are not affected by preanalytical variation produced by prolonged transport and/or storage of whole blood, serum, or heparin-containing plasma. Our findings underscore the robustness of the Roche fifth-generation hs-cTnT assay around the 99th percentile and extend the previously published data on the stability of cTnT in vitro (2, 3, 5).

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**Fig. 1.** Effect of different conditions for storage of heparin-containing plasma on detectable cTnT concentrations measured with the fifth-generation hs-cTnT assay from Roche (n = 28).

The mean relative difference ± 2 SDs (compared with the FF reference) is plotted for the 13 storage conditions. The mean cTnT concentration was 58 ng/L (range, 4–451 ng/L; median, 17 ng/L); 18 of the 28 samples had a cTnT concentration between 4 and 25 ng/L. RT, room temperature.

**Persistent Increases in Cardiac Troponin Concentrations As Measured with High-Sensitivity Assays after Acute Myocardial Infarction**

**To the Editor:**

We read with interest the report by Koenig et al. (1) showing the value of high-sensitivity cardiac troponin T (hs-cTnT)1 assays for predicting long-term cardiovascular events in patients after an acute coronary syndrome (ACS) or coronary artery bypass grafting. Al-
though studies have demonstrated long-term cardiovascular events with measurements of hs-cTnI or hs-cTnT in patients who present with symptoms suggestive of ACS (2, 3), Koenig et al. found a relationship with hs-cTnT concentrations after patients had been discharged from a cardiac rehabilitation program (mean time to discharge and hs-cTnT measurement was 43 days from the index event) (1). hs-cTnT concentrations ≥3 ng/L (limit of blank) remained detectable in 84% of patients and were ≥14 ng/L (99th percentile) in 37.1% of the patients. These findings raise important questions about how gradually hs-cTnT concentrations decrease in the absence of recurrent ACS and have implications regarding the use of high-sensitivity cardiac troponin assays for diagnosing subsequent events in patients who are stable after an ACS.

To address these questions, we conducted a prospective observational study to assess whether cardiac troponin concentrations normalize by 30 days after an acute myocardial infarction (AMI). After obtaining ethics approval, we recruited a convenience sample of Hamilton General Hospital patients who consented to return 30 days after their first AMI (index event) to provide a follow-up sample (plasma from EDTA-anticoagulated blood) for cTnT analyses (Roche fourth-generation assay, used clinically). Samples were frozen at −80 °C and were subsequently thawed for the first time for hs-cTnT analysis (Roche Diagnostics E Modular Analytics analyzer; CV, 2.4% at 30 ng/L) and thawed a second time for the hs-cTnI assay (Abbott Diagnostics precommercial prototype assay, ARCHITECT i1000SR analyzer; CV, 6.1% at 21 ng/L). We used the following thresholds, which were obtained from the literature for cTnT and from the manufacturer for hs-cTnI, as evidence of a persistent abnormal increase: cTnT ≥10 ng/L, hs-cTnT 99th percentiles [≥14 ng/L (overall), ≥9 ng/L (women), and ≥16 ng/L (men)], and hs-cTnI 99th percentiles [≥26 ng/L (overall), ≥16 ng/L (women), and ≥34 ng/L (men)]. We collected samples from 46 patients, 38 with ST-elevation myocardial infarction (STEMI) and 8 non-STEMI patients. Two of the patients had a recurrent myocardial infarction during the 30-day follow-up. We assessed the remaining 44 patients [38 men and 6 women; mean (SD) age, 60 (12) years] who had remained event free. Similar to the results of Koenig et al., we found that 80% of the patients had hs-cTnT values ≥3 ng/L and 27% had hs-cTnT values ≥14 ng/L by 30 days after their AMI (Fig. 1). In ad-

![Fig. 1. hs-cTnT and hs-cTnI concentrations in stable, event-free participants 30 days after AMI.](image-url)
dition, 84% of the patients had a detectable hs-cTnI concentration (≥1.3 ng/L, limit of blank). Persistent increases, however, were not as common for cTnI values >10 ng/L (2% of patients) or for hs-cTnI values greater than the overall 99th percentile (7% of patients had values ≥26 ng/L) by 30 days after an AMI. The use of sex-specific 99th percentile cutoffs further reduced the overall prevalence of persistent hs-cTnT increases (20% of patients) and hs-cTnI (2% of patients). When overall or sex-specific 99th percentile cutoffs were used, the hs-cTnI assay classified participants differently than the hs-cTnT assay (P = 0.007, and P = 0.011, respectively, by the McNemar test). The probabilities of persistent increases in hs-cTnT or hs-cTnI were not affected by sex (male, female), age (<60 years, ≥60 years), or type of index event (STEMI, non-STEMI) (P > 0.10, χ² test).

There is evidence that increases in hs-cTnT ≥99th percentile may last up to 7 weeks after an ACS. Another recent cohort study showed that a similar proportion of patients (31.3%) had persistent hs-cTnT increases ≥14 ng/L at 7 weeks after an ACS (4). The risk of a cardiovascular event in patients who had a persistent hs-cTnT increase was 3-fold higher than in patients whose hs-cTnT values normalized by 7 weeks after an ACS (4). It remains unclear, however, how long hs-cTnT increases persist beyond 7 weeks or whether this effect is observed with the hs-cTnI assays, because it appears that cTnI concentrations may fall below the 99th percentile cutoffs during the healing phase (approximately 5 to 6 weeks) after an AMI (5).

In conclusion, although there may be prognostic value for cardiac troponin concentrations measured by high-sensitivity assays during the convalescence phase of stable patients after an ACS, our data suggest that diagnosis of subsequent events (reinfarction) is not possible with a single hs-cTnT measurement. A substantial number of patients will have increased hs-cTnT concentrations for at least 30 days after an AMI without showing increases with either the fourth-generation cTnT assay or the hs-cTnI assay with the manufacturer’s 99th percentile cutoffs. Observations of persistent increases in cardiac troponin with high-sensitivity assays after an AMI are consistent with the new guidelines from the Third Universal Definition of Myocardial Infarction (5), which recommend serial measurements and possibly sex-specific cutoffs to distinguish chronic from acute increases (i.e., reinfarction). Limitations of our study include the short 30-day observation period and the limited laboratory and imaging data before and after ACS; thus, one cannot distinguish between increases due to the slow process of “healing” and those caused by persistent left ventricular dysfunction. Larger and longer studies are needed to determine when hs-cTnI and hs-cTnT concentrations normalize across different patient subgroups after ACS, and during and after the healing phase.

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