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ORIGINAL RESEARCH

High Sensitivity Troponin Level and Benefits of Chronic Total Occlusion Revascularization

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BACKGROUND: The survival benefit of revascularization of chronic total occlusion (CTO) of the coronary arteries remains a subject of controversy. We measured high sensitivity troponin-I (hsTn-I) levels as an estimate of myocardial ischemia in patients with stable coronary artery disease, with the hypothesis that (1) patients with CTO have higher levels of hsTn-I than patients without CTO, (2) hsTn-I levels will predict adverse cardiovascular events in patients with CTO, and (3) patients with elevated hsTn-I levels will have a survival benefit from CTO revascularization.

METHODS AND RESULTS: In 428 patients with stable coronary artery disease and CTO undergoing coronary angiography, adverse event rates were investigated. Cox proportional hazards models and Fine and Gray subdistribution hazard models were performed to determine the association between hsTn-I level and incident event rates in patients with CTO. HsTn-I levels were higher in patients with compared with those without CTO (median 6.7 versus 5.6 ng/L, P=0.002). An elevated hsTn-I level was associated with higher adverse event rates (adjusted all-cause mortality hazard ratio, 1.19 [95% CI, 1.08–1.32]; P=0.030) for every doubling of hsTn-I level. CTO revascularization was performed in 28.3% of patients. In patients with a high (>median) hsTn-I level, CTO revascularization was associated with substantially lower all-cause mortality (adjusted hazard ratio, 0.26 [95% CI, 0.08–0.88]; P=0.030) compared with those who did not undergo revascularization. In patients with a low (≤median) hsTn-I level, event rates were similar in those with and without CTO revascularization.

CONCLUSIONS: HsTn-I levels may help identify individuals who benefit from CTO revascularization.

Key Words: chronic total occlusion ■ coronary artery bypass graft ■ high sensitivity troponin-I ■ percutaneous coronary intervention

Patients with a chronic total occlusion (CTO) of a coronary artery have been shown to have higher mortality compared with those with coronary artery disease (CAD) without CTOs.[1] This is possibly due to persistent ischemia from the CTO,[2–4] because CTO is more likely to be associated with myocardial ischemia than non-CTO lesions.[5] CTOs are encountered in 15% to 30% of patients undergoing diagnostic coronary angiography, yet despite the higher associated mortality rate, percutaneous coronary intervention (PCI) to revascularize the CTO is attempted in <10% and coronary artery bypass graft surgery in <25% of individuals.[6,7] Although CTO revascularization can improve the ischemic burden and symptoms, there is a lack of data regarding its mortality benefit.[5,8–16] In fact, the American College of Cardiology/American Heart Association PCI guidelines provide a Class IIb/Level of Evidence B recommendation for PCI for CTOs in patients with refractory angina after performing PCI of non-CTO lesions.[17] Whether specific populations of patients with CTO experience a survival benefit from CTO revascularization remains unknown.

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CLINICAL PERSPECTIVE

What Is New?

- Our findings suggest that a high or low baseline high sensitivity troponin-I level may identify individuals with chronic total occlusion who are most likely to obtain a survival benefit from revascularization of their chronic total occlusion.

What Are the Clinical Implications?

- In clinical practice, obtaining a baseline high sensitivity troponin-I level can help physicians make management decisions.

Nonstandard Abbreviations and Acronyms

CTO	chronic total occlusion
HsTn-I	high sensitivity troponin-I

The circulating level of high sensitivity troponin (hsTn), a biomarker of myocardial ischemia or injury, can be elevated in the absence of an acute coronary syndrome.[18–26] Higher circulating levels of hsTn-I predict incident adverse cardiovascular events and mortality in patients with and without CAD.[27–31] Patients with CTOs with poorly developed collaterals have higher levels of ischemia than those with well-developed collaterals[32] and have higher hsTn levels.[33,34] Whether the hsTn levels predict mortality risk in patients with CTO, a population with elevated ischemic burden, remains unknown. Furthermore, whether individuals with CTO and elevated hsTn levels benefit from CTO revascularization remains to be studied. The aim of this investigation was to determine whether (1) hsTn-I levels are higher in patients with CTO compared with those with significant CAD, without CTO; (2) hsTn-I levels predict incident adverse events in patients with CTO; and (3) patients with elevated hsTn-I levels have a survival benefit from revascularization of the CTO. In this prospective study of patients with stable CAD and CTO with long-term follow-up, we hypothesized that patients with CTO will, on average, have higher levels of hsTn-I than patients without CTO, and higher hsTn-I levels will predict adverse cardiovascular events and survival benefit from revascularization in those with a CTO.

