HHS Public Access

Author manuscript

Mayo Clin Proc. Author manuscript; available in PMC 2016 November 01.

Published in final edited form as:

Mayo Clin Proc. 2015 November ; 90(11): 1482–1491. doi:10.1016/j.mayocp.2015.08.016.

Troponin T as a predictor of end-stage renal disease and all-cause death among African-Americans and whites from hypertensive families

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Abstract

Objective—To evaluate cardiac troponin T (cTnT) as a predictor of end-stage renal disease (ESRD) and death in a cohort of African-American and white community dwelling adults with hypertensive families.

Patients & Methods—3,050 participants (whites from Rochester, Minnesota; African-Americans from Jackson, Mississippi) of the Genetic Epidemiology Network of Arteriopathy study were followed from baseline exam (June 1996–August 2000) through January 22, 2010. Cox regression models were used to examine the association of cTnT with ESRD and death adjusting for traditional risk factors.

Results—Cohort demographics and measurements included: whites (46%), hypertensive (71%), eGFR<60 mL/min/1.73m^2 (32%), high-sensitivity C-reactive protein>3 mg/L (52%), and abnormal cTnT (≥0.01 ng/mL) (2%). At 10 years, 27% with abnormal cTnT developed ESRD compared to 1% with normal cTnT. Similarly, at 10 years, 47% with an abnormal cTnT had died

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Disclosure

Data for these analyses were provided by United States Renal Data System (USRDS), but the analysis and conclusions are those of the authors and do not represent the USRDS or National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Financial disclosure: **A.S.J. has or presently consults with most of the major diagnostic companies (troponin)**.

compared to 7% with a normal cTnT. Abnormal cTnT was strongly associated with ESRD and death. This effect was attenuated but was still highly significant after adjustment for demographics, eGFR, and traditional risk factors for ESRD (unadjusted hazard ratio [HR] 23.91 (95% CI 12.9, 44.2); adjusted HR 2.81 (CI 1.3, 5.9) and death (unadjusted HR 8.43 [CI 6.0, 11.9]); adjusted HR 3.46 (CI 2.3, 5.1).

Conclusion—cTnT makes an independent contribution beyond traditional risk markers to the prediction of ESRD and all-cause death in community-dwelling individuals. Further studies may be needed to determine if cTnT screening among individuals with hypertension or within a subset of hypertensives would help identify those at risk for ESRD and all-cause death.

Keywords

blood pressure; coronary artery disease; diabetes mellitus; nephrology; renal disease

INTRODUCTION

Hypertension remains a priority health condition,[1–3] and by 2030 it is estimated that greater than 40% of United States (US) adults will have one or more forms of cardiovascular disease, including hypertension, leading to significant economic cost.[4] Hypertensive adults have up to a 4-fold increase in cardiovascular disease-associated death with disproportionate rates seen in racial and ethnic minorities.[5–7] Hypertension-associated morbidity extends to kidney disease, comprising one of the most common causes of end-stage renal disease (ESRD), a condition affecting approximately 600,000 people and costing nearly $50 billion in public and private funds in the US.[8,9]

Persons with hypertension represent a high-risk population for the development of ESRD and death, likely due to the interplay of other cardiovascular diseases and associated morbidity. Recently published guidelines by the American College of Physicians[10] suggest that screening for chronic kidney disease stages 1 to 3 is not clearly beneficial in the general population despite the increased risk for adverse cardiovascular and renal outcomes in these patients.[11] Instead, it may be more beneficial to identify the higher-risk patients who need close monitoring for ESRD and other comorbid events. Identification of risk markers that improve risk assessment for death and the prediction of ESRD may be more cost effective, improve medical decision-making, and help target interventions in those who will clearly benefit.

Cardiac troponin T (cTnT) is a sensitive and specific biomarker for myocyte injury in the setting of acute coronary syndromes.[12] In the general population, minimally increased cTnT as measured by the standard, readily-available assay is rare among subjects without chronic conditions such as heart failure, left ventricular hypertrophy, chronic kidney disease, or diabetes mellitus.[13–15] However, minimally elevated cTnT levels in asymptomatic, older individuals and in patients with chronic kidney failure are associated with all-cause death.[14,16–23] Whether cTnT can distinguish those at greatest risk of ESRD in addition to death is less clear. To address this question, we used the Genetic Epidemiology Network of Arteriopathy (GENOA) multi-ethnic cohort study of hypertensive families sampled from the

community. We tested the hypothesis that cTnT would predict death and ESRD independent of traditional cardiovascular risk factors and kidney function.

SUBJECTS AND METHODS

Design Overview

The study design is a prospective cohort study of individuals from hypertensive families. The association of baseline cTnT with subsequent ESRD or all-cause death was assessed.

