High Cardiac Troponin T Doubles Event Risk

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FROM THE ANNUAL SCIENTIFIC SESSIONS OF THE AMERICAN HEART ASSOCIATION

CHICAGO – Higher serum concentrations of cardiac troponin T independently predicted an increased rate of new-onset heart failure and cardiovascular death in a longitudinal study of more than 4,000 elderly, community-dwelling Americans with a median follow-up of 12 years.

"Measurement of cTnT [cardiac troponin T] may be useful in cardiovascular risk stratification in older adults," Dr. Christopher R. deFilippi said at the scientific sessions.

Assessing cTnT's role as a risk predictor became possible with the recent availability of high-sensitivity assays. Previous studies using conventional cTnT assays found roughly 4% of the general elderly population had detectable levels; in Dr. deFilippi's new study, 66% of community-dwelling U.S. adults with a median age of 71 had detectable cTnT levels. The high-sensitivity test produces "about a 10-fold increase in the number of people with detectable cTnT; that's what gives us a dynamic range," said Dr. deFilippi, a cardiologist at the University of Maryland in Baltimore.

Over 12 years, the rates of heart failure and cardiac death tracked along with baseline cTnT levels.

DR. DEFILIPPI

Results from two other studies presented at the meeting and a third study published in early December showed similar links between high levels of cTnT and cardiovascular events, cardiac structure, and death (see box).

The consistent findings from all these studies show that cTnT "is a pretty good risk predictor. Cardiac troponin offers a very easy way for a physician to say that a person is at high risk" for new-onset heart failure, cardiovascular death, or other cardiovascular disease events, Dr. deFilippi said in an interview.

"I look at cardiac troponin T as early biochemical evidence of pathology. Finding a high level in a person could be a wake-up call. It gives some of the earliest, direct evidence with a cardiac-specific molecule that pathology is taking place," independent of traditional risk markers, he said.

"Cardiac troponin T could be the summation of all other risk factors. We use cholesterol level as a motivator, even though it is much less effective for measuring risk," Dr. deFilippi explained.

Another attractive feature of measuring cTnT is that the evidence collected by Dr. deFilippi and his associates suggest that in some people high levels are reversible, and when levels drop a person's risk drops.

VITALS

Major Finding: Community-dwelling older adults in the highest quartile for their serum cardiac troponin T level, as measured with a high-sensitivity assay, had a two- to threefold increased risk for new-onset heart failure and for cardiovascular death during a median follow-up of 12 years.

Data Source: The 4,221 unselected U.S. residents age 65 or older (median age of 71) enrolled in the Cardiovascular Health Study.

Disclosures: The study was partially funded by Roche Diagnostics, which markets a high-sensitivity cardiac troponin T assay. Dr. deFilippi said that he has served as a consultant to and has received honoraria and grant support from Roche Diagnostics and from Siemens Healthcare Diagnostics. He has also been a consultant to and received grant support from Critical Diagnostics and BG Medicine.

In the analyses so far, the strongest correlation with a lowered serum level of cTnT has been a person's level of activity and exercise, he said.

The high-sensitivity cardiac troponin T test has not yet received marketing approval from the Food and Drug Administration, but is commercially available in Europe.

To examine the prognostic ability of cTnT, Dr. deFilippi and his associates used serum specimens collected from 4,221 community-dwelling Americans aged 65 or older enrolled in the Cardiovascular Health Study.

At baseline, 2,794 (66%) of the participants had a detectable level of cTnT, at least 3 pg/mL, and their median age was 71.

During a median follow-up of almost 12 years, the incidence of heart failure and cardiovascular death tracked along with baseline levels of cTnT. Among the one-third of patients with an undetectable level at baseline the rate of new-onset heart failure during follow-up averaged 1.6% per year. Among people in the highest quintile of cTnT level, greater than 12.9 pg/mL, the incident heart failure rate averaged 6.4% per year. "It's a huge difference," he said.

In an analysis that adjusted for demographic differences and traditional risk factors including systolic blood pressure, smoking status, serum creatinine, and left ventricular size, people with baseline cTnT levels above the median all had a significantly increased risk for both end points.

The quintile of people with the highest cardiac troponin T level had a 2.5-fold increased risk of new-onset heart failure and a threefold increased risk of cardiovascular death compared with those who had an undetectable level at baseline.

