Weekly and 90-Minute Biological Variations in Cardiac Troponin T and Cardiac Troponin I in Hemodialysis Patients and Healthy Controls

Kristin M. Aakre,1,2* Thomas Røraas,3 Per Hyltoft Petersen,3 Einar Svarstad,4,5 Hilde Sellevoll,5 Øyvind Skadberg,6 Kristin Sæle,5 and Sverre Sandberg1,3

BACKGROUND: Myocardial infarction (MI) is diagnosed by the finding of a single cardiac troponin value above the 99th percentile and a significant time-dependent change in cardiac troponin concentration. The aim of this study was to determine the 90-min and weekly biological variations, the reference change value (RCV), and the index of individuality (II) of high-sensitivity cardiac troponin T (hs-cTnT) (Roche Diagnostics) and hs-cTnI (Abbott Diagnostics) in patients receiving hemodialysis (HD) and in healthy individuals.

METHOD: Blood samples were collected from 19 HD patients (on an HD-free day) and 20 healthy individuals at 90-min intervals over a 6-h period (between 08:30 and 14:30) and before the midweek HD treatment for 10 weeks. The within-person variation (CVi), between-person variation, RCV, and II were calculated.

RESULTS: During the 6-h sampling period, the concentrations of hs-cTnT (both groups) and hs-cTnI (HD patients only) decreased on average by 0.8% to 1.7% per hour, respectively. These declining trends were included in the calculation of a 90-min asymmetric RCV: −8%/+5% in HD patients (hs-cTnT), −18%/+21% in HD patients (hs-cTnI), −27%/+29% in healthy individuals (hs-cTnT), and −39%/+64% in healthy individuals (hs-cTnI). The II was low in both groups for both assays. The weekly CVi values were approximately 8% (hs-cTnT) and 15% (hs-cTnI) in both groups.

CONCLUSIONS: When using a cardiac troponin change of 20%–50% to diagnose an MI, the false-positive rate is likely to be lower for the hs-cTnT assay than for the hs-cTnI assay. The low II suggests that use of a diagnostic cutoff value can be omitted.

© 2014 American Association for Clinical Chemistry

Chronic kidney disease (CKD)7 is an important risk factor for cardiovascular morbidity and mortality, and the risk is even more important in patients receiving hemodialysis (HD) (1). In the presence of clinical symptoms and signs of an acute myocardial infarction (MI), the universal definition includes the finding of a serum cardiac troponin concentration above the 99th percentile for the assay as defined in healthy individuals, together with a significant time-dependent increase or decrease in cardiac troponin concentrations (2). In contrast to individuals with healthy kidney function, the cardiac troponin concentrations in patients with CKD may be constantly increased at concentrations higher than the 99th percentile of a healthy population. This finding is most frequent for the cardiac troponin T (cTnT) assay (3–5). Therefore, the diagnosis of an MI in HD patients is often based solely on the dynamics of the measured cardiac troponin concentration. However, the magnitude of the concentration change (i.e., the δ criterion) is a matter of debate, with relative δ values ranging from 20% to 250% having been discussed (6–12). Some argue that an absolute δ in high-sensitivity (hs)-cTnT of 7–9 ng/L is optimal for differentiating between diseased and nondiseased individuals (6, 13, 14). However, such studies rarely include patients receiving HD. The European Society of Cardiology suggests that in the clinical context of MI, a concentration change of 20% (baseline cardiac troponin concentration above the 99th

1 Laboratory of Clinical Biochemistry, Haukeland University Hospital, Bergen, Norway; 2 Norwegian Clinical Chemistry EQA Program, Bergen, Norway; 3 Norwegian Quality Improvement of Primary Care Laboratories (NOKLUS), Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway; 4 Department of Clinical Medicine, University of Bergen, Bergen, Norway; 5 Department of Medicine, Haukeland University Hospital, Bergen, Norway; 6 Laboratory of Clinical Biochemistry, Stavanger University Hospital, Stavanger, Norway.

* Address correspondence to this author at: Laboratory of Clinical Biochemistry, Haukeland University Hospital, 5021 Bergen, Norway. Fax + 47-55975976; e-mail kristin.moberg.aakre@helse-bergen.no.

Received October 1, 2013; accepted February 21, 2014. Previously published online at DOI: 10.1373/clinchem.2013.216978

Nonstandard abbreviations: CKD, chronic kidney disease; HD, hemodialysis; MI, myocardial infarction; cTnI, cardiac troponin I; hs, high-sensitivity; CVi, within-person biological variation; RCV, reference change value; CVa, analytical variation; II, index of individuality; CVb, between-person variation.
percentile) to 50% (baseline cardiac troponin concentration below the 99th percentile) over 3–6 h is sufficient for a diagnosis of MI (15). However, for the hs cardiac troponin assays, there are limited data to support the use of a 20% change in cardiac troponin in HD patients, and there is conflicting evidence regarding the use of a 50%  δ  value in individuals with cardiac troponin concentrations that are below to within the 99th percentile (11, 13, 16–24). One study used a fourth-generation cTnT assay to explore the weekly within-person biological variation (CVi) value for cTnT in HD patients (25), and several studies have measured the long-term hs cardiac troponin CVi in healthy individuals and in patients with chronic diseases (16, 17, 19, 22, 26).