Setting and Participants

GENOA Cohort—Study participants were members of sibships enrolled in the GENOA study designed to identify genetic determinants of hypertension in multiple racial groups.[24,25] The GENOA sibships were ascertained based on two or more members of the sibships having primary hypertension diagnosed prior to age 60 years. In Rochester Minnesota, a Mayo Clinic diagnostic index was used to identify all non-Hispanic white residents of Olmsted County with a diagnosis of essential hypertension made before the age of 60, who were then recruited for enrollment. In Jackson, Mississippi, subjects were recruited through hypertensive probands from the Atherosclerosis Risk in Communities cohort, a probability sample of 45–64 year-old, non- Hispanic black or African American residents of that community.[26] All siblings of recruited subjects from these cohorts were invited to participate in the GENOA study. Sibships in which the index sibling was known to have a cause of secondary hypertension (e.g., renal artery stenosis) including severely impaired kidney function (e.g., serum creatinine ≥2.0 mg/dL) were not recruited. All available members of the recruited sibships, including normotensive siblings, were invited to the initial (baseline) study visit conducted between June 1996 and August 2000. Participants were excluded if they lacked stored serum samples at the baseline visit or had kidney failure at their baseline visit. This study was approved by the Mayo Clinic and University of Mississippi Medical Center Institutional Review Boards.

Cohort Baseline Assessment—The initial GENOA study visit consisted of a questionnaire regarding personal medical history, comorbid conditions, family history; blood pressure (BP) measurement; and blood draw for measurements of serum glucose, lipids (total cholesterol, high density lipoprotein, triglycerides), and creatinine. Hypertension was confirmed if a prior diagnosis and prescription antihypertensive medication were reported, or if the average systolic blood pressure (SBP) or diastolic blood pressures (DBP) was ≥140 mm Hg or ≥90 mm Hg, respectively. Diabetes was diagnosed if the subject reported treatment with insulin or oral hypoglycemic agents or the fasting serum glucose concentration was ≥126 mg/dL. Serum creatinine measurements were obtained with a standardized enzymatic assay.[27] Estimated glomerular filtration rate (eGFR) at the baseline exam was calculated using the Modification of Diet in Renal Disease (MDRD) study equation.[28,29] eGFR was also calculated using the CKD–EPI 2009 equation[30] but this led to no meaningful difference in the study findings compared to using the MDRD study equation and was thus not reported. cTnT and high-sensitivity C-reactive protein (hsCRP) were measured in stored serum samples from the baseline exam (June 1996–August 2000) in Rochester, MN. cTnT was measured using immunoassay methods on Roche® e-modulers

using an electrochemiluminescent immunoassay (Roche Diagnostics, Indianapolis, IN) in the Central Clinical Laboratory at Mayo Clinic in Rochester, MN. The limit of detection for this assay is <0.01 ng/mL, which is also the 99th percentile of the upper reference range.[31,32] The 10% coefficient of variation for this assay is 0.035 ng/mL. In our laboratory, at the limit of detection the coefficient of variation is 18%. hsCRP was measured using the Roche Cobas® 6000, latex-enhanced immunoturbidimetric assay (Roche Diagnostics, Indianapolis, IN).

Outcomes and Follow-up

The primary outcome measures were all-cause death and ESRD. Vital status and death date were queried using Accurint (www.accurint.com). For study participants who were deceased as of January 22, 2010, death certificates were obtained for death verification and to determine primary cause of death. Primary causes of death were grouped into the following categories: malignancy, cardiac, sepsis/infection, pulmonary, cerebrovascular, trauma, renal, and unknown/other. ESRD events (i.e., initiation of maintenance dialysis therapy or kidney transplantation) as of May 2008 were determined via query conducted in 2010 of the United States Renal Data System (USRDS), a comprehensive national database of ESRD in the United States (www.usrds.org).

Statistical Analysis

Because 98% of cTnT values were undetectable, cTnT was stratified into normal (undetectable; <0.01 ng/mL) and abnormal (detectable; ≥0.01 ng/mL) values.[13,21,22,33] Both hsCRP and triglycerides were assessed as continuous variables, and measurements were log-transformed due to skewness. hsCRP was also analyzed as a categorical variable with two categories: low-average risk (≤3 mg/L) and high-risk (>3 mg/L).[34,35] Demographic and clinical variables were compared between abnormal and normal cTnT groups using the 2-sample rank-sum test for quantitative variables and the Chi square test for categorical variables. Cumulative rates of all-cause death and kidney failure (ESRD) events were estimated using the Kaplan-Meier method, and log rank tests were used for group comparisons. Proportional hazards regression (Cox) models were used to examine the association between cTnT and all-cause death (or ESRD) in univariable and multivariable models. Multi-variable regression models were used to adjust for potential confounding variables. Age, sex, race, diabetes, hypertension, low density lipoprotein cholesterol, cigarette smoking, history of myocardial infarction, hsCRP, and eGFR were evaluated as covariates in multivariable models.[36,37] Due to the limited number of ESRD events, the number of covariates used in the multivariable models for predicting ESRD was restricted. Event times were defined as the time elapsed from study entry to the time of death or ESRD. Subjects free of death event were censored at time of death survey, January 22, 2010. Subjects free of ESRD events were censored at death or time of most recent USRDS ESRD survey data availability (two year reporting delay), May 2008. For both outcomes, the presence of an interaction between eGFR and cTnT was tested using a likelihood ratio test comparing nested Cox models (with vs. without interaction). The C-statistic was used to assess the impact of cTnT in different models. Results were expressed as hazard ratios (HRs) with 95% confidence intervals (CIs). A secondary analysis for ESRD was conducted using the regression method of Fine and Gray to obtain the subdistribution HR for ESRD.[38]

This method accounts for subjects who died before occurrence of ESRD (competing risk). Subjects lost to follow-up before ESRD or death were censored. Subjects who died before ESRD remained in the risk set with an adjusted weight. All analyses were done in Statistical Analysis System (SAS version 9.3; SAS Institute, Cary, NC).

RESULTS

Baseline characteristics

Of 3,431 GENOA participants, the final study cohort consisted of 3,050 due to exclusions for the following: lack of stored serum samples available for both cTnT and hsCRP measurements (n=361); kidney failure based on documented ESRD prior to baseline exam (n=8) or estimated GFR <15 mL/min/1.73m2 (n=6); and missing data (n=6). Baseline characteristics are presented in Table 1 for participants with abnormal cTnT (≥0.01 ng/mL) and normal cTnT (<0.01 ng/mL) levels. Overall, cTnT was abnormal or detectable in 66 (2.1%) with measurements ranging from 0.01–0.63 ng/mL. Participants with abnormal cTnT were older, more likely to be male and have comorbidities including hypertension, diabetes, myocardial infarction, and stroke compared to those with normal cTnT. However, no significant racial difference was observed. eGFR was lower while the cardiovascular biomarker, hsCRP, was higher in those with abnormal cTnT.

Outcome: All-cause death—During a median follow-up period of 11.5 years (25^{th}, 75^{th} percentile: 10.6, 12.4 years), 308 participants died (incidence density 0.90/100 person-years). An abnormal cTnT was significantly associated with risk of all-cause death (Log rank *P*<.001, Figure 1 and Table 2). At 10 years, 47% (95% CI 33.5%, 55.8%) with an abnormal cTnT died compared to 7.3% (95% CI 6.3%, 8.2%) with a normal cTnT. The leading cause of death was cardiac among those with and without an abnormal cTnT at baseline (52.8% vs. 35.3%, respectively), Figure 2. There was an increased risk of all-cause death with an abnormal cTnT that remained significant even after multivariable adjustment (Table 2, HR 3.46; 95% CI 2.3, 5.1). The final model for mortality without cTnT had a C-statistic of 0.779 (95% CI 0.75, 0.8) that increased to 0.784 (95% CI 0.76, 0.81) with cTnT. A forest plot showing the effect of cTnT within subgroups made no suggestion that the effect of cTnT differed between other subgroups (Supplemental Figure 1). While the death risk with an abnormal cTnT was higher with eGFR≥60 mL/min/1.73 m^2 than with eGFR<60 mL/min/1.73 m^2 (HR 10.47 vs. 6.35), the interaction was not statistically significant (*P*=.2) even when eGFR was modeled as continuous (*P*=.7).

Outcome: ESRD—During a median follow-up period of 9.8 years (25^{th}, 75^{th} percentile: 8.9, 10.8 years), 52 participants developed ESRD (incidence density 0.18/100 person-years). An abnormal cTnT was significantly associated with risk of ESRD (Log rank *P*<.001, Figure 3 and Table 3). At 10 years, 27.4% (12.3, 39.8 %) with abnormal cTnT developed ESRD compared to 1.3% (0.9, 1.8%) with normal cTnT. The primary cause of ESRD was attributed to diabetes in 59.6%, and other causes were due to glomerulonephritis, multiple myeloma, unspecified, or unknown. There was an increased risk of ESRD with an abnormal cTnT that remained significant even after adjusting for demographics, hypertension, diabetes, and eGFR (HR 2.81; 95% CI 1.34, 5.90). This adjusted risk remained significant

with death modeled as a competing risk in the fully adjusted model (HR 2.37; 95% CI 1.02, 5.53). The final model for ESRD without cTnT had a C-statistic of 0.901 (95% CI 0.85, 0.95) that increased to 0.909 (95% CI 0.86, 0.96) with cTnT. A forest plot showing the effect of cTnT within subgroups suggested that the effect of cTnT differed between those with and without diabetes (Supplemental Figure 2). The likelihood ratio test suggested evidence of an interaction between cTnT and diabetes (P=.008). Inspection of the interaction between diabetes and cTnT (Figure 4) revealed that subjects with normal cTnT and no diabetes were at very low risk for ESRD.

DISCUSSION

In this study of community-dwelling individuals sampled for hypertension, abnormal cTnT concentration (≥0.01 ng/mL) independently predicted death and ESRD events. Our GENOA study participants with abnormal cTnT were generally older with comorbid conditions and reduced kidney function. However, abnormal cTnT provided prognostic information independent of traditional cardiovascular disease or ESRD risk factors. Findings in our predominantly hypertensive population are similar to other reports wherein a mildly-increased or detectable cTnT level in patients with heart failure, kidney disease, or even healthy older individuals portends worsened prognosis.[19,39] However, our study is the first to demonstrate the ability of cTnT to predict ESRD beyond traditional risk markers and kidney function.

Despite the known relationship between hypertension, kidney function, and cTnT, cTnT has not previously been studied as a risk marker for ESRD. Recently, Bansal et al. found that cTnT, measured by high-sensitivity assays not yet clinically available in the US, and N-terminal pro-B-type natriuretic peptide were associated with rapid decline of kidney function and incident chronic kidney disease in elderly patients free of heart failure.[39] Our investigations to date are plausible given the well-described biologic interaction between cardiac and kidney function.[40–45] Dysfunction of the heart often leads to dysfunction of the kidney, and vice versa. In patients with chronic kidney disease, the high cardiovascular morbidity and all-cause death rates observed are believed to be multifactorial in etiology from accelerated atherosclerotic vascular disease, congestive heart failure, left ventricular hypertrophy, and toxicity from the circulating uremic milieu.[43,46] Hence, cTnT serves as a marker of this cardiorenal interplay allowing for selection of a higher risk group for ESRD.

