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EDITORIAL

Troponin in Stable Patients Undergoing Coronary Angiography: Should It Be Routinely Assessed?

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Cardiovascular diseases are one of the leading causes of death globally, with ≈19 million fatalities per year.[1] Death from cardiovascular causes increased by 18.7% between 2010 and 2020, and a further increase is expected without adequate preventive interventions. Approximately half of cardiovascular deaths are attributable to coronary artery disease (CAD).[1,2] Despite guideline-recommended primary or secondary prevention, several patients remain at high risk of adverse cardiovascular events.[3–6]

See Article by Brunner et al.

Cardiac troponins (cTns) are proteins enabling the calcium-mediated interaction of actin and myosin. Because cardiac and skeletal isoforms are distinct, high-sensitivity cTns (hs-cTns) are highly specific for the detection of cardiac damage and represent the preferred biomarkers for the evaluation of patients with suspected myocardial injury or infarction.[7] Conversely, the role of hs-cTn in stable patients with suspected or known CAD is still controversial.[8]

In this issue of the *Journal of the American Heart Association* (*JAHA*), Bay et al compared the prognostic value of hs-cTnI and hs-cTnT in 1829 patients with stable symptoms suggestive of CAD referred for coronary angiography to a single center in Germany.[9] Consistent with previous observations, the authors showed that higher values of hs-cTnI or hs-cTnT, even at low concentrations (ie, <99th percentile upper reference limit), were independently associated with all-cause mortality.[8,10–12] The risk models were adjusted for several relevant confounders, including traditional cardiovascular risk factors, renal function, other biomarkers, and CAD severity according to Gensini and synergy between percutaneous coronaryintervention with TAXUS and cardiac surgery (SYNTAX) scores. Unfortunately, some key information was missing, such as left ventricular ejection fraction or heart failure. Including these variables in the adjusted model may have yielded slightly different results.

One of the most interesting findings of the analysis of Bay et al was that only hs-cTnI was significantly associated with major adverse cardiovascular events. Previous studies showed the superiority of hs-cTnI over hs-cTnT in predicting cardiovascular events.[13,14] The mechanistic explanation of this association is not fully understood; a higher specificity of hs-cTnI for myocardial injury has been advocated. However, other reports that do not directly compare hs-cTnT and hs-cTnI demonstrated that both biomarkers predict major adverse cardiovascular events.[8,10–12,15–18] Although some uncertainty remains about the predictive superiority of hs-cTnI over hs-cTnT in stable patients with suspected or confirmed CAD, the association of hs-cTn values with adverse outcomes in this population is consistent throughout the literature. Hence, the question is whether hs-cTns should be routinely measured

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For Disclosures, see page 2.

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in stable patients with suspected or known CAD. This practice would be problematic for several reasons. First, in this population, there are no established hs-cTn cutoffs above which hs-cTn is considered elevated and a management decision would be recommended. Indeed, different thresholds have been used across studies.

Second, a broad range of diseases impacting patient's prognosis may cause an elevation of hs-cTn, especially at lower-range concentrations.[19] Elevated hs-cTn can be attributable to heart failure with reduced or preserved ejection fraction, left ventricular hypertrophy, infiltrative cardiomyopathies, pericarditis or myocarditis, arrhythmias (eg, atrial fibrillation), or even noncardiac disease, such as sepsis, stroke, pulmonary hypertension, chronic kidney disease, and cancer on chemotherapy.[19] Intuitively, it can be expected that in patients with CAD and/or cardiovascular risk factors, elevated hs-cTn values are more likely to be associated with myocardial ischemia than in an unselected population. However, a substudy of the objective randomised blinded investigation with optimal medical therapy of angioplasty in stable angina trial recently questioned this assumption, showing that in symptomatic patients with known obstructive single-vessel disease, reversible myocardial ischemia is not the only mechanism underlying cTn increase.[20] Knowing the direct cause of hs-cTn elevation is essential to providing the right treatment and reducing the risk of adverse events. Selected patients with higher troponin levels were proven to have the largest benefit from statins, angiotensin-converting enzyme inhibitors, or vorapaxar.[11,16,17] Yet, it remains unclear how exactly hs-cTn values should impact the decision to initiate or up-titrate a cardiovascular treatment in stable patients with suspected or known CAD; and whether such strategy would improve the prognosis.[3,6] In the fourth universal definition of myocardial infarction document, experts suggested that if myocardial infarction has been excluded, an elevated troponin should trigger a workup to understand the cause of troponin increase rather than begin any treatment.[7]

In conclusion, in stable patients with suspected or known CAD, increased hs-cTn values are associated with a higher risk of adverse events and hs-cTnI might be a more specific predictor of cardiovascular complications than hs-cTnT. However, the routine assessment of hs-cTn in this population is currently not advisable. Trials showing improved outcomes following management decisions based on hs-cTn values are needed to support such an approach.

ARTICLE INFORMATION

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