METHODS

Patients

The data that support the findings of this study are available from the corresponding author upon reasonable request. We studied participants enrolled in the Emory Cardiovascular Biobank (NCT00378924), a prospective cohort of patients referred for clinically indicated cardiac catheterization at 3 Emory health care sites in Atlanta, GA, between May 2004 and March 2018.[35] Exclusion criteria included (1) history of cardiac transplantation, (2) history of coronary artery bypass graft, and (3) acute coronary syndrome at presentation. Patients without a CTO were excluded from outcomes analyses.

A CTO was defined as 100% luminal diameter stenosis with absence of antegrade flow on angiography of known or assumed 3 months duration.[36] Significant CAD was defined as CAD >50% in any major coronary artery. Three-vessel or left main disease was defined as patients with >50% stenosis in the left anterior descending artery, right coronary artery and left circumflex artery, or in the left main artery. Demographic and clinical data were obtained from questionnaires, and medical records included age, sex, race, body mass index, history of smoking, estimated glomerular filtration rate (eGFR), use of angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers, β-blockers or statins, history of myocardial infarction (MI), history of chronic kidney disease, history of heart failure (HF), left ventricular ejection fraction (LVEF) (defined by most recent transthoracic echocardiography or ventriculography), diabetes (HbA_{1c} >6.5 or treatment with insulin or oral antidiabetic medications), hypertension (systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, or treatment with antihypertensive medications), dyslipidemia (total cholesterol >200 mg/dL, low-density lipoprotein >130 mg/dL, high-density lipoprotein <40 mg/dL or treatment with lipid-lowering medications) as previously described.[35] The study was approved by the Emory University institutional review board. All subjects provided written informed consent.

Revascularization

Patients were revascularized as clinically indicated after angiography. Revascularization of the CTO was defined as PCI that decreased the stenosis grade by at least 50% and restored TIMI (Thrombolysis in Myocardial Infarction) grade 2 or 3 flow, or coronary artery bypass graft that bypassed the CTO lesion within 90 days of enrollment. The nonrevascularization group included those who were managed medically or had revascularization of the non-CTO lesions only.

HsTn-I Assay

Blood samples were collected on the same day as cardiac catheterization, before the procedure, and were stored at −80 °C. Measurements were performed using the Architect analyzer (Abbott Laboratories, North Chicago, IL), with a detection limit of 1.2 ng/L and an interassay coefficient of variation of <10% at 4.7 ng/L.

Follow-Up

Follow-up was conducted for up to 3 years for determination of all-cause mortality, cardiovascular death, MI, HF hospitalization, and the composite end point of all-cause mortality, nonfatal MI, and HF hospitalizations. Follow-up data were collected by personnel blinded to the biomarker and clinical data through telephone interview, chart review, and query of the Social Security Death Index and State records as previously described.[35] Two independent cardiologists, both blinded to the biomarker and clinical data, adjudicated the cause of death. Cardiovascular death was defined as death attributable to an ischemic cardiovascular cause (ie, fatal MI, stroke, or peripheral arterial disease) or sudden death because of an unknown or presumed cardiovascular cause in high-risk patients. Medical records were accessed to validate all self-reported events.

Statistical Analysis

Patient characteristics were summarized using medians, interquartile ranges, frequency counts, and percentages as appropriate. Baseline differences between patients with CTO and significant CAD without CTO, between patients with CTO and hsTn-I levels above and below the median, and between patients with CTO with and without CTO revascularization, were assessed using Mann–Whitney *U* tests for continuous variables or the χ^2 test for categorical variables.

Incident event rates were evaluated in patients with CTO only, based on hsTn-I levels. HsTn-I levels were examined both as a binary variable stratified by median (6.7 ng/L) and as a continuous variable by $\log_2$ transformation to evaluate cumulative incidence. Cumulative incidence function was used to visualize differences in survival outcomes across groups coupled with log-rank tests. Incident event rates in patients with and without revascularization of CTO were examined and stratified by hsTn-I median (6.7 ng/L). Cox proportional hazards models were used to examine the association between groups and time to all-cause death and the composite outcomes of all-cause death, MI, or HF hospitalization. Fine and Gray subdistribution hazard models were performed for time to cardiovascular death, with noncardiovascular deaths treated as competing risk events. Model 1 of the analyses was adjusted for age, sex, race (Black race versus non-Black race), body mass index, LVEF, history of smoking, hypertension, diabetes, dyslipidemia, eGFR, history of MI, use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, β-blockers, and statins. Model 2 of the analyses included the aforementioned variables, CAD severity, and revascularization at enrollment. All analyses were performed using SPSS software, Stata/BE 17.0. *P* values <0.05 were considered statistically significant.

RESULTS

Baseline characteristics of the 1912 enrolled patients (430 with, and 1482 without CTO) are shown in Table S1. The unadjusted median hsTn-I level in patients without CTOs was lower compared with those with CTOs (median 5.6 versus 6.7 ng/L, *P*=0.002) (Table S1; Figure S1).

HsTn-I Levels and Incident Outcomes in Patients With a CTO

There were 2 patients with CTO who were lost to follow-up. In the 428 patients with available outcome data, those with higher hsTn-I levels (>median of 6.7 ng/L) were older, more likely to be Black, have lower eGFR, lower LVEF, and a history of MI and HF when compared with those with lower hsTn-I levels (≤ median) (Table 1). Disease severity was similar between the 2 groups. Both groups had a similar proportion of women, and the median hsTn-I levels were similar between women and men (6.6 versus 6.8 ng/mL; *P*=0.88).

During follow-up, 14.2% of the patients with CTO had deaths from all causes, 9.3% had cardiovascular death, 7.2% had a MI, and 8.3% were hospitalized with HF exacerbations (Table 1). A higher hsTn-I level was associated with a greater risk of all-cause and cardiovascular death and the composite outcome of all-cause death, MI, and HF hospitalizations in unadjusted analyses (Table 2). In models adjusted for age, sex, race, body mass index, smoking history, hypertension, diabetes, dyslipidemia, MI history, eGFR, LVEF, use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, β-blockers, and statins, these differences remained significant (Table 2). When compared with patients with a hsTn-I level ≤median, those with elevated hsTn-I (>median) values had a 5.8-fold higher adjusted rate of cardiovascular mortality, a 5-fold higher adjusted rate of all-cause mortality, and a 3.8-fold higher adjusted rate of the composite event rate (all-cause mortality, MI, HF hospitalization), all *P*<0.001 (Figure 1). There was no interaction between sex, hsTn-I levels, and outcomes.

Revascularization and Outcomes

Of the total cohort of 428 patients, 121 (28.3%) underwent CTO revascularization (91 with PCI and 30 with coronary artery bypass graft), 93 (21.7%) patients received non-CTO revascularization only, and 214 (50.0%) patients were medically managed. Patients who received CTO revascularization were younger, more likely to be male, and less likely to

Table 1. Characteristics of Patients With CTO Stratified by Median HsTn-I Level

Variable	HsTn-I >6.7 ng/L (N=212)	HsTn-I <6.7 ng/L (N=216)	*P* value
HsTn-I, ng/L	15.0 (9.2–30.1)	3.7 (2.8–5.0)	<0.001*
Age	66.0 (58.8–74.5)	63.0 (55.3–70.0)	0.004*
Sex: Male	157 (74.1%)	157 (72.7%)	0.75
Race: Black	50 (23.6%)	26 (12.0%)	0.002*
BMI	28.7 (25.5–32.8)	29.1 (25.5–32.7)	0.88
History of smoking	145 (68.4%)	151 (69.9%)	0.74
Hypertension	186 (87.7%)	178 (82.4%)	0.12
Diabetes	83 (39.2%)	72 (33.3%)	0.21
Dyslipidemia	166 (78.3%)	174 (80.6%)	0.56
Chronic kidney disease	34 (16.0%)	18 (8.3%)	0.015*
History of MI	88 (41.7%)	61 (28.4%)	0.004*
History of HF	91 (42.9%)	38 (17.6%)	<0.001*
eGFR, mL/min per 1.73 m^2	68.9 (52.2–83.0)	80.1 (63.9–93.8)	<0.001*
LVEF (%)	50.0 (40.0–55.0)	55.0 (50.0–60.0)	<0.001*
Disease severity			
1 Vessel	64 (30.2%)	86 (39.8%)	0.11
2 Vessels	81 (38.2%)	70 (32.4%)	
3 Vessels	67 (31.6%)	60 (27.8%)	
Medications			
ACEi/ARB	137 (64.6%)	131 (60.6%)	0.40
β-blocker	164 (77.4%)	152 (70.4%)	0.10
Statin	175 (82.5%)	185 (85.6%)	0.38
3-y outcomes			
All-cause death	49 (23.1%)	12 (5.6%)	<0.001*
Cardiovascular death	33 (15.6%)	7 (3.2%)	<0.001*
MI	19 (9.0%)	12 (5.6%)	0.17
HF hospitalizations	30 (14.2%)	6 (2.8%)	<0.001*
Composite	50 (23.6%)	15 (7.0%)	<0.001*

Median (interquartile range) and frequency count (percentage) are shown. Composite events included all-cause death, MI, and HF hospitalizations. ACEi/ARB indicates angiotensin-converting enzyme inhibitors/angiotensin-receptor blocker; BMI, body mass index; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; HF, heart failure; HsTn-I, high sensitivity troponin-I; LVEF, left ventricular ejection fraction; and MI, myocardial infarction.

*Significance $P<0.05$.

have chronic kidney disease or a history of MI compared with patients who did not receive CTO revascularization. HsTn-I levels were similar between the 2 groups (Table S2). The proportion of patients with CTO revascularization between the >median and ≤median hsTn-I groups were similar (Table S3). During follow-up, the unadjusted event rates were significantly higher in the group without, compared with those with CTO

Table 2. Associations Between HsTn-I Level and Incident Adverse Events in Patients With CTO

Outcomes	Unadjusted HR (95% CI)	*P* value	Adjusted Model 1 HR (95% CI)	*P* value	Adjusted Model 2 HR (95% CI)	*P* value
For every 100% increase in HsTn-I level						
All-cause death	1.21 (1.11–1.31)	<0.001*	1.18 (1.07–1.30)	0.001*	1.19 (1.08–1.32)	0.001*
Cardiovascular death	1.15 (1.07–1.25)	<0.001*	1.11 (0.99–1.25)	0.077	1.11 (0.97–1.28)	0.12
All-cause death/MI/HF hospitalization	1.21 (1.12–1.31)	<0.001*	1.19 (1.08–1.32)	0.001*	1.17 (1.07–1.29)	0.001*

Cox regression was used for all-cause mortality and all-cause death/MI/HF hospitalization. Fine and Gray subdistribution model was used for cardiovascular death. In adjusted model 1, covariates included age, sex, race (Black vs non-Black), BMI, history of smoking, left ventricular ejection fraction, hypertension, diabetes, hyperlipidemia, eGFR, history of MI, use of ACEi/ARB, β-blockers, and statins. Adjusted model 2 included the covariates in adjusted model 1, with the addition of disease severity and any revascularization at enrollment. ACEi/ARB indicates angiotensin-converting enzyme inhibitors/angiotensin-receptor blocker; BMI, body mass index; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; HsTn-I, high sensitivity troponin-I; and MI, myocardial infarction.

*Significance $P<0.05$.

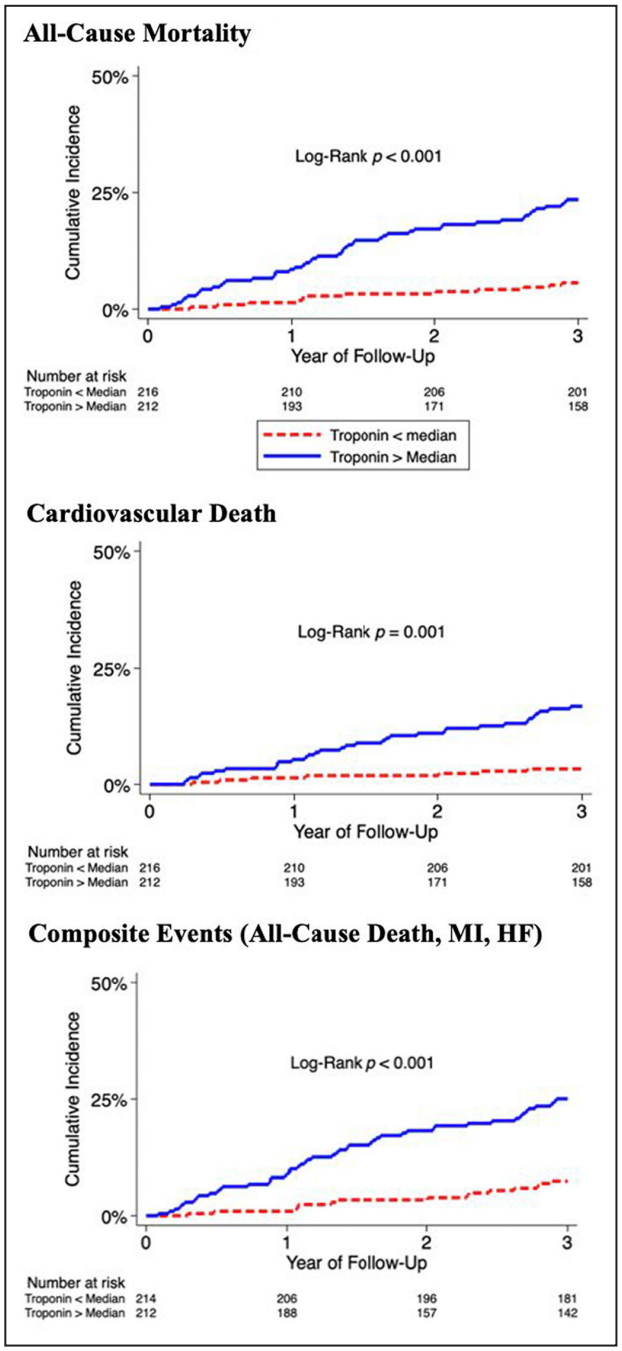

Figure 1. Cumulative incidence of adverse events in patients with a CTO, with or without elevated (>median 6.7 ng/L) HsTn-I level.
Cumulative incidence function as used to visualize differences in outcomes in patients with CTO with above (n=212) and below (n=216) hsTn-I level (6.7 ng/L), coupled with log-rank tests. CTO indicates chronic total occlusion; HF, heart failure hospitalization; HsTn-I, high sensitivity troponin-I; and MI, myocardial infarction.

revascularization (Table 3). After further adjustment for age, sex, race, body mass index, smoking history, hypertension, diabetes, dyslipidemia, MI history, eGFR, LVEF, use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, β-blockers, and statins, all-cause mortality and cardiovascular death remained significant.

HsTn-I Levels and Outcomes With Revascularization

The outcomes of CTO revascularization were further explored based on hsTn-I levels. In patients with elevated hsTn-I (>median) levels, the rates of all-cause mortality, cardiovascular death, and the composite end point were all significantly lower by >50% in patients who underwent CTO revascularization, compared with those who did not receive CTO revascularization, a difference that persisted even after adjustment for the aforementioned covariates (all-cause mortality hazard ratio, 0.26 [95% CI, 0.08–0.88]; *P*=0.030). In contrast, in patients with low hsTn-I (≤median) levels, adverse event rates were similar in those with or without CTO revascularization, even after adjustment (Table 3, Figure 2, Table S3). The adjusted interaction term between hsTn-I levels (above/below median) and CTO revascularization on the composite outcome trended to be significant, *P*=0.086.

DISCUSSION

Novel findings of our study include the following: patients with CTO have an elevated hsTn-I level compared with those without a CTO. Moreover, a higher hsTn-I level was an independent predictor of adverse outcomes in patients with CTO, similar to findings in other individuals with or without CAD.[27–34] Finally, although CTO revascularization was associated with a reduced event rate in the entire cohort, there was a dramatic improvement in outcomes in those with high hsTn-I level, while there was no improvement in those with low hsTn-I level. Our findings suggest that patients with a greater burden of ischemia, as demonstrated by elevated hsTn-I levels, are most likely to benefit from CTO revascularization.

It is also important to note that the median level of hsTn-I in our CTO cohort was lower than the 99th percentile of both men and women.[37] In addition to myocardial cell death, reversible ischemia and increased metabolic demand leads to cleavage and release of troponin and its degradation products into in the circulation,[21–26] resulting in higher circulating hsTn levels. Inducible myocardial ischemia has been reported to be greater in the presence of CTO compared with those with obstructed CAD without CTO.[5] One novel finding from our study includes the presence of higher hsTn-I levels in patients with CTO compared with patients without CTO, likely due to greater ischemia in these patients. Additionally, there are extensive data showing that women have lower troponin levels compared with men.[37] However, in our cohort of patients with CTO,

Table 3. Incident Adverse Events in Revascularized Compared With Nonrevascularized Patients With CTO

Outcomes	Unadjusted HR (95% CI)	*P* value	Adjusted Model 1 HR (95% CI)	*P* value	Adjusted Model 2 HR (95% CI)	*P* value
Overall						
All-cause death	0.36 (0.17–0.76)	0.007*	0.40 (0.16–1.05)	0.060	0.43 (0.16–1.12)	0.083
Cardiovascular death	0.27 (0.10–0.76)	0.013*	0.22 (0.05–0.92)	0.039*	0.22 (0.05–0.91)	0.036*
All-cause death/MI/HF hospitalization	0.40 (0.20–0.80)	0.010*	0.57 (0.25–1.31)	0.19	0.59 (0.25–1.35)	0.21
HsTn-I ≤6.7 ng/L						
All-cause death	0.83 (0.23–3.08)	0.79	1.18 (0.41–7.9)	0.86	1.42 (0.18–11.32)	0.74
Cardiovascular death	0.41 (0.05–3.40)	0.42	1.13 (0.07–18.3)	0.94	0.80 (0.11–5.68)	0.83
All-cause death/MI/HF hospitalization	0.95 (0.30–3.00)	0.94	1.47 (0.27–8.00)	0.66	1.72 (0.30–9.92)	0.54
HsTn-I >6.7 ng/L						
All-cause death	0.26 (0.10–0.65)	0.004*	0.25 (0.08–0.83)	0.023*	0.26 (0.08–0.88)	0.030*
Cardiovascular death	0.24 (0.07–0.77)	0.014*	0.12 (0.02–0.94)	0.043*	0.13 (0.02–1.08)	0.059
All-cause death/MI/HF hospitalization	0.26 (0.10–0.66)	0.004*	0.40 (0.14–1.10)	0.088	0.41 (0.14–1.18)	0.097

Cox regression model was used for all-cause mortality and all-cause death/MI/HF hospitalization. Fine and Gray subdistribution model was used for cardiovascular death. In adjusted model 1, covariates included age, sex, race (Black vs non-Black), BMI, history of smoking, left ventricular ejection fraction, hypertension, diabetes, hyperlipidemia, eGFR, history of MI, use of ACEi/ARB, β-blockers, and statins. Adjusted model 2 included the covariates in adjusted model 1, with the addition of disease severity and non-CTO revascularization at enrollment. ACEi/ARB indicates angiotensin-converting enzyme inhibitors/angiotensin-receptor blocker; BMI, body mass index; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; HsTn-I, high sensitivity troponin-I; and MI, myocardial infarction.

*Significance $P<0.05$.

men and women had similar levels of hsTn-I, and there was no interaction between sex and troponin levels and outcomes.

Higher circulating levels of hsTn-I predict incident adverse cardiovascular events and mortality in patients with CAD[27–34] as well as elderly individuals.[38] Herein, we demonstrate the independent prognostic value of hsTn-I levels in predicting incident adverse events in patients with a CTO, a population with greater ischemia and overall higher hsTn-I levels. This indicates that among this population, patients with greater ischemia are at higher risk of adverse events and vice versa.

Patients with CTO with poorly developed collaterals have higher levels of ischemia than those with well-developed collaterals,[32] and hsTn levels have been shown to correlate with the extent of collateralization.[33] We demonstrate that CTO revascularization was associated with improved outcomes only in patients with greater ischemia, evident as elevated hsTn-I levels, likely due to the improvement in ischemic burden. Patients with low levels of ischemia, as shown by lower hsTn-I levels, likely had a well-developed collateral circulation and little change in ischemic burden by CTO revascularization.

The survival benefit of CTO revascularization remains a subject of controversy. Although meta-analyses and observational studies of patients with CTO demonstrate reduction in mortality with revascularization,[39–42] the randomized controlled Decision-CTO (Drug-Eluting Stent Implantation versus Optimal Medical Treatment in Patients with Chronic Total Occlusion) trial found no difference in outcomes with revascularization of CTOs.[43] However, this trial was limited by failure to reach the final sample size and therefore had low power to demonstrate improvement in the mortality end point. Additionally, this trial did not stratify patients by hsTn levels and did not assess the relationship between ischemia burden and outcomes.[43] Additionally, the EURO CTO (Randomized Multicentre Trial to Compare Revascularization With Optimal Medical Therapy for the Treatment of Chronic Total Occlusions) trial found that CTO PCI improves health status assessed by the Seattle angina questionnaire but had no difference in major adverse events compared with medical management alone.[15] This trial, however, was limited by slow patient recruitment and very low event rates, likely due to selection bias of excluding patients with severe symptoms. Our data, after adjustment for clinical covariates, showed that CTO revascularization was associated with substantial survival benefit in the subset of patients with greater ischemia, evident as higher hsTn-I levels, while the subset with less ischemia, evident as lower hsTn-I levels, had no survival benefit.

Beyond the mortality benefit, our data also found that there were fewer HF hospitalizations in patients with elevated hsTn-I levels who underwent CTO revascularization by 3-fold. In patients with CTO, meta-analyses have shown that PCI of the CTO improves LVEF compared with medical therapy,[44,45] but randomized controlled clinical trials such as EXPLORE (Evaluating Xience and Left Ventricular Function in Percutaneous