Race also plays an important role in the all-cause death risk, with African Americans having life expectancy 3–8 years less than white counterparts.[47–49] One advantage of our cohort was the balanced racial sampling, which allowed testing for racial differences in the cTnT relationships. Most prior investigations of cTnT had few African American participants. Wallace et al. assessed the prevalence and determinants of cTnT elevations with conventional cTnT assays in 3,557 subjects of the Dallas Heart study, a multi-ethnic study of subclinical cardiovascular disease, which oversampled African Americans (~52%).[13] They found that African American race was associated with detectable cTnT levels on univariate analysis, but in multivariable analyses, only diabetes, left ventricular hypertrophy, chronic kidney disease, and congestive heart failure were associated with detectable cTnT. Similarly, we did not find race to be a determinant of abnormal cTnT levels in our GENOA

cohort. Taken together, these studies suggest that cTnT, as a composite marker of myocardial or endothelial damage resulting from comorbid conditions, identifies a high-risk group regardless of race, albeit this is generally more common in African Americans.

The prevalence (2.1%) of an abnormal cTnT may appear low in this study. However, in healthy populations previously studied, the prevalence of a detectable or abnormal cTnT is rare, ranging 0.7% to 4%.[13,17] The prevalence of cTnT increases with age and with multimorbidity, hence illustrating why we intentionally examined a higher-risk, community-based cohort. Despite the small number of participants with an abnormal cTnT, cTnT proved to be an independent predictor of all-cause death and ESRD in our study population. Recently, a more sensitive assay for cTnT not yet clinically available in the United States has been associated with death and cardiovascular morbidity in community-based samples.[50–52] In a study of 4,221 community-dwelling adults aged 65 years or older from the Cardiovascular Health Study (51% hypertensives and 16% African Americans), very low levels of cTnT measured with a highly-sensitive assay were significantly associated with cardiovascular death and incident heart failure independent of other biomarkers, including C-reactive protein and N-terminal pro-type B natriuretic peptide. Other investigations revealed that variations of levels in this marker over time were associated with concordant changes in the risk of heart failure and cardiovascular death.[50,52] The additive information from high-sensitivity assays for cTnT has allowed for identification of individuals at high risk for death who have both increased high-sensitivity cTnT and left ventricular hypertrophy.[53,54] Given these observations, it is possible that slight elevations in high-sensitivity cTnT levels previously undetected by our conventional cTnT assay may predict a significant proportion of deaths in the remaining participants from our study who died having had undetectable levels at baseline.

Our study had some limitations. The aim of the GENOA baseline exam was not to identify genetic predictors of target organ damage. Hence, we lacked baseline measurements of urine protein excretion rates in addition to electrocardiogram and echocardiogram studies, which may have provided insight into the presence of left ventricular hypertrophy, a condition previously associated with abnormal cTnT. The limitation from lack of urine samples is important, particularly given the findings in the Prevention of Renal and Vascular Endstage Disease study that albuminuria added significantly to the identification of individuals at risk of cardiovascular morbidity and all-cause death,[55] development of progressive albuminuria,[56] and its association with high-sensitivity cTnT assays.[57] Second, we were unable to determine the impact of changes in medical therapy, cardiac interventions, and subsequent cardiac or renal events leading to adverse outcomes over time. Third, our cohort consists of individuals belonging to hypertension-enriched families and therefore may limit applicability to the general population. Fourth, multiple factors influence cTnT, and a single measurement may not appropriately represent a subject's true baseline.

In conclusion, we report that cTnT provides prognostic information with respect to all-cause death and ESRD independent of traditional risk factors and baseline kidney function in community-dwelling individuals at potentially higher risk by virtue of ascertainment through hypertension. As patient populations grow older with increasing multimorbidity,[58] identifying those at highest risk for death or ESRD could improve patient management

strategies. Unfortunately, abnormal cTnT, measured with the standard assay, is relatively uncommon and thus does not improve risk prediction enough to support routine use. Further study is needed to determine if there is a particular patient group in which cTnT screening would meaningfully improve discrimination between the low- and high-risk patients for these sequelae.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We would like to acknowledge the contribution of Jodie van de Rostyne for laboratory support, Daniel Crusan, Cindy Crowson, and Dr. Eric Bergstralh for statistical support, and Drs. Fernando Cosio, Mira Keddis, and Ziad el-Zoghby for critical review of manuscript and study design.