Even when also adjusted for baseline levels of NT-pro brain natriuretic peptide and C-reactive protein, people in the highest quintile for baseline level had about a twofold higher rate of heart failure and cardiovascular death during follow-up, Dr. deFilippi reported.

Records on follow-up cTnT levels, measured 2-3 years after baseline in 86% of the study participants, showed that among those with a detectable cTnT level at baseline, nearly two-thirds stayed at about the same level, 22% increased by more than 50%, and 14% decreased by more than 50%.

The high increasers had their subsequent heart failure and cardiovascular death rates rise by about 50% compared with people with more moderate changes.

In contrast, among those whose levels fell by more than 50% during follow-up subsequent event rates dropped by about 25% compared with those with less change in their cTnT level.

Concurrent with Dr. deFilippi's talk at the meeting. the findings also appeared in an article published online in JAMA (2010; 304:doi:10.1001/jama.2010.1708).

The results also identified some people with very high levels at baseline that then fell to an undetectable level at their second cTnT measurement. Few people showed this kind of change, but it occurred often enough for Dr. deFilippi to speculate that certain actions can effectively lower serum cardiac troponin T levels.

The source of the cTnT isn't clear. Dr. deFilippi believes it's caused by a chronic process, although the specifics remain unknown. "It's unlikely an ischemic cause," he said. "The issue is, once you see [a high level] can you intervene? Right now, that's an open question." ■

Other Studies Using High-Sensitivity Test Support cTnT's Risk-Marker Role

CHICAGO – In addition to the report by Dr. deFilippi, three other research groups recently reported finding significant links between elevated serum levels of cardiac troponin T and an increased risk for cardiovascular events:

► Researchers measured cardiac troponin T (cTnT) using a high-sensitivity assay in 10,820 Americans aged 53-75 without prevalent cardiovascular disease enrolled in the Atherosclerosis Risk in Communities (ARIC) study. In these people, with an average age of 63 years, 61% had a detectable level of serum cTnT at baseline using the high-sensitivity test. During an average follow-up of 10 years, Researchers found a significant link between detectable levels at baseline and death and hospitalization for heart failure during follow-up, Dr. Justin T. Saunders from Baylor College of Medicine in Houston reported at the scientific sessions.

► In a second, independent study, researchers measured serum cTnT with the high-sensitivity assay in women enrolled in the Women's Health Study. The current analysis focused on 512 women with diabetes at the time of their serum sampling and 564 women without diabetes. Among the women with diabetes, detectable levels of cTnT excisted in 56% of those who had cardiovascular disease events during follow-up and in 42% of the women who did not later have an event, a statistically significant difference. The event that seemed most responsible for this difference was cardiovascular disease death. Among the women without diabetes, detectable levels of cTnT appeared to have no significant relationship to subsequent cardiovascular disease events. Detectable cTnT appeared in 34% of the women with a subsequent event and in 30% of those without a later event, Dr. Brendan M. Everett from Brigham and Women's Hospital in Boston reported at the scientific sessions.

► In the third study, researchers ran high-sensitivity cTnT measures on 3,546 people aged 30-65 enrolled in the Dallas Heart Study. They found detectable levels in 25% of the participants. The prevalence of detectable levels depended on age and gender. People younger than 40 had a prevalence rate of 14% compared with a prevalence of 58% in people aged 65 or older. Men had a prevalence rate of 37%, compared with a rate of 13% in women. During a median follow-up of 6.4 years, in an analysis that adjusted for a series of baseline variables and risk factors, people in the highest quintile for serum cTnT level had a statistically significant, greater than fourfold increased risk for both all-cause death and cardiovascular death, said Dr. James A. de Lemos, from the University of Texas Southwestern Medical Center, and his associates in a report published in the Dec. 8, 2010, issue of JAMA (2010;304:2503-12).

Dr. Saunders had no disclosures.

Dr. Everett said he had received research grants from Roche Diagnostics.

Dr. de Lemos said that he has received research grants from Roche Diagnostics and Biosite, and consulting fees, lecture honoraria, or both from Tethys Biomedical, Johnson & Johnson, Roche Diagnostics, Biosite/Invemess, Siemens, AstraZeneca, Pfizer, Bristol Myers Squibb/Sanofi Aventis, and Merck.

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