High Cardiac Troponin T Doubled Event Risk

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CHICAGO – Higher serum levels 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.

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

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.

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.

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. deFillipi said in an interview.

"I look at [cTnT] 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.

"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. deFillipi noted.

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. 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 cTnT test has not yet received marketing approval from the Food and Drug Administration, but is commercially available in Europe.

To examine the prognostic capability 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.

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

DR. DEFILIPPI

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 new-onset heart failure and cardiovascular death. The quintile of people with the highest cTnT 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 the investigators adjusted the anaysis 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.

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 on-line (JAMA 2010; 304:doi:10.1001/jama.2010.1708).

The results of the study also identified a number of 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 cTnT levels.

The source of the cTnT isn't clear. Dr. deFilippi said that he 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." ■

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.

Catheter Ablation Supported

Atrial Fibrillation *from page 1*

ministration when the committee was making its decisions, it was not included in the guidelines, according to the report.

The updated guidelines also suggest the use of dronedarone for some atrial fibrillation patients to reduce hospitalizations for cardiovascular events.

Recent studies such as the DIONYSOS study (Efficacy and Safety of Dronedarone Versus Amiodarone for the Maintenance of Sinus Rhythm in Patients With Persistent Atrial Fibrillation) showed that dronedarone was less effective than amiodarone for reducing the recurrence of atrial fibrillation. However, in a placebo-controlled, double-blind, parallel-arm trial to assess the efficacy of dronedarone 400 mg b.i.d. for the prevention of cardiovascular hospitalization or death from any cause in patients with atrial fibrillation/atrial flutter (the ATHENA trial), dronedarone reduced the "the combined end point of death and cardiovascular hospitalizations, largely by reducing hospitalizations related to atrial fibrillation," the reviewers wrote. However, dronedarone should not be given to patients with NYHA class IV heart failure or patients with decompensated heart failure within the past 4 weeks, they noted.

To maintain normal sinus rhythm, the updated guidelines support the use of catheter ablation based on data from more than 6,900 patients. In one multicenter study (the ThermoCool trial), symptomatic patients with paroxysmal atrial fibrillation who were treated with catheter ablation showed significant improvement after 3 months, compared with control patients. Currently, catheter ablation treatment is recommended for atrial fibrillation patients without severe lung disease who have not had success with drug therapy.

Dr. L. Samuel Wann, a cardiologist at Wheaton Franciscan Healthcare in Wauwatosa, Wis., served as chair of the 2011 Writing Group Committee. Dr. Wann and his colleagues wrote that the 2006 full-text guidelines for the management of atrial fibrillation that are not mentioned in the 2011 update remain unchanged at this time. "The guidelines attempt to define practices that meet the needs of most patients in most circumstances," the reviewers said.

"The last time the guidelines were published was in 2006, and there have been several new drugs and treatments that have been developed since that time. Physicians want to know where they stand in terms of the hierarchy of treatment of patients with atrial fibrillation," explained Dr. Curtis, chair of the department of medicine at the University of Buffalo, N.Y. "In order to be timely, we did a limited, focused update," she said.

The clinical implications of more lenient heart rate control are unclear at this time, Dr. Curtis said. In the Rate Control Efficacy in Permanent Atrial Fibrillation (RACE II) study, on which the recommendations were based, the difference in heart rate control between lenient control and strict control groups was limited, she noted.

But the study emphasized the need for clinicians to be careful about going too far in trying to control patients' heart rates, Dr. Curtis said, because too much control could lead to bradycardia and unnecessary pacemaker use.

As for additional research, "We need to know how to prevent [atrial fibrillation] in the first place, and we need to understand thoroughly the long-term outcomes of ablation therapy," Dr. Curtis said.

Dr. Wann had no financial conflicts to disclose. Several of the writing group members, including Dr. Curtis, disclosed serving as a speaker or consultant, or receiving research funding from multiple pharmaceutical companies including Medtronic, Boston Scientific, AstraZeneca, Sanofi-Aventis, and GlaxoSmithKline. ■