The reference change value (RCV) defines the maximum difference between 2 consecutive results that might be caused by analytical variation (CVa) and CVi (27, 28). If the RCV value is larger than the  δ  criterion used to define a disease, there is a risk of misinterpreting physiological changes as abnormal (i.e., a higher rate of false-positive test results may lead to a lower test specificity). The index of individuality (II) describes the utility of conventional population-based reference values and diagnostic cutoffs (e.g., the 99th percentile). In view of the current recommendations for diagnosing MI, the aim of the current study was to determine the 90-min CVi, between-person variation (CVb), RCV, and II for the hs-cTnT assay and for an hs-cTnI (Abbott Diagnostics) assay in patients receiving HD and in healthy individuals. The same assays were also used to estimate the parameters for weekly measurements.

**Materials and Methods**

**INCLUSION OF STUDY PARTICIPANTS**

This study was carried out according to the principles of the Declaration of Helsinki, and the protocol was approved by the Regional Committee for Medical and Health Research Ethics. Informed written consent to participate was obtained from each individual. One cohort included 19 patients with CKD who had been receiving HD at least twice weekly for at least 2 months, and the other cohort consisted of 20 healthy volunteers from the laboratory staff. The median age of the HD group was 71 years (range 35–84 years) and 21% were females (Table 1). The patients with CKD had been treated with HD for a median duration of 16.5 months at the time of inclusion. The main etiology of CKD stage 5 was nephrosclerosis (8 patients), followed by glomerulonephritis (6 patients), miscellaneous (3 patients), and postrenal causes (2 patients). The median age of the healthy individuals was 61 years (range 46–68 years) and half of them were females.

<table>
<thead>
<tr>
<th>Table 1. Patient characteristics (n = 19).a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
</tr>
<tr>
<td>Female sex</td>
</tr>
<tr>
<td>HD treatment duration, median (range), months</td>
</tr>
<tr>
<td>Receiving antihypertensive medications</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Earlier MI or angina pectoris</td>
</tr>
<tr>
<td>Heart valve disease</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
</tbody>
</table>

* Except where stated otherwise, the data are n values.

**COLLECTION OF SAMPLES**

The samples were collected in 2011. Two series of blood samples were collected from the participants; one series included 5 samples that were collected at 90-min intervals over a 6-h period (i.e., samples were collected at 0830, 1000, 1130, 1300, and 1430). In the HD group, these blood samples were obtained on a day that the patients did not receive HD. Additionally, weekly samples were collected over a period of 10 weeks. The samples were obtained from HD patients before a midweek HD session and from healthy individuals during morning hours between 08:30 and 09:30.

**ASSAY INFORMATION**

The samples were centrifuged within 1 h of being collected and the serum was frozen immediately to −80°C and stored until April 2013. The serum samples were then thawed and analyzed in one run using the hs-cTnT assay on a Modular E system from Roche Diagnostics (limit of detection 3.0 ng/L; 99th percentile 14 ng/L; reagent lot recalibrated according to the 2009 99th percentile) (29) and the hs-cTnI STAT assay (limit of detection 1.6 ng/L; 99th percentile 23 ng/L) (30) on an Architect i2000SR system from Abbott Diagnostics. The samples from half of the patients and half of the healthy individuals were analyzed in duplicate to estimate CVa. Samples for duplicate analysis were selected randomly for each sex. Testing regarding heterophilic antibodies or human antimouse antibodies was not conducted, since a chronically increased hs cardiac troponin concentration is a very common finding in patients with renal failure and is known to be of clinical importance (3–5).

**EXCLUSION OF PATIENTS BECAUSE OF CLINICAL EVENTS DURING THE STUDY PERIOD**

The medical records for each HD patient were carefully reviewed by 2 independent medical doctors with several years of training in internal medicine to identify clinical events that could possibly be related to cardiac...
ischemia (e.g., angina pectoris, MI, pulmonary embolism, tachy/bradyarrhythmia, deteriorating congestive heart failure, myocarditis, sepsis, severe hypotension or hypertension, or aortic dissection). Four patients suffered events during the study period and were therefore excluded from all or some of the calculations (see Table 1 in the Data Supplement that accompanies the online version of this report at http://www.clinchem.org/content/vol60/issue6). Patient 3 had an episode of atrial fibrillation and dyspnea and was admitted to hospital (excluded from calculation of weekly biological variation); patient 8 developed recurrent infections diagnosed as endocarditis (excluded from all calculations); patient 13 developed hypertension and dyspnea that led to increased antihypertensive medication, diuretic treatment, and changes in HD treatment (excluded from calculation of weekly biological variation); and patient 16 was admitted to the hospital for treatment of infection and hypotension (excluded from calculation of the weekly biological variation).

**EXCLUSION OF HEALTHY INDIVIDUALS OWING TO NONMEASURABLE RESULTS**

Individuals with more than 1 (90-min variation) or 2 (weekly variation) nonmeasurable results (defined as hs-cTnT <3.0 ng/L or hs-cTnI <1.6 ng/L) within one series were excluded from the calculations in that particular sample sequence (see online Supplemental Table 1). Four individuals were excluded from the calculation of hs-cTnT variