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Troponin T as a Predictor of End-Stage Renal Disease and All-Cause Death in 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 and Methods: A total of 3050 participants (whites from Rochester, Minnesota; African Americans from Jackson, Mississippi) of the Genetic Epidemiology Network of Arteriopathy study were followed from baseline examination (June 1, 1996, through August 31, 2000) through January 22, 2010. Cox proportional hazards regression models were used to examine the association of cTnT with ESRD and death after adjusting for traditional risk factors.

Results: Cohort demographic characteristics and measurements included 1395 whites (45.7%), 2174 hypertensive (71.3%), 992 estimated glomerular filtration rate of less than 60 mL/min per 1.73 m^2 (32.5%), 1574 high-sensitivity C-reactive protein level of greater than 3 mg/L (51.6%), and 66 abnormal cTnT level of 0.01 ng/mL or higher (2.2%). The estimated cumulative incidence of ESRD at 10 years was 27.4% among those with abnormal cTnT levels compared with 1.3% for those with normal levels. Similarly, the estimated cumulative incidence of death at 10 years was 47% among those with abnormal cTnT compared with 7.3% among those with normal cTnT. Abnormal cTnT levels were strongly associated with ESRD and death. This effect was attenuated but was still highly significant after adjustment for demographic characteristics, estimated glomerular filtration rate, and traditional risk factors for ESRD (unadjusted hazard ratio [HR], 23.91; 95% CI, 12.9-44.2; adjusted HR, 2.81; 95% CI, 1.3-5.9) and death (unadjusted HR, 8.43; 95% CI, 6.0-11.9; adjusted HR, 3.46; 95% CI, 2.3-5.1).

Conclusion: Cardiac troponin T makes an independent contribution to the prediction of ESRD and all-cause death in community-dwelling individuals beyond traditional risk markers. Further studies may be needed to determine whether cTnT screening in individuals with hypertension or in a subset of hypertensive individuals would help identify those at risk of ESRD and all-cause death.

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Hypertension is a priority health condition,[1-3] and it is estimated that by 2030 more than 40% of the US adults will have 1 or more forms of cardiovascular disease, including hypertension, leading to significant economic costs.[4] Hypertensive adults have up to a 4-fold increase in cardiovascular disease–related deaths, with disproportionate rates seen in racial and ethnic minorities.[5-7] Hypertension-related 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 United States.[8,9]

Persons with hypertension represent a high-risk population for the development of ESRD and death, likely because of 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 of 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 at those who will clearly benefit.

Cardiac troponin T (cTnT) is a sensitive and specific biomarker for myocyte injury in the setting of acute coronary syndrome.[12] In the general population, minimally elevated cTnT levels as measured with the standard, readily-available assay are rare in individuals 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 the highest risk of ESRD in addition to death is less clear. To address this question, we used the Genetic Epidemiology Network of Arteriopathy (GENOA) multiethnic 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.

PATIENTS 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 sibships from the GENOA study were ascertained on the basis of 2 or more members of the sibships having primary hypertension diagnosed before the age of 60. 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, individuals were recruited through hypertensive probands from the Atherosclerosis Risk in Communities cohort, a probability sample of 45- to 64-year-old non-Hispanic black or African American residents of that community.[26] All siblings of individuals recruited 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 (eg, renal artery stenosis) including severely impaired kidney function (eg, serum creatinine level$\geq$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 from June 1, 1996, through August 31, 2000. Participants were excluded if they lacked stored serum samples or had kidney failure at their baseline visit. This study was approved by the Mayo Clinic Institutional Review Board and the institutional review board of the University of Mississippi Medical Center.

Cohort Baseline Assessment. The initial GENOA study visit involved the administration of a questionnaire enquiring about personal medical history, comorbid conditions, and family history; blood pressure measurement; and blood drawn for measurements of serum glucose, lipids (total cholesterol, high-density lipoprotein cholesterol, triglycerides), and creatinine. Hypertension was confirmed if a previous diagnosis and prescription antihypertensive medication were reported or if the average systolic blood pressure or diastolic blood pressure was 140 mm Hg or higher or 90 mm Hg or higher, respectively. Diabetes was diagnosed if the individual reported treatment with insulin or oral hypoglycemic agents or the fasting serum glucose concentration was 126 mg/dL or higher. Serum creatinine measurements were obtained with a standardized enzymatic assay.[27] The estimated glomerular filtration rate (eGFR) at the baseline examination was calculated using the Modification of Diet in Renal Disease Study equation.[28,29] The eGFR was also calculated using the CKD-EPI 2009 equation,[30] but it led to no meaningful difference in the study findings compared with using the Modification of Diet in Renal Disease Study equation and was thus not reported. Cardiac troponin T and high-sensitivity C-reactive protein (hsCRP) levels were measured

in stored serum samples from the baseline examination (June 1996 to August 2000) in Rochester. The cTnT level was measured by means of immunoassay methods on Roche e-modulers using an electrochemiluminescent immunoassay (Roche Diagnostics) in the Central Clinical Laboratory at Mayo Clinic in Rochester. The limit of detection for this assay is less than 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, the coefficient of variation is 18% at the limit of detection. The hsCRP level was measured with the Roche Cobas 6000, latex-enhanced immunoturbidimetric assay (Roche Diagnostics).

Outcomes and Follow-Up

The primary outcome measures were all-cause death and ESRD. Vital status and death date were obtained using Accurint (www.accurint.com). For study participants who were deceased as of January 22, 2010, death certificates were obtained to verify death and to determine the 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. End-stage renal disease events (ie, initiation of maintenance dialysis therapy or kidney transplantation) as of May 2008 were determined in 2010 via a query conducted in the United States Renal Data System, a comprehensive national database which collects, analyzes, and distributes information about ESRD in the United States (www.usrds.org).

Statistical Analyses

Because 98% of cTnT values were undetectable, they were stratified into 2 categories: normal (undetectable; <0.01 ng/mL) and abnormal (detectable; ≥0.01 ng/mL).[13,21,22,33] Both hsCRP and triglyceride levels were assessed as continuous variables, and measurements were log-transformed due to skewness. The hsCRP level was also analyzed as a categorical variable with 2 categories: low to 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. Cox proportional hazards regression models were used to examine the association between cTnT and all-cause death (or ESRD) in univariable and multivariable models. Multivariable regression models were used to adjust for potential confounding variables. Age, sex, race, diabetes, hypertension, low-density lipoprotein cholesterol level, cigarette smoking, history of myocardial infarction, hsCRP level, and eGFR were evaluated as covariates in multivariable models.[36,37] Because of the limited number of ESRD events, the number of covariates used in 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. Individuals free of death events were censored at the time of death survey, that is, January 22, 2010. Individuals free of ESRD events were censored at the time of death or at the time of most recent United States Renal Data System ESRD survey data availability (2-year reporting delay), that is, May 2008. For both outcomes, the presence of an interaction between the eGFR and the cTnT level was tested using a likelihood ratio test comparing nested Cox proportional hazards models (with vs without interaction). The C statistic was used to assess the effect of cTnT in different models. The results were expressed as hazard ratios (HRs) with 95% CIs. A secondary analysis for ESRD was conducted using the regression method of Fine and Gray[38] to obtain the subdistribution HR for ESRD. This method accounts for individuals who died before the occurrence of ESRD (competing risk). Individuals lost to follow-up before ESRD or death were censored. Individuals who died before the occurrence of ESRD remained in the risk set with an adjusted weight. All analyses were performed using SAS version 9.3 (SAS Institute).

RESULTS

Baseline Characteristics

Of 3431 participants of the GENOA study, only 3050 comprised the final study cohort because of exclusions for the following: lack of stored serum samples available for both cTnT and hsCRP measurements (n=361);

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kidney failure based on documented ESRD before the baseline examination (n=8) or eGFR less than 15 mL/min per 1.73 m^2 (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 levels were abnormal or detectable in 66 (2.2%), with measurements ranging from 0.01 to 0.63 ng/mL. Participants with abnormal cTnT levels were older and more likely to be male and have comorbidities including hypertension, diabetes, myocardial infarction, and stroke compared with those with normal cTnT levels. However, no significant racial difference was observed. The eGFR

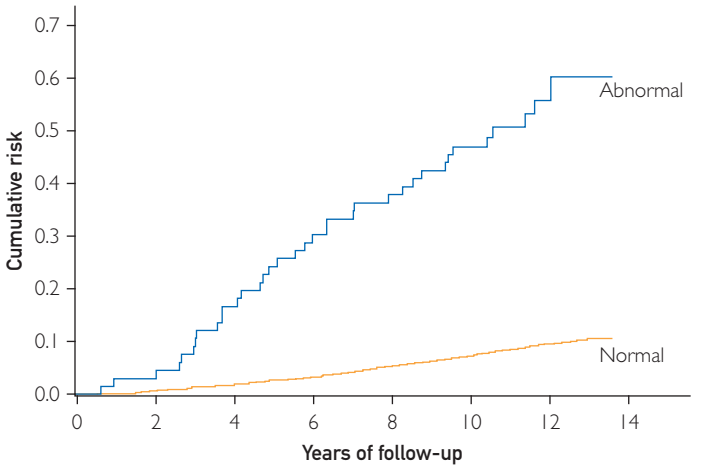
TABLE 1. Comparison of Baseline Characteristics Between Participants With Abnormal cTnT and Normal cTnT Levels[a,b]

Characteristic	Abnormal cTnT Levels (n=66)	Normal cTnT Levels (n=2984)	*P* value[c]
Demographic and cardiovascular risk factors			
Age (y)	67 (59, 72)	57 (49, 64)	<.001 (1)
Race: African American	41 (62.1)	1614 (54.1)	.2 (2)
Sex: 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 blockade 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)
Examination measurements			
Systolic blood pressure (mm Hg)	143 (126, 166)	132 (120, 146)	<.001 (1)
Systolic blood pressure>150 mm Hg	26 (39.4)	607 (20.3)	<.01 (2)
Diastolic blood pressure (mm Hg)	76 (67, 87)	78 (71, 85)	.64 (1)
Pulse (beats/min)	70 (62, 80)	68 (62, 76)	.34 (1)
Laboratory measurements			
Serum creatinine level (mg/dL)	1.4 (1.2, 1.9)	1.1 (1.0, 1.3)	<.001 (1)
eGFR (mL/min per 1.73 m^2)	52 (41, 63)	66 (57, 74)	<.001 (1)
eGFR			<.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 level (mg/dL)	103 (93, 157)	93 (86, 105)	<.001 (1)
Total cholesterol level (mg/dL)	195 (159, 229)	204 (178, 231)	.07 (1)
Low-density lipoprotein level (mg/dL)	115 (85, 145)	124 (98, 150)	.09 (1)
High-density lipoprotein level (mg/dL)	49 (37, 60)	52 (42, 63)	.04 (1)
Triglyceride level (mg/dL)	171 (121-217)	140 (105-196)	.02 (1)
Log triglyceride level	7.4 (6.9, 7.8)	7.1 (6.7, 7.6)	.01 (1)
hsCRP level (mg/L)	3.9 (1.9, 10.6)	3.2 (1.4, 7.0)	<.001 (1)
hsCRP level>3 mg/L	40 (60.6)	1534 (51.4)	.14 (2)
Log hsCRP level	1.9 (0.9, 3.3)	1.7 (0.5, 2.8)	.03 (1)

[a]BMI = body mass index; cTnT = cardiac troponin T; eGFR = estimated glomerular filtration rate; HMG Co-A = 3-hydroxy-3-methyl-glutaryl-CoA; hsCRP = high-sensitivity C-reactive protein; RAAS = renin-angiotensin-aldosterone system.

[b]Values are presented as median (25th, 75th percentile) or as No. (percentage).

[c]*P* value from the (1) 2-sample rank sum test or (2) χ^2 test, as appropriate.



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. Risk of all-cause death by abnormal vs normal cardiac troponin T (cTnT) levels.

was lower, whereas the cardiovascular biomarker, hsCRP level, was higher in those with abnormal cTnT levels.

Outcome: All-Cause Death

During a median follow-up period of 11.5 years (25th, 75th percentile, 10.6, 12.4 years), 308 participants died (incidence density, 0.90 per 100 person-years). An abnormal cTnT level was significantly associated with the risk of all-cause death (log-rank, $P<.001$) (Figure 1 and Table 2). At 10 years, the estimated cumulative incidence of death was 47% (95% CI, 33.4%-57.7%) among those with abnormal cTNT levels compared with 7.3% (95% CI, 6.3%-8.2%) among those with normal cTNT. The leading cause of death was cardiac in those with and without abnormal cTnT levels at baseline (52.8% vs 35.3%, respectively) (Figure 2). There was an increased risk of all-cause death with an abnormal cTnT level that remained significant even after multivariable adjustment (HR, 3.46; 95% CI, 2.3-5.1) (Table 2). The final model for mortality without cTnT had a C statistic of 0.779 (95% CI, 0.75-0.8), which 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, available online at http://www.mayoclinicproceedings.org). Although the risk of death with an abnormal cTnT level was higher with an eGFR of 60 mL/min per 1.73 m^2 or higher than with an eGFR of less than 60 mL/min per 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 (25th, 75th percentile, 8.9, 10.8 years), 52 participants developed ESRD (incidence density, 0.18 per 100 person-years). An abnormal cTnT level was significantly associated with the risk of ESRD (log-rank, $P<.001$) (Figure 3 and Table 3). At 10 years, the estimated cumulative incidence of ESRD was 27.4% (95% CI, 12.4%-39.8%) among those with abnormal cTNT levels compared with 1.3% (95% CI, 0.9%-1.8%) among those 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 level that remained significant even after adjusting for demographic characteristics, 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), which 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, available online at http://www.mayoclinicproceedings.org). The likelihood ratio test provided evidence of an interaction between cTnT status and diabetes ($P=.008$). Inspection of the interaction between cTnT status and diabetes (Figure 4) revealed that individuals with normal cTnT levels and no diabetes were at a low risk of ESRD.

DISCUSSION

In this study of community-dwelling individuals with hypertension, an abnormal cTnT level (≥0.01 ng/mL) independently predicted death

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TABLE 2. Risk of All-Cause Death With Abnormal cTnT Levels[a]

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

[a]cTnT = cardiac troponin T; eGFR = estimated glomerular filtration rate; hsCRP = high-sensitivity C-reactive protein.
[b]Hypertension, diabetes, myocardial infarction, low-density lipoprotein cholesterol level, and smoking.

and ESRD events. Our GENOA study participants with abnormal cTnT levels were generally older with comorbid conditions and reduced kidney function. However, abnormal cTnT levels provided prognostic information independent of traditional risk factors for cardiovascular disease or ESRD. Findings in our predominantly hypertensive population are similar to those of other reports in which a mildly increased or detectable cTnT level in patients with heart failure or 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[39] found that cTnT levels, measured with high-sensitivity assays not yet clinically available in the United States, and N-terminal pro-B-type natriuretic peptide levels were associated with a rapid decline in kidney function and incident chronic kidney disease in elderly patients without heart failure. Our investigations to date are plausible, given the well-described biological 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 the selection of a group with higher risk of ESRD.

Race also plays an important role in the risk of all-cause death, with African Americans having life expectancy 3 to 8 years less than that of 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 previous investigations of cTnT had few African American participants. Wallace et al[13] assessed the prevalence and determinants of cTnT level elevations with conventional cTnT assays in 3557 participants of the Dallas Heart Study, a multiethnic study of subclinical cardiovascular disease, which oversampled African Americans (~52%). They found that African American race was associated with detectable cTnT levels in univariable analysis, but in multivariable analysis, only diabetes, left ventricular hypertrophy, chronic kidney disease, and congestive heart failure

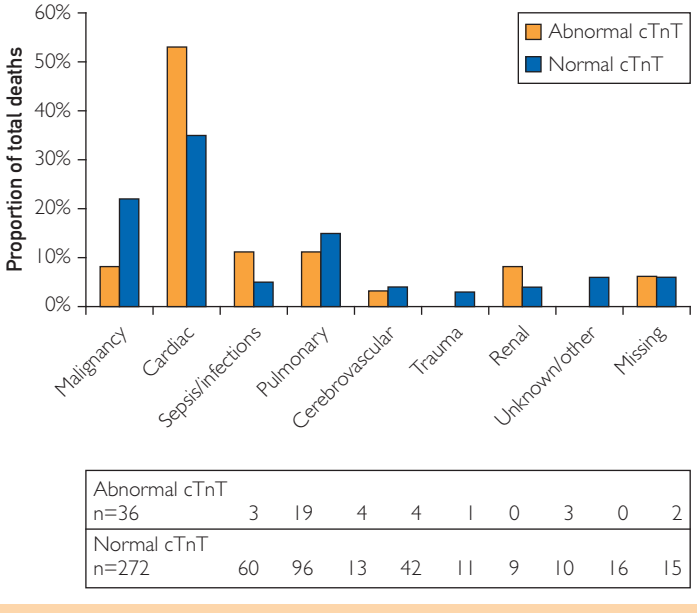
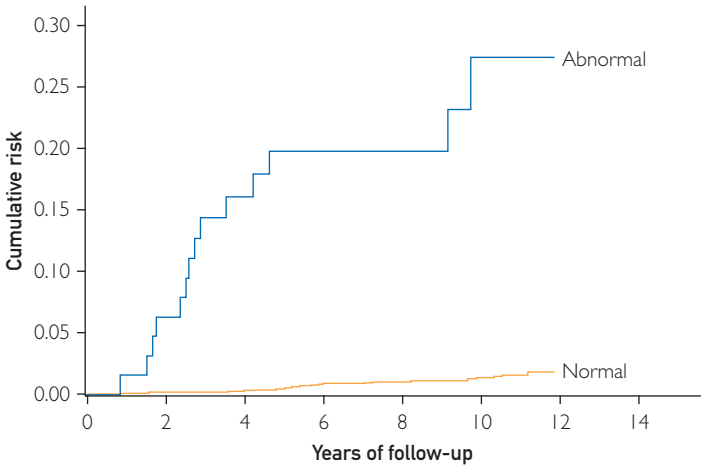


FIGURE 2. Primary cause of death by baseline cardiac troponin T (cTnT) status.



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. Risk of end-stage renal disease by abnormal vs normal cardiac troponin T (cTnT) levels.

were associated with detectable cTnT levels. Similarly, we did not find race to be a determinant of abnormal cTnT levels in our GENOA study cohort. Taken together, these studies suggest that cTnT, as a composite marker of myocardial or endothelial damage caused by comorbid conditions, identifies a high-risk group regardless of race, albeit this is generally more common in African Americans.

The prevalence (2.2%) of an abnormal cTnT level may appear low in this study. However, in healthy populations studied previously,[13,17] the prevalence of a detectable or abnormal cTnT level is rare, ranging from 0.7% to 4%. The prevalence of a cTnT level 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 abnormal cTnT levels, 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 4221 community-dwelling adults aged 65 years and older from the Cardiovascular Health Study (51% hypertensives and 16% African Americans), very low levels of cTnT measured with a highly sensitive assay were associated with cardiovascular death and incident heart failure independent of other biomarkers, including C-reactive protein and N-terminal pro-B-type natriuretic peptide. Other investigations[50,52] revealed that variations in levels of this marker over time were associated with concordant changes in the risk of heart failure and cardiovascular death. The additive information from high-sensitivity assays for cTnT has allowed for the identification of individuals at high risk of death who have both elevated high-sensitivity cTnT levels 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 of our study who died having had undetectable levels at baseline.

Our study had some limitations. First, the aim of the baseline examination in the GENOA study 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

TABLE 3. Risk of End-Stage Renal Disease With Abnormal cTnT Levels

Model	Hazard ratio	95% CI	*P* value	C statistic
1. Unadjusted	23.91	12.92-44.24	<.001	0.635
2. Adjusted for demographic factors (age, sex, and race)	20.84	10.58-41.05	<.001	0.757
3. Adjusted 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

cTnT = cardiac troponin T; eGFR = estimated glomerular filtration rate.

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levels. The limitation due to the lack of urine samples is important, particularly given the findings of 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 hypertensive families and therefore may limit applicability to the general population. Fourth, multiple factors influence cTnT levels, and a single measurement may not appropriately represent an individual's true baseline.

CONCLUSION

We report that cTnT levels provide 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, identifying those at the highest risk of death or ESRD could improve patient management strategies. Unfortunately, abnormal cTnT levels, measured with the standard assay, are relatively uncommon and thus do not improve risk prediction enough to support routine use. Further study is needed to determine whether there is a particular patient group in which cTnT screening would meaningfully improve discrimination between the low- and high-risk patients for these sequelae.

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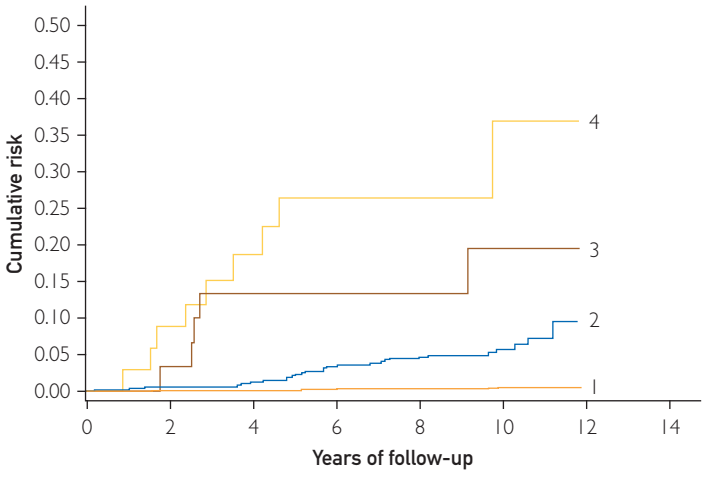
SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at: http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.



Numbers at risk

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

FIGURE 4. Risk of end-stage renal disease by diabetes and cardiac troponin T (cTnT) status.

Abbreviations and Acronyms: **cTnT** = cardiac troponin T; **eGFR** = estimated glomerular filtration rate; **ESRD** = end-stage renal disease; **GENOA** = Genetic Epidemiology Network of Arteriopathy; **HR** = hazard ratio; **hsCRP** = high-sensitivity C-reactive protein

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Potential Competing Interests: Dr Jaffe has or presently consults with most of the major diagnostic companies (troponin).

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