						
Mortality	21 (18.4)	30 (26.1)	35 (30.7)	33 (30.3)	54 (47.8)	

MACE	17 (14.9)	19 (16.5)	28 (24.6)	18 (16.5)	28 (24.8)

DVT indicates deep vein thrombosis; PE, pulmonary embolism; CHD, coronary heart disease; PVD, peripheral vascular disease; hs-cTnT, high sensitivity cardiac troponin T; CRP, C-reactive protein; PTH, parathyroid hormone; MACE, major adverse cardiovascular events.

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