Prognostic Value of Cardiac Troponin T Is Independent of Inflammation, Residual Renal Function, and Cardiac Hypertrophy and Dysfunction in Peritoneal Dialysis Patients

Angela Yee-Moon Wang,1* Christopher Wai-Kei Lam, 2 Mei Wang, 1 Iris Hiu-Shuen Chan, 2 William B. Goggins, 3 Cheuk-Man Yu, 1 Siu-Fai Lui, 1 and John E Sanderson 1†

Background: We investigated whether cardiac troponin T (cTnT) independently predicted outcome and added prognostic value over other clinical risk predictors in chronic peritoneal dialysis (PD) with end-stage renal disease.

Methods: Baseline cTnT, echocardiography, indices of dialysis adequacy, and biochemical characteristics were assessed in 238 chronic PD patients who were followed prospectively for 3 years or until death.

Results: Using multivariable Cox regression analysis, cTnT remained predictive of all-cause mortality [hazard ratio 4.43, 95% CI 1.87–10.45, \(P = 0.001\)], cardiovascular death (4.12, 1.29–13.17, \(P = 0.017\)), noncardiovascular death (8.06, 1.86–35.03, \(P = 0.005\)), and fatal and nonfatal cardiovascular events (CVEs) (3.59, 1.48–8.70, \(P = 0.005\)) independent of background coronary artery disease, inflammation, residual renal function, left ventricular hypertrophy, and systolic dysfunction. cTnT alone had better predictive value than C-reactive protein (CRP) alone for mortality [area under the ROC curve (AUC) 0.774 vs 0.691; \(P = 0.089\)] and first CVE (AUC 0.711 vs 0.593; \(P = 0.009\)) at 3 years. Survival models including age, sex, and clinical, biochemical, and echocardiographic characteristics yielded AUCs of 0.813 (95% CI, 0.748–0.877), 0.800 (95% CI, 0.726–0.874), and 0.769 (95% CI, 0.708–0.830), respectively, in relation to all-cause mortality, cardiovascular death, and fatal and nonfatal cardiovascular events. After addition of cTnT, AUCs of the above models increased significantly to 0.832 (95% CI, 0.669–0.894; \(P = 0.0037\)), 0.810 (95% CI, 0.739–0.883; \(P = 0.0036\)), and 0.780 (95% CI, 0.720–0.840; \(P = 0.0002\)), respectively; no AUCs increased when CRP was added.

Conclusions: cTnT is an independent predictor of long-term mortality, cardiovascular death and events, and noncardiovascular death in PD patients.

© 2007 American Association for Clinical Chemistry

The mortality of patients with end-stage renal disease (ESRD)4 remains high because of increased prevalence of cardiovascular complications (1). Hence, a clinical goal is to identify serum biomarkers useful for cardiovascular risk prediction and stratification in this population. Cardiac troponin T (cTnT) is a highly sensitive and specific marker of myocardial damage. It is useful in diagnosing acute myocardial infarction and predicts mortality in non–renal failure patients with unstable coronary disease (2–3). In addition, patients with heart failure have in-
creased cTnT in the absence of acute ischemia (4–5), suggesting that an increase in cTnT may reflect subclinical myocardial damage.

cTnT is frequently increased in ESRD patients without evidence of acute myocardial ischemia (6–7) and is associated with all-cause and cardiovascular death (8–13). Recently, the Netherlands Cooperative Study on the Adequacy of Dialysis showed that although cTnT predicts mortality, it has limited added predictive value over other clinical risk factors in dialysis patients (14). On the other hand, our recent study indicated an incremental value of cTnT to conventional echocardiography in predicting circulatory congestion in peritoneal dialysis (PD) patients (15). cTnT correlates with left ventricular (LV) hypertrophy in ESRD patients without acute myocardial ischemia (9, 11). The important question—whether cTnT remains prognostically significant after adjusting for important potential confounders such as coronary artery disease (CAD), cardiac hypertrophy and dysfunction, inflammation, and residual renal function (RRF)—has remained unanswered.

We studied PD patients to determine, first, whether the long-term prognostic value of cTnT remained independent of other outcome predictors and potential confounders for cTnT and, second, whether cTnT has added predictive value over other clinical risk predictors, including C-reactive protein (CRP).

**Materials and Methods**

**Patients**

The Clinical Research Ethics Committee of the Chinese University of Hong Kong approved the study. Patients were eligible for study inclusion if they had ESRD and were on continuous ambulatory PD therapy for ≥3 months. All patients used conventional lactate-buffered glucose-based PD solutions. Exclusion criteria included acute coronary syndrome, underlying malignancy, chronic liver disease, systemic lupus erythematosus, chronic rheumatic heart disease, congenital heart disease, and refusal to give consent. Of the 270 total PD patients in our center, 32 were excluded; the remaining 238 (88%) patients were included in the study. Informed consent was obtained from all study patients. Study enrollment started in September 1999 and ended in December 2000.

**Study Design**

This prospective cohort study was conducted in a single dialysis center of a university teaching hospital in Hong Kong. At study enrollment, all patients underwent baseline echocardiography, measurement of RRF, dialysis indices, and biochemical characteristics. In patients who developed volume overload, peritonitis, exit site infections, or other infective complications, all the above assessments were deferred for at least 1 month after complete resolution of the complication.

**Data Collection**

At baseline, we collected demographic data including age, sex, dialysis duration, cause of renal failure, smoking history, and diabetes status. We defined known clinical atherosclerotic vascular disease as CAD, which included the presence of ischemic heart disease, history of angina, previous myocardial infarction with or without coronary artery bypass surgery or stenting, ischemic cerebrovascular event, transient ischemic attack, or peripheral vascular disease with or without amputation. An experienced cardiologist blinded to all clinical details of patients performed 2-dimensional echocardiography in patients lying in the left decubitus position by use of a GE-VingMed System 5 echocardiographic machine (GE-VingMed Sound AB) with a 3.3-mHz multiphase array probe. All echocardiographic data were recorded according to the guidelines of the American Society of Echocardiography (16, 17).

We measured residual glomerular filtration rate (GFR) at the time of echocardiography as the average of 24-h urine urea and creatinine clearance (18). We estimated adequacy of dialysis by measuring total weekly urea and creatinine clearance using conventional methods (19). We corrected creatinine concentration in dialysate for interference by glucose according to the reference formula derived in our laboratory (20). Contribution of PD and renal component to the total urea clearance was estimated separately.

At study entry, we collected EDTA and heparin blood samples for measurement of cTnT, high-sensitivity CRP, albumin, and hemoglobin after patients completed the first PD exchange of the day. We measured cTnT in EDTA plasma by use of a 3rd-generation electrochemiluminescence immunoassay (Roche Modular analyzer, Roche Diagnostic GmbH) with detection limit 0.01 μg/L and interfere CVs of 5.9%, 4.8%, and 1.5% at 0.024, 0.18, and 1.76 μg/L, respectively. We measured CRP and albumin in heparin plasma by use of the Tina-quant CRP latexulsensitive assay (detection limit 0.01 mg/L and CV 1.6% at 2.0 mg/L) and the bromcresol purple method (CV 2.8% at 45 g/L) on the Roche analyzer.

**Follow-up and Outcome Measures**

All patients were followed up prospectively in the hospital clinic for 3 years from the day of study entry (when they had all of the baseline assessments) or until death. Cause of death and nature of the 1st cardiovascular event (CVE; fatal or nonfatal) were determined by the attending physicians, who had no knowledge of the baseline cTnT and CRP results. This information was retrieved from the computerized Clinical Management System of the Hong Kong Hospital Authority and the Renal Registry Database that keeps detailed records of all hospitalization episodes. In case of death out of hospital, family members were interviewed by telephone to ascertain the circumstances surrounding death. No patient was lost to follow-up. The outcome measures evaluated were death from all causes,
continuous variables for the Cox models were evaluated of proportional hazards. The functional forms of the all-cause mortality, cardiovascular and noncardiovascular death, and fatal CVEs as defined below. Sudden cardiac death was defined as unexpected natural death within 1 h from symptom onset and without any prior condition that would appear fatal (21,22). Fatality and nonfatal CVEs included angina with electrocardiographically-documented changes of myocardial ischemia, myocardial infarction, electrocardiographically-documented arrhythmia, transient ischemic attacks, thromboembolic or hemorrhagic stroke (all defined according to conventional clinical criteria), peripheral vascular disease, cardiovascular congestion, and sudden cardiac death. Peripheral vascular disease was defined as the presence of intermittent claudication with angiographic or sonographic detection of ≥50% stenosis of the major arteries of the lower limb, with or without revascularization procedures, ischemic leg ulceration, gangrene, amputation, and aortic aneurysm. Cardiovascular congestion was defined clinically by the presence of symptoms and signs of heart failure including dyspnea, increased jugular venous pressure, and basal crepitations together with radiographic evidence of pulmonary venous congestion or interstitial edema (23) and resolution of symptoms, signs, and radiographic changes with hypertonic peritoneal dialysis exchanges. For patients who had multiple CVEs, survival analysis in relation to CVE was limited to the 1st CVE.

STATISTICAL ANALYSIS

We used the Kolmogorov–Smirnov test for gaussian distribution of continuous data, and we expressed data as mean (SD) or median [interquartile range (IQR)] depending on the distribution. We stratified patients by conventional cTnT cutoffs <0.01 µg/L (99th percentile), 0.03 µg/L (10% CV), and 0.10 µg/L (clinical threshold). Comparisons among groups were performed using ANOVA. We tested the trend across the groups of cTnT using the trend test. Variables not in gaussian distribution were log-transformed before performing the trend test. We generated survival curves stratified by cTnT groups using the Kaplan-Meier method and compared between-group survival using the log-rank test. In this analysis, patients who underwent kidney transplantation or transferred to hemodialysis during the 3-year period were censored at the time of transfer to alternative renal replacement therapy. If a patient died within 3 months of transfer to hemodialysis, he or she was not censored, as the early mortality was considered to reflect the health status during the period of failing PD treatment. We used Cox proportional hazards model to estimate the hazard ratios of all-cause mortality, cardiovascular and noncardiovascular death, and fatal and nonfatal CVEs in relation to cTnT and other variables. We checked that all variables considered in the regression analysis met the assumption of proportional hazards. The functional forms of the continuous variables for the Cox models were evaluated by examining scatter plots of the Martingale residuals from the null Cox model vs each covariate (24). A backward stepwise procedure was used to choose the final basic model, with variables significant at $P < 0.10$ being retained in the model. To have adequate confounder control, before dropping a covariate from the model, we made sure that its absence from the model did not result in a substantial change in the risk estimates for the other covariates. Background CAD, CRP, residual GFR, and LV mass and function were retained in all models regardless of their statistical significance.

We performed ROC curves analysis to investigate the predictive value of cTnT, CRP, cTnT and CRP together, echocardiographic measures, and cTnT in addition to other covariates with or without CRP. All-cause mortality, cardiovascular death, noncardiovascular death, and fatal and nonfatal CVE at 3 years were the events of interest. We calculated a risk score for each individual based on each model by multiplying the coefficient estimate for each variable from the fully adjusted Cox model by the value of the variable for each patient and then adding these Figs. for each patient. This risk score was then used in the ROC analysis. The best cutoff of cTnT in predicting all-cause mortality and CVE was derived from the ROC curves and was defined as the value that gave the best combination of sensitivity and specificity. We considered $P$ values <0.05 to be statistically significant, and all tests were 2-sided. All statistical analyses were performed using SAS software, version 8.2 (SAS Institute), SPSS software, version 11.0 (SPSS), and MedCalc Software version 7.50.