Support: Mary Kathryn and Michael B. Panitch Career Development Award and funds from the Mayo Foundation (L.J.H); Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Mayo Clinic (L.J.H.); NIH grants R01 HL054464 and R01 DK073537 (S.T.T), U01 HL054463-10 (T. Mosley), K23 DK078229 (A.D.R), and UL1 TR000135 from the National Center for Advancing Translational Sciences (NCATS). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

Abstract Abbreviations

cTnT	Cardiac troponin T
CI	Confidence Interval
eGFR	Estimated glomerular filtration rate
ESRD	End-stage renal disease

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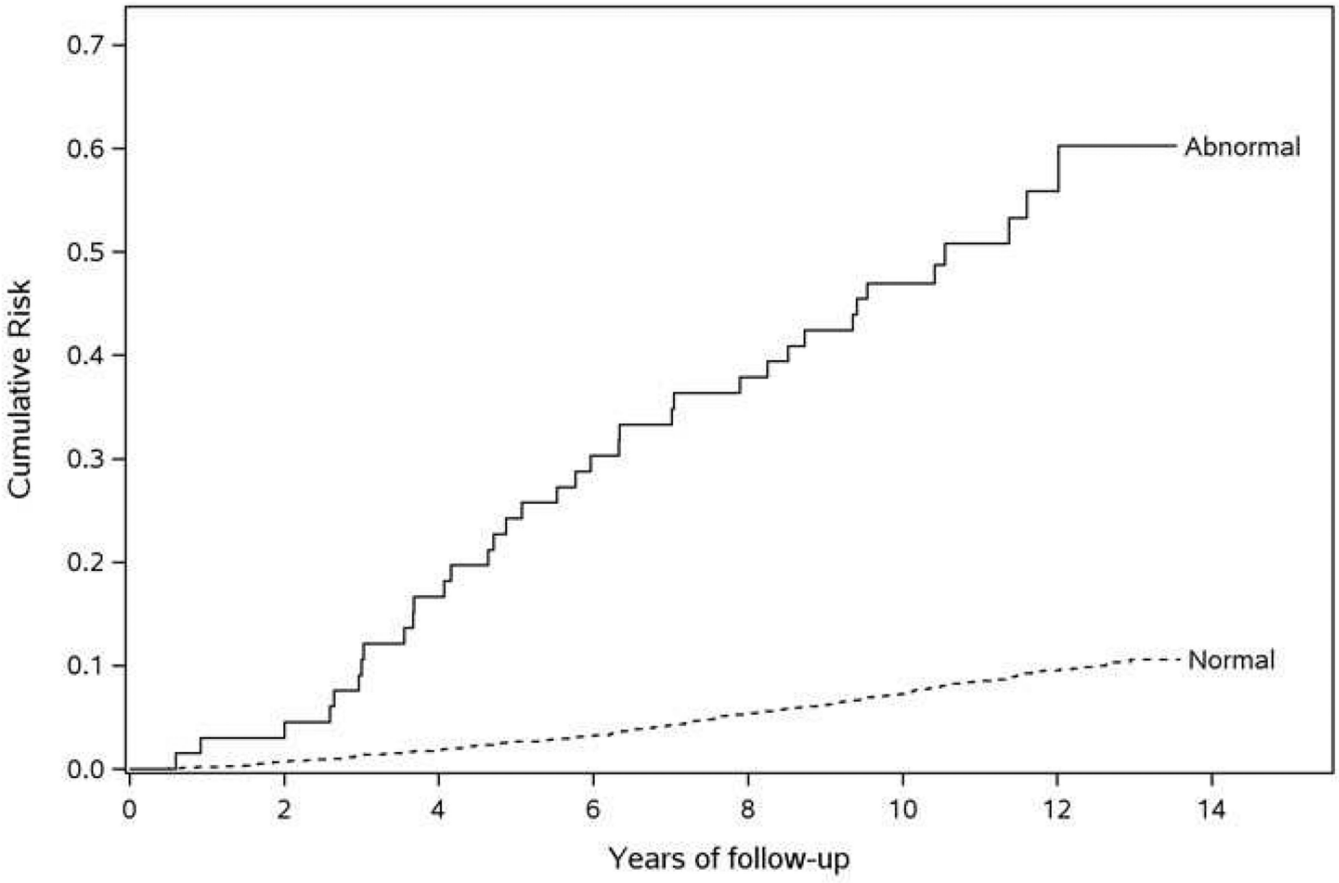


Number at risk

Years of follow-up	0	2	4	6	8	10	12
Abnormal cTnT	66	64	55	46	41	34	11
Normal cTnT	2984	2963	2929	2888	2824	2563	1050