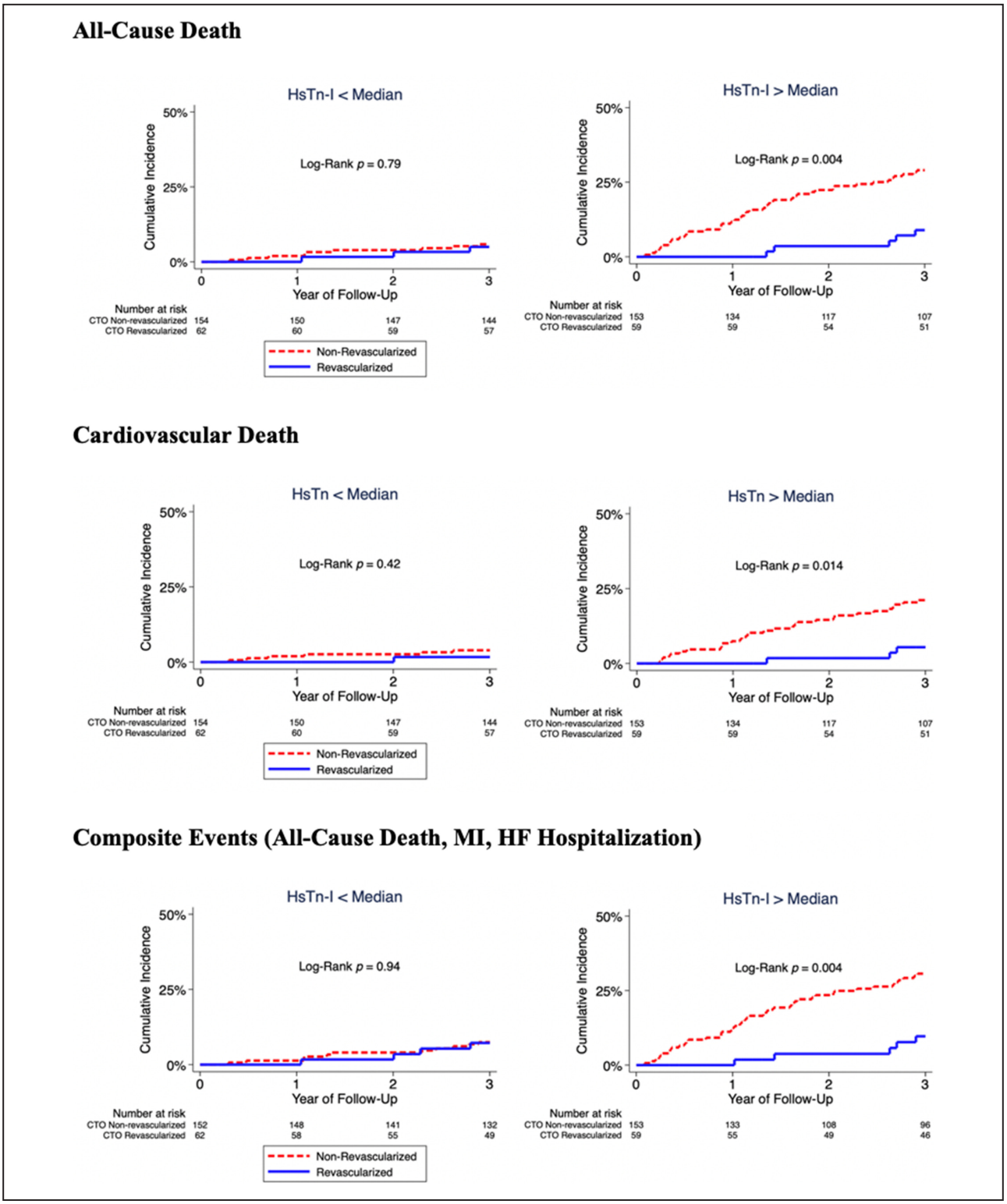

Figure 2. Cumulative incidence of adverse events in patients with CTO revascularization compared with the nonrevascularized group in those with elevated (>median 6.7 ng/L, right), or Low (≤median 6.7 ng/L, left) HsTn-I levels.
Incident event rates in patients with (n=121) and without (n=307) CTO revascularization were examined and stratified by a hsTn-I level of 6.7 ng/L. Cumulative incidence function was used to visualize the differences in outcomes across groups, coupled with log-rank tests. CTO indicates chronic total occlusion; HF, heart failure; HsTn-I, high sensitivity troponin-I; and MI, myocardial infarction.

Coronary Intervention on Occlusions After ST-Elevation Myocardial Infarction) and REVASC (Recovery of Left Ventricular Function After Stent Implantation in Chronic Total Occlusion of Coronary Arteries) did not confirm these findings, except in the subset of patients with left anterior descending artery CTO.[46,47] However, ischemia quantification or hsTn data are not available in these trials. Our data suggest that patients with CTO and greater ischemic burden, evident as higher hsTn-I levels, have lower HF hospitalization rates after CTO revascularization.

The decision to revascularize a CTO is currently reserved for those with significant symptoms, or presence of reversible ischemia on noninvasive testing.[48] Revascularization of CTOs has been shown to improve ischemia on myocardial perfusion imaging.[5,8–13] Moreover, those with the greatest ischemic burden appear to have the greatest reduction in ischemia after revascularization of the CTO on myocardial perfusion imaging.[14] Importantly, patients undergoing revascularization who had the greatest reduction in ischemia measured by positron emission tomography had better event-free survival than those with less reduction of ischemia.[49] Together, these studies suggest that the decrease in the ischemic burden by revascularization may be driving improved outcomes in patients with CTOs.

STRENGTHS AND LIMITATIONS

Strengths of our study include enrollment of a diverse population including women and Black participants with a wide range of LVEF and long-term follow-up with availability of adjudicated event rates. HsTn-I measurements were performed at 1 time, which minimized variability. Limitations include a lack of postrevascularization hsTn-I measurements, and thus assessment of the link between relief of ischemia and outcomes. Second, revascularization was not randomized and was performed for clinical reasons, and there were differences in the clinical characteristics among patients who did and did not undergo revascularization. However, to address this, we adjusted for differences in the clinical variables in all of our analyses and found that substantial benefit of revascularization persisted. Another limitation was the lower numbers of cardiovascular death events in subgroup analyses based on high and low hsTn-I levels. Nevertheless, our findings regarding the value of hsTn-I levels in identifying a subset of patients with CTO who benefit from revascularization need to be replicated in a randomized trial.

CONCLUSIONS

Patients with CTO have higher hsTn-I levels compared with those with CAD without CTO, and this elevation is associated with higher rates of adverse events. Only patients with elevated hsTn-I levels experienced a survival benefit from revascularization. Thus, measurement of hsTn-I levels can assist in identifying individuals who may experience survival benefit from revascularization of CTOs.

ARTICLE INFORMATION

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Affiliations

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Disclosures

Dr Murtagh is a full-time Abbott employee and shareholder of Abbott. The remaining authors have no disclosures to report.

Supplemental Material

Table S1–S3
Figure S1

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