The 28 patients with STEMI had sufficient sample remaining to allow for determination of cTnI (2). The characteristics of this group have previously been reported (2), but in brief the mean age (SD) was 56 (11) years, and 17.4% of patients were women. Mean (SD) body mass index was 26.46 (3.5) kg/m², and 71.4% of patients were hypertensive, 64.3% were current smokers, 60.7% had hypercholesterolemia, and 14.3% had diabetes. Blood samples were available at admission and at 24, 48, 72, and 96 h after onset of symptoms. cTnI concentrations were measured at a laboratory in Heidelberg, Germany, with the AccuTnI assay (Beckman-Coulter). The assay has a limit of detection of 0.01 μg/L, with a 99th percentile as low as 0.02–0.03 μg/L. In the laboratory performing the measurements, a cutoff value of 0.03 μg/L was used. Cardiac MRI was performed as described elsewhere (2). Plasma concentrations of cTnI are reported as median with the corresponding interquartile range (IQR). For all analyses, a value of \( P < 0.05 \) was considered statistically significant. Correlation coefficients were calculated by the Spearman test.

Of the 28 study patients with STEMI, 7.1% of patients (2 of 28) received fibrinolytic agents before percutaneous coronary intervention; the remainder underwent primary percutaneous coronary intervention. Preinterventional thrombolysis in myocardial infarction flow grade 3 was present in 12 of 28 patients (42.3%) before PCI and in 27 of 28 patients (96.4%) after. The median time delay from onset of symptoms to balloon angioplasty was 6.25 h. MRI was performed at median of 4 days (range 3–4 days). All patients manifested delayed hyperenhancement observed with MRI; in 60.71% of patients (17 of 28) hyperenhancement was transmural. Mean infarct size relative to heart weight was 18.2% (IQR 7%–49%). Ventricular function evaluated by MRI revealed a mean ejection fraction of 54.4% (27.9%–63.6%) and a mean stroke volume of 91.32 mL (42.4–109.3 mL). The median absolute value for infarct size was 29.3 g (IQR 16.6–53.0 g). Spearman analysis demonstrated a strong correlation between cTnI values and infarct mass at 24 (\( n = 24 \)), 48 (\( n = 26 \)), 72 (\( n = 23 \)), and 96 h (\( n = 28 \)) after onset of symptoms (Fig. 1A and B). As with other studies (2, 3), correlations between the infarct size and cTnI were significant for all time-points except for admission (Spearman correlation coefficient Rho = 0.2; data not shown).

These data document that cTnI values provide accurate estimates of infarct size in patients with STEMI. As with cTnT (2, 3), cTnI correlated with infarct size in reperfused STEMI patients at 24–96 h as well (Fig. 1A). These data indicate that clinicians can rely on values on days 1–4 to provide an approximation to MRI-determined reperfused infarct size. Importantly, the slopes of the correlation curves are different for each day (Fig. 1B). The parallelism of these data with the data for cTnT suggest that similar relationships, as with cTnT, are also likely to occur with non-STEMI. It is also likely that there will be differences with and without reperfusion. The use of imaging techniques such as positron-emission tomography and contrast-enhanced MRI (4) to enable determination of infarct size are currently impeded owing to limited availability and high cost. Small infarcts may escape visualization because of inadequate resolution. We now show with MRI that single-point values of cTnI between 24 and 96h, as with sestamibi measurements (5), correlate well. Troponin measurements are not only cheaper and more available but provide an esti-
mate of the size of infarction not confounded by prior infarction. This investigation shows that for patients with reperfused STEMI, early as well as later measurements of cTnI are reliable estimates of infarct size. The fact that cTnI measurement at time-points earlier than 96 h correlate well with MRI-determined infarct size should allow for an earlier evaluation of prognosis in of these patients. Larger prospective and controlled studies are needed to confirm our results.