Figure 1.
All-cause death risk by Abnormal versus Normal cTnT

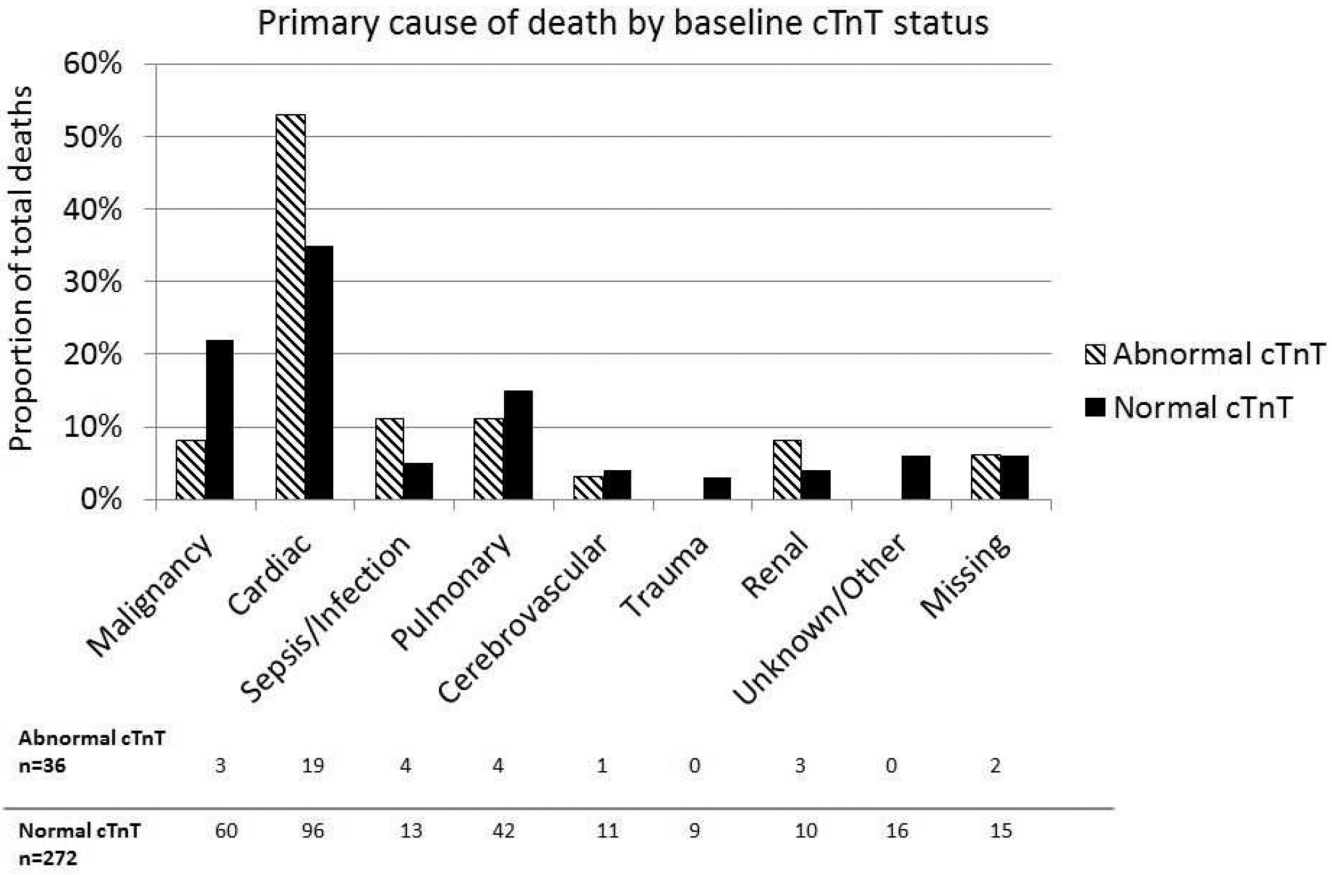
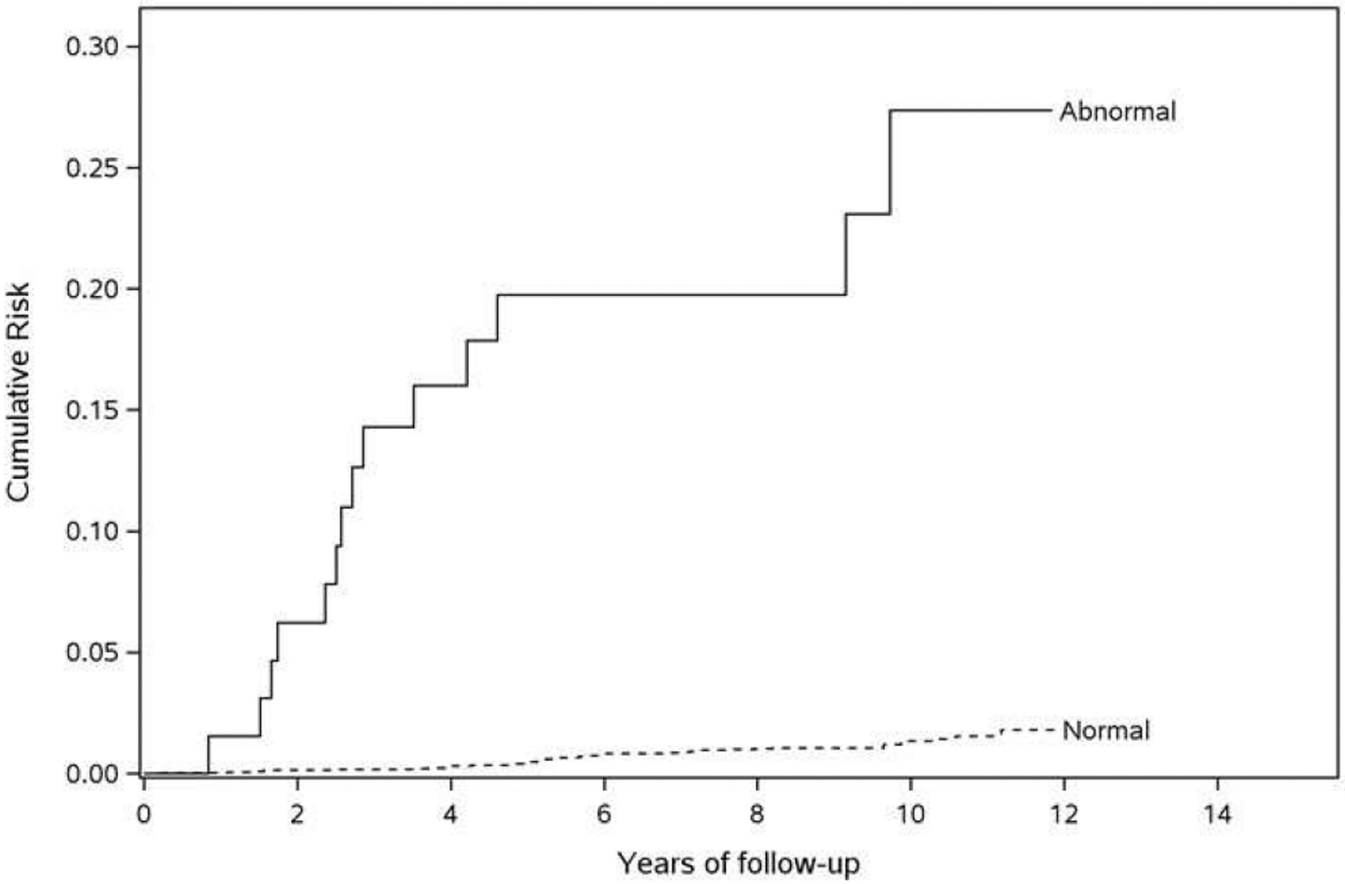


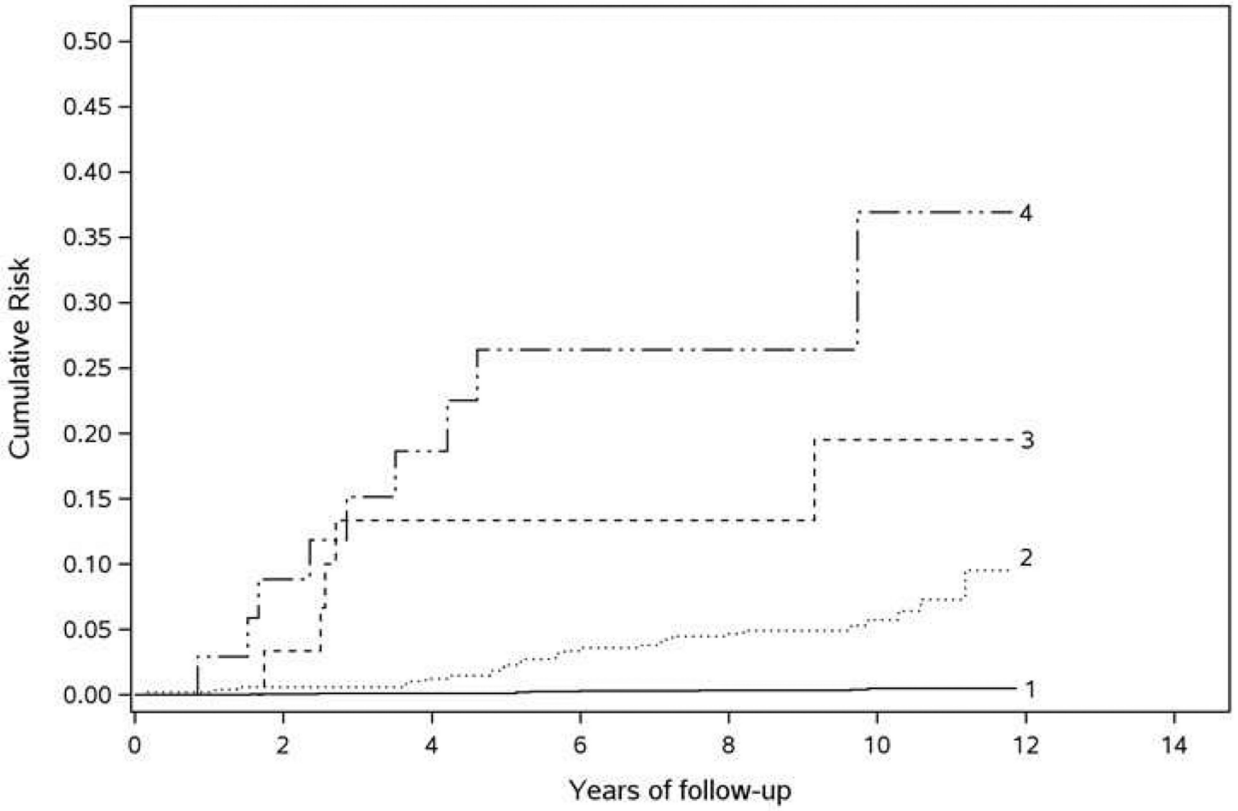
Figure 2.
Primary cause of death by baseline cTnT status



Number at risk

Years of follow-up	0	2	4	6	8	10	12
Abnormal cTnT	66	60	47	39	36	17	0
Normal cTnT	2984	2960	2922	2867	2740	1286	0

Figure 3.
End-stage renal disease risk by Abnormal versus Normal cTnT



Numbers at Risk

Years of follow-up	0	2	4	6	8	10	12
1, No diabetes & normal cTNT	2491	2473	2449	2416	2319	1092	0
2, Diabetes & normal cTNT	493	487	473	451	421	194	0
3, No diabetes & abnormal cTNT	32	29	24	23	21	11	0
4, Diabetes & abnormal cTNT	34	31	23	16	15	6	0

Figure 4.
End-stage renal disease risk by Diabetes and cTnT status

Table 1

Comparison of Variables[a] between Subjects with Abnormal cTnT versus Normal cTnT Concentrations.