Results

The baseline characteristics of the study population are shown in Table 1. The underlying renal disease was chronic glomerulonephritis in 75 patients (31.5%), diabetic nephropathy in 58 patients (24.4%), hypertensive nephropathy in 32 patients (13.4%), and other causes or not identified in 73 patients (30.7%). cTnT concentration was <0.01 µg/L in 77 patients (32.4%), 0.01 to 0.029 µg/L in 15 patients (6.3%), 0.03 to 0.099 µg/L in 63 patients (26.5%), and ≥0.1 µg/L in 83 patients (34.8%). Excluding the 77 patients with cTnT <0.01 µg/L, the median cTnT concentration was 0.06 (range 0.01–3.95) µg/L. The clinical, biochemical, and echocardiographic characteristics of patients in the different cTnT categories are detailed in Table 1. Patients with cTnT 0.01–0.029 and 0.03–0.099 µg/L were combined as a group for analysis because there were only 15 patients with cTnT 0.01–0.029 µg/L. LV end-diastolic (P <0.001) and end-systolic (P <0.001) volume indexed by body surface area showed significant increasing trend with increasing cTnT. Body mass index (P = 0.057), diastolic blood pressure (P = 0.058), and PD urea clearance (P = 0.45) showed no significant trend with increasing cTnT. There was no significant trend in the use of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (P = 0.32), beta-blocker (P = 0.33), calcium-channel blocker (P = 0.44), hydroxymethylglu-
Table 1. Baseline characteristics of study population in the cardiac troponin T categories.

<table>
<thead>
<tr>
<th>Initial plasma cardiac troponin T, µg/L</th>
<th>&lt;0.01</th>
<th>0.01–0.099*</th>
<th>≥0.10</th>
<th>P value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>238</td>
<td>77</td>
<td>78</td>
<td>83</td>
</tr>
<tr>
<td>Age, years</td>
<td>55.7 (11.6)</td>
<td>52.1 (12.4)</td>
<td>57.0 (11.0)</td>
<td>57.9 (10.6)</td>
</tr>
<tr>
<td>Male, %</td>
<td>51.3</td>
<td>40.3</td>
<td>50.0</td>
<td>62.7</td>
</tr>
<tr>
<td>Positive smoking history, %</td>
<td>37.0</td>
<td>26.0</td>
<td>37.2</td>
<td>47.0</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>30.7</td>
<td>13.0</td>
<td>29.5</td>
<td>48.2</td>
</tr>
<tr>
<td>Coronary artery disease, %</td>
<td>20.2</td>
<td>6.5</td>
<td>23.1</td>
<td>30.1</td>
</tr>
<tr>
<td>Atherosclerotic vascular disease, %</td>
<td>23.1</td>
<td>6.5</td>
<td>21.8</td>
<td>39.8</td>
</tr>
<tr>
<td>Median dialysis duration, months (IQR)</td>
<td>27 (15–51)</td>
<td>23 (14–40)</td>
<td>26 (13–57)</td>
<td>40 (16–60)</td>
</tr>
<tr>
<td>Total weekly urea clearance</td>
<td>1.81 (0.45)</td>
<td>1.94 (0.39)</td>
<td>1.81 (0.45)</td>
<td>1.68 (0.45)</td>
</tr>
<tr>
<td>Total weekly creatinine clearance, L/week per 1.73 m²</td>
<td>56 (22)</td>
<td>67.1 (25.0)</td>
<td>56.5 (21.9)</td>
<td>49.2 (15.3)</td>
</tr>
<tr>
<td>No residual renal function, %</td>
<td>38.7</td>
<td>13.0</td>
<td>38.5</td>
<td>62.7</td>
</tr>
<tr>
<td>Hemoglobin, g/L</td>
<td>92 (17)</td>
<td>99 (17)</td>
<td>92 (17)</td>
<td>88 (16)</td>
</tr>
<tr>
<td>Serum albumin, g/L</td>
<td>28.6 (5.1)</td>
<td>29.4 (5.4)</td>
<td>28.6 (5.1)</td>
<td>26.5 (4.4)</td>
</tr>
<tr>
<td>Median CRP, mg/L (IQR)</td>
<td>2.72 (0.92–9.00)</td>
<td>1.33 (0.67–3.97)</td>
<td>4.29 (0.63–13.67)</td>
<td>5.28 (1.37–16.36)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>147 (17)</td>
<td>143 (17)</td>
<td>147 (17)</td>
<td>149 (19)</td>
</tr>
<tr>
<td>LV mass index, g/m²</td>
<td>224 (84)</td>
<td>172 (47)</td>
<td>236 (81)</td>
<td>263 (90)</td>
</tr>
<tr>
<td>Ejection fraction &lt;40%, %</td>
<td>6.6</td>
<td>0</td>
<td>2.6</td>
<td>16.3</td>
</tr>
</tbody>
</table>