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Cross-Reactivity of BNP, NT-proBNP, and proBNP in Commercial BNP and NT-proBNP Assays: Preliminary Observations from the IFCC Committee for Standardization of Markers of Cardiac Damage

To the Editor:

B-type natriuretic peptide (BNP) is a 32 amino acid cardiac-synthesized hormone that reduces blood pressure and increases sodium excretion (1). Following proteolytic cleavage of proBNP, a 108-amino acid precursor, an N-terminal fragment (NT-proBNP) and BNP are released (2). Increased concentrations of BNP and NT-proBNP can be used clinically to monitor heart failure, but lack of alignment between commercial BNP and NT-proBNP assays (3) can lead to confusion when clinicians or laboratorians compare results measured for the same analyte on different instruments. Some of this confusion arises from variable assay specificity regarding what peptides are being measured. We studied whether (a) BNP assays demonstrated cross-reactivity with NT-proBNP or proBNP, and (b) whether NT-proBNP assays demonstrated cross-reactivity with BNP or proBNP, by using 5 commercial BNP and 3 commercial NT-proBNP assays with 2 BNP, 2 NT-proBNP, and 2 proBNP materials.

The NPs studied were: Peptide Institute synthetic BNP (aa 77–108), Scios human recombinant BNP (aa 77–108), HyTest human recombinant NT-proBNP (aa 1–76), Roche modified (amidated for stabilization) synthetic NT-proBNP, HyTest human recombinant proBNP (aa 1–108), and Scios glycosylated human recombinant proBNP. BNP assays evaluated were Abbott Architect, Abbott AxSYM, Bayer Centaur, Biosite Triage, and Beckman Access (Biosite assay packaged for use by Beckman). NT-proBNP assays (all based on Roche reagents) were Dade-Behring Dimension, Ortho-Clinical Diagnostics Vitros, and Roche Elecsys 2010. All assays, for which epitopes of the antibodies used have been previous described (3), were run according to the manufacturers’ guidelines. BNP, NT-proBNP, and proBNP materials were diluted with normal (low NP concentration) EDTA-plasma pools and lithium-heparin plasma (Dade assay only) pools, collected from healthy donors after institutional review board approval was obtained, to achieve target concentrations of 250, 500, and 1000 ng/L. Baseline BNP and NT-proBNP were quantified first in the pools and then after the pools were spiked with NP peptides. All measurements were performed in duplicate. Baseline BNP or NT-proBNP concentrations were subtracted from each spiked pool measurement. Percent cross-reactivity was calculated by dividing the measured concentration for the spiked pool into the expected peptide concentration, multiplying by 100, and then averaging across all 3 expected concentrations.

Recoveries and cross-reactivity percentages between peptides and BNP and NT-proBNP assays are displayed in Table 1. The BNP assays were more specific for the BNP peptides, with recovery ranging from 79% to 199%, compared to 5% to 38% cross-reactivity to the proBNP peptides and <1% to 7% cross-reactivity to the NT-proBNP peptides. Similarly, the NT-proBNP assays were more specific for the NT-proBNP peptides, showing 47% to 243% recovery, with substantial cross-reactivity to proBNP peptides (<1% to 249%), and no cross-reactivity to the BNP peptides (<1% across all assays).

This study demonstrates that the BNP peptides used do not substantially cross-react with NT-proBNP assays, and that the NT-proBNP peptides do not substantially cross-react with BNP assays. We confirm that there is substantial cross-reactivity between proBNP peptides and commercially available BNP and NT-proBNP assays. Variations depended on the different sources and types of peptide tested in each assay. We observed minimal cross-reactivity with the glycosylated Scios proBNP peptide, compared with substantial cross-reactivity to the non-glycosylated HyTest proBNP peptide with the NT-proBNP assays. Glycosylation likely interfered with peptide antibody binding. The mechanisms responsible for different reactivities between the HyTest and Roche NT-proBNP peptides using different NT-proBNP assays, which use the same antibodies but different assay architectures, cannot be explained presently. The modest differences in reactivities for the recombinant (Scios) and synthetic (Peptide Institute) BNP materials using different BNP assays also requires additional study; with different assay architectures for the same reagents (Biosite, Beckman) showing diverse recovery.

Little is known about which NP forms are circulating physiologically. The clinical significance of measured cross-reactivities will

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