	Abnormal cTnT (N=66)	Normal cTnT (N=2984)	*P* value[b]
Demographic and Cardiovascular Risk Factors:			
Age, years	67 (59,72)	57 (49, 64)	<.001[1]
African American	41 (62.1%)	1614 (54.1%)	.2[2]
Male	41 (62.1%)	1067 (35.8%)	<.001[2]
Education			.14
Precollege	46 (69.7%)	1615 (55.3%)	
University	13 (19.7%)	846 (28.4%)	
Graduate	4 (6.1%)	242 (8.1%)	
Trade	3 (4.6%)	245 (8.2%)	
BMI, kg/m^2	29 (27, 35)	30 (26,34)	.65[1]
Hypertension	62 (93.9%)	2112 (70.8%)	<.001[2]
Diabetes	34 (51.5%)	493 (16.5%)	<.001[2]
Myocardial Infarction	19 (28.8%)	131 (4.4%)	<.001[2]
Stroke	12 (18.2%)	97 (3.3%)	<.001[2]
Medications:			
Hypertension medication	58 (87.9%)	1832 (61.4%)	<.001[2]
RAAS agent	31 (47.0%)	673 (22.6%)	<.001[2]
Lipid Lowering medication	13 (19.7%)	328 (11.0%)	.03[2]
HMG Co-A reductase inhibitor	13 (19.7%)	286 (9.6%)	.006[2]
Exam Measurements:			
Systolic BP, mmHg	143 (126,166)	132 (120, 146)	<.001[1]
Systolic BP > 150 mmHg	26 (39.4%)	607 (20.3%)	<.01[2]
Diastolic BP, mmHg	76 (67, 87)	78 (71, 85)	.64[1]
Pulse, beats per minute	70 (62, 80)	68 (62, 76)	.34[1]
Laboratory measurements:			
Serum Creatinine, mg/dL	1.4 (1.2, 1.9)	1.1 (1.0, 1.3)	<.001[1]
Estimated GFR, ml/min/1.73m^2	52 (41, 63)	66 (57, 74)	<.001[1]
Estimated GFR			<.001[2]
>=60	21 (31.8%)	2037 (68.3%)	
45–59	22 (33.3%)	815 (27.3%)	
30–44	13 (19.7%)	122 (4.1%)	
15–29	10 (15.2%)	10 (0.3%)	
Glucose, mg/dL	103 (93,157)	93 (86, 105)	<.001[1]
Total cholesterol, mg/dL	195 (159, 229)	204 (178,231)	.07[1]
Low density lipoprotein, mg/dL	115 (85, 145)	124 (98,150)	.09[1]
High density lipoprotein, mg/dL	49 (37,60)	52 (42,63)	.04[1]
Triglycerides, mg/dL	171 (121–217)	140 (105–196)	.02[1]

	Abnormal cTnT (N=66)	Normal cTnT (N=2984)	*P* value[b]
Log triglycerides	7.4 (6.9,7.8)	7.1 (6.7,7.6)	.01[1]
hsCRP, mg/L	3.9 (1.9, 10.6)	3.2 (1.4, 7.0)	<.001[1]
hsCRP > 3 mg/L	40 (60.6%)	1534 (51.4%)	.14[2]
Log hsCRP	1.9 (0.9,3.3)	1.7 (0.5,2.8)	.03[1]

Abbreviations: BMI, body mass index; BP: blood pressure; GFR: glomerular filtration rate (calculated using the Modification of Diet in Renal Disease equation); HMG Co-A reductase inhibitor, 3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitor; hsCRP: high-sensitivity C-reactive protein; RAAS: renin angiotensin aldosterone system blockade agent

[a] Values are median (25^{th}, 75^{th}) or n (percent) as appropriate.

[b] *P* value from (1) rank sum test or (2) chi-square test as appropriate.

Table 2

Risk of all-cause death with abnormal cTnT

Model	cTnT Hazard Ratio	95% Confidence Interval	*P*-value	C-statistic
1. Unadjusted	8.43	5.95, 11.94	<.001	0.552
2. Adjusted for demographic factors (age, sex, race)	4.49	3.13, 6.43	<.001	0.768
3. Adjusted for demographic factors and traditional risk factors[a]	3.75	2.57, 5.47	<.001	0.783
4. Adjusted for demographic factors, traditional risk factors[a], and eGFR	3.52	2.40, 5.18	<.001	0.783
5. Adjusted for demographic factors, traditional risk factors[a], eGFR, and Log hsCRP	3.46	2.35, 5.09	<.001	0.784

Abbreviations: eGFR: estimated glomerular filtration rate; hsCRP: high-sensitivity C-reactive protein;

[a]Hypertension, diabetes, myocardial infarction, low-density lipoprotein cholesterol, smoking

Table 3

Risk of end-stage renal disease with abnormal cTnT

Model	cTnT Hazard Ratio	95% Confidence Interval	*P* value	C-statistic
1. Unadjusted	23.91	12.92, 44.24	<.001	0.635
2. Adjusted for demographic factors (age, sex, race)	20.84	10.58, 41.05	<.001	0.757
3. Adjus ted for demographic factors, hypertension, and diabetes	11.95	6.05, 23.60	<.001	0.853
4. Adjusted for demographic factors, hypertension, diabetes, and eGFR	2.81	1.34, 5.90	.01	0.909

Abbreviation: eGFR: estimated glomerular filtration rate