Data are mean (SD) unless specified otherwise.

* Patients with cTnT 0.01–0.029 and cTnT 0.03–0.099 µg/L were combined as a group for analysis.

During follow-up, 70 patients (29.4%) died, 25 patients (10.5%) underwent kidney transplantation, and 25 patients (10.5%) switched to hemodialysis. There were 44 deaths from cardiovascular causes, including ischemic heart disease/myocardial infarction in 6, cardiovascular congestion in 2, arrhythmia in 1, sudden death in 19, cerebrovascular disease in 12, and peripheral vascular disease in 4 patients. The remaining 26 noncardiovascular deaths were due to peritonitis in 10, other infections in 11, malignancy in 2, and miscellaneous causes including termination of dialysis in 3 patients. Excluding patients who underwent kidney transplantation (n = 25) or who were switched to hemodialysis (n = 25), patients who died (n = 70) had higher median (IQR) cTnT at study baseline than those who remained alive on PD by the end of the 3-year follow-up (n = 118) [0.16 (0.08–0.28) vs 0.03 (0.01–0.08) µg/L, P <0.001].

During follow-up, 129 patients developed one or more fatal and nonfatal CVEs: 15 patients had ischemic heart disease, 18 patients had cerebrovascular disease, 5 patients had peripheral vascular disease, 78 patients had cardiovascular congestion, 6 patients had arrhythmia, and 7 patients had sudden cardiac death as their first CVE. Those who developed one or more CVEs had a higher median (IQR) cTnT at study baseline than those who had no CVEs during the 3-year follow-up [0.1 (0.02–0.20) vs 0.02 (0.01–0.07) µg/L, P <0.001]. Fig. 1 shows the Kaplan-Meier survival curves in relation to all-cause mortality, cardiovascular mortality, and 1st fatal or nonfatal CVE of patients in the 3 groups of cTnT. In the final multivariable Cox regression models (Table 2), cTnT remained a significant predictor of mortality, cardiovascular, and noncardiovascular death [adjusted hazard ratio, 8.06 (95% confidence interval [CI], 1.86–35.03), P = 0.005], and fatal and nonfatal CVE independent of background CAD, CRP, residual GFR, LV mass index, and ejection fraction. There was no synergism between cTnT and CRP in relation to the different outcomes.

The ability of cTnT and other variables to predict the different outcomes at 3 years was investigated by ROC analysis (Table 3). Compared to CRP alone, cTnT alone showed higher predictive value across all outcomes including all-cause mortality (P = 0.089), cardiovascular death, noncardiovascular death, and fatal and nonfatal CVE (P = 0.009). Adding cTnT to the model including age, sex, and clinical, biochemical, and echocardiographic features further increased the areas under the curves (AUCs) across all outcomes, whereas adding CRP did not increase the AUCs for any of the outcomes.

According to ROC curve analysis, the cTnT cutoff that best discriminated patients who died from those who survived and between patients with and without CVE at 3 years was 0.075 µg/L. This cutoff of 0.075 µg/L had a
similar sensitivity and specificity in predicting mortality [76% (95% CI 64%–85%) and 71% (63%–78%), respectively] and had a positive and negative predictive value of 52% and 88%, respectively, for mortality. The diagnostic sensitivity for CVE using a cTnT cutoff of 0.075 μg/L was 61% (52%–69%), and the specificity was 78% (69%–85%); this corresponded to a positive and negative predictive value of 77% and 63%, respectively, for CVE.
**Discussion**

In this prospective study, we showed that a single random cTnT provides important prognostic value for long-term mortality, CVE, fatality, and noncardiovascular death in chronic PD patients independent of other risk predictors including CAD, CRP, RRF, LV hypertrophy, and systolic dysfunction. Our findings clearly extend the usefulness of cardiac cTnT as a biomarker for long-term cardiovascular risk stratification and outcome prediction to ESRD patients receiving long-term PD. As in hemodialysis patients (7–10, 12, 13), two-thirds of our PD patients had cTnT ≥0.01 μg/L, and one-third ≥0.1 μg/L. In addition, cTnT was linked to LV mass (9, 25) but predicted mortality and cardiovascular death and events independent of LV mass. This contrasts with the study by deFilippi et al. (10) that showed no relation between cTnT and LV mass or function, but is similar to other studies in hemodialysis patients (9, 25). So far, only 2 studies have been done in a PD population (11, 12). Both reported prognostic value of cTnT but were limited by very small sample size. The recent Netherlands Cooperative Study on the Adequacy of Dialysis reported limited predictive power of cTnT over other clinical risk factors in a mixed cohort of hemodialysis and PD patients (14). This is in contrast to our current finding that troponin T has added predictive value over other clinical, biochemical, and echocardiographic measures in chronic PD patients for all-cause mortality and cardiovascular death and events. Our study has the largest number of PD patients and extends our previous observation that cTnT adds significant value to echocardiography in identifying PD patients at risk of cardiovascular congestion (15). cTnT testing may not replace echocardiography, but our data clearly confirm the additional value of cTnT testing for prognostication in chronic PD patients without acute myocardial ischemia.

The cTnT cutoffs used to evaluate mortality and cardiovascular risk differed in different studies. Some studies (8, 9), including a recent metaanalysis (27), suggested that a cTnT concentration >0.1 μg/L identified a subgroup of asymptomatic ESRD patients with poor survival and high risk of cardiac death. There is increasing evidence, however, that an even lower cTnT cutoff of <0.1 μg/L (clinical threshold) was predictive of an increased

---

**Table 2. Final stepwise multivariable Cox regression models for all-cause mortality, cardiovascular and noncardiovascular death, and fatal and nonfatal CVE.**

<table>
<thead>
<tr>
<th>n</th>
<th>All-cause mortality</th>
<th>P value</th>
<th>Cardiovascular death</th>
<th>P value</th>
<th>Fatal and nonfatal CVE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>CRP, mg/L</td>
<td>1.02 (1.01–1.04)</td>
<td>0.006</td>
<td>1.02 (1.00–1.04)</td>
<td>0.019</td>
<td>1.00 (0.99–1.02)</td>
</tr>
<tr>
<td>44</td>
<td>Residual GFR, mL/min per 1.73 m²</td>
<td>0.64 (0.50–0.81)</td>
<td>&lt;0.001</td>
<td>0.61 (0.45–0.83)</td>
<td>0.002</td>
<td>0.86 (0.76–0.97)</td>
</tr>
<tr>
<td>129</td>
<td>LV mass index, g/m²</td>
<td>1.003 (1.000–1.006)</td>
<td>0.072</td>
<td>1.003 (0.999–1.007)</td>
<td>0.15</td>
<td>1.004 (1.002–1.006)</td>
</tr>
<tr>
<td></td>
<td>LV ejection fraction, %</td>
<td>0.97 (0.94–1.00)</td>
<td>0.039</td>
<td>0.99 (0.95–1.02)</td>
<td>0.41</td>
<td>0.97 (0.94–0.99)</td>
</tr>
<tr>
<td></td>
<td>cTnT, μg/L</td>
<td>4.43 (1.87–10.45)</td>
<td>0.001</td>
<td>4.12 (1.29–13.17)</td>
<td>0.017</td>
<td>3.59 (1.48–8.70)</td>
</tr>
</tbody>
</table>

Data are hazard ratio (95% CI).

- a Includes age and background CAD.
- b Includes age, background CAD, and diabetes.
- c Includes age and hemoglobin.
- d Includes age, sex, background CAD, diabetes, duration of dialysis, and hemoglobin.

---

**Table 3. Predictive value of cTnT, CRP, and other risk predictors for different outcomes: ROC curve analysis.**

<table>
<thead>
<tr>
<th>Model</th>
<th>All-cause mortality</th>
<th>Cardiovascular death</th>
<th>Non-cardiovascular death</th>
<th>Fatal and non-fatal cardiac events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: cTnT</td>
<td>0.774 (0.706–0.841)</td>
<td>0.720 (0.638–0.802)</td>
<td>0.744 (0.638–0.850)</td>
<td>0.711 (0.645–0.776)</td>
</tr>
<tr>
<td>2: hsCRP</td>
<td>0.691 (0.619–0.763)</td>
<td>0.668 (0.584–0.752)</td>
<td>0.646 (0.537–0.754)</td>
<td>0.593 (0.519–0.666)</td>
</tr>
<tr>
<td>3: cTnT + hsCRP</td>
<td>0.747 (0.680–0.815)</td>
<td>0.699 (0.620–0.779)</td>
<td>0.722 (0.614–0.831)</td>
<td>0.703 (0.630–0.763)</td>
</tr>
<tr>
<td>4: echocardiographic features</td>
<td>0.691 (0.614–0.768)</td>
<td>0.657 (0.561–0.752)</td>
<td>0.664 (0.559–0.769)</td>
<td>0.713 (0.646–0.780)</td>
</tr>
<tr>
<td>5: age, sex, and clinical and biochemical features</td>
<td>0.813 (0.751–0.875)</td>
<td>0.776 (0.701–0.850)</td>
<td>0.774 (0.670–0.877)</td>
<td>0.719 (0.655–0.784)</td>
</tr>
<tr>
<td>6: model 5 and echocardiographic features</td>
<td>0.813 (0.748–0.877)</td>
<td>0.800 (0.726–0.874)</td>
<td>0.779 (0.673–0.885)</td>
<td>0.769 (0.708–0.830)</td>
</tr>
<tr>
<td>7: model 5 + hsCRP</td>
<td>0.809 (0.746–0.873)</td>
<td>0.773 (0.696–0.850)</td>
<td>0.764 (0.661–0.866)</td>
<td>0.712 (0.647–0.777)</td>
</tr>
<tr>
<td>8: model 5 + cTnT</td>
<td>0.823 (0.761–0.885)</td>
<td>0.783 (0.709–0.857)</td>
<td>0.787 (0.682–0.892)</td>
<td>0.743 (0.681–0.805)</td>
</tr>
<tr>
<td>9: model 5 + cTnT + hsCRP</td>
<td>0.816 (0.752–0.879)</td>
<td>0.776 (0.700–0.853)</td>
<td>0.778 (0.674–0.883)</td>
<td>0.741 (0.679–0.803)</td>
</tr>
<tr>
<td>10: model 6 + hsCRP</td>
<td>0.812 (0.746–0.877)</td>
<td>0.795 (0.718–0.872)</td>
<td>0.776 (0.673–0.879)</td>
<td>0.758 (0.697–0.820)</td>
</tr>
<tr>
<td>11: model 6 + cTnT</td>
<td>0.832 (0.669–0.894)</td>
<td>0.810 (0.739–0.883)</td>
<td>0.790 (0.682–0.898)</td>
<td>0.780 (0.720–0.840)</td>
</tr>
<tr>
<td>12: model 6 + cTnT + hsCRP</td>
<td>0.828 (0.764–0.891)</td>
<td>0.810 (0.735–0.884)</td>
<td>0.789 (0.687–0.891)</td>
<td>0.779 (0.719–0.838)</td>
</tr>
</tbody>
</table>

Data are calculated AUC (95% CI). hsCRP, high-sensitivity C-reactive protein. Clinical features include background CAD, diabetes, and duration of dialysis. Biochemical features include hemoglobin and residual GFR. Echocardiographic features include LV mass index and ejection fraction.
all-cause and cardiovascular mortality (10, 11, 14). There was some suggestion from our Kaplan-Meier analysis that a cTnT >0.01 μg/L was associated with more adverse cardiovascular outcomes. Conversely, a cTnT cutoff <0.01 μg/L may be useful in defining a subgroup of PD patients with better health status and lower cardiovascular risk, as evident from our study. This concept was reinforced by Apple et al. (12), who showed that an increased cTnT defined by any cutoff concentrations was associated with an increased risk of death in hemodialysis patients. All these observations agreed with a study of the general population, suggesting that even a minimally increased cTnT (0.01 to 0.029 μg/L) reflects subclinical cardiac injury and predicts a greater risk of mortality (28).

Although previous studies have established the importance of CRP in predicting mortality and cardiovascular death in ESRD patients (29–31), our ROC analysis showed that CRP had little added value over other clinical risk factors and was inferior to cTnT in predicting long-term outcome of PD patients. In the multivariable Cox regression analysis, CRP retained significance for all-cause mortality and cardiovascular death but became insignificant in predicting CVE. This is somewhat contrary to what we might expect and differs from the study by Apple et al. (32) showing that high-sensitivity CRP was more powerful than cTnT in predicting mortality in hemodialysis patients. As shown in our study and others (10–11, 27), CRP correlates with cTnT. However, CRP may be increased as a result of chronic infections, dialysis, or malnutrition (33) as well as vascular inflammation and myocardial injury. In contrast, cTnT represents a highly specific and sensitive marker of myocardial injury. Cardiovascular congestion may raise the concentration of cTnT but is unlikely to increase CRP (16). This may explain the disparity in the ROC analysis between cTnT and CRP in predicting CVE and why CRP did not retain independent significance for CVE. Furthermore, adding CRP to the models including cTnT did not increase the AUCs for any of the outcomes, indicating that combining cTnT and CRP did not increase predictive efficiency for any of the outcomes in PD patients. Again, our results were different from those of deFilippi et al. (10) in hemodialysis patients showing that the combination of troponin T and CRP testing provided additional prognostic information.

This study has several potential limitations. First, a relatively large number of covariates was considered in the multivariable analysis for cardiovascular and noncardiovascular death despite the relatively small event numbers. Some of our results thus require interpretation with caution and need confirmation with larger prospective studies before being generally accepted. Second, the inclusion of prevalent but not incident patients into our study may introduce survival bias. In addition, further study is needed to confirm whether the best cutoff values derived from the ROC analysis in our PD population are also applicable to other dialysis populations. In this study, cTnT was measured postPD; it is currently not known whether cTnT concentration differs pre- and postPD.

Multiple factors contribute to cTnT increases in PD patients. In keeping with a study in hemodialysis patients that showed a positive association between cTnT increase and severity of angiographic CAD (11), we observed more atherosclerotic vascular disease and CAD among PD patients with increased cTnT. Our PD patients with increased cTnT had greater LV hypertrophy and dilation as well as worse systolic function as reported in other studies (10, 12, 26). Uremic LV hypertrophy was associated with cardiomyocyte/capillary mismatch (34) and increased risk of subclinical myocardial ischemic insults, resulting in leakage of cardiac troponins into the circulation. There is pathological evidence that increased cTnT is associated with subclinical myocardial necrosis or microinfarct (35–36). On the other hand, kidney function may contribute to the elimination of troponins (37–38). However, cTnT circulates predominantly in free, intact form in patients with kidney failure, as in patients with acute coronary syndrome (39), providing important evidence that circulating cTnT in kidney failure reflects cardiac pathology. This concurs with our findings that irrespective of its association with RRF, the prognostic importance of cTnT for mortality and cardiovascular death and events in PD patients is largely independent of RRF.

Grant/funding Support: The study was supported by grant from the Hong Kong Health Service Research Fund. Financial Disclosures: None declared

References
9. Mallamaci F, Zoccali C, Parlongo S, Tripepi G, Benedetto FA, Cutrupi S, et al. Troponin is related to left ventricular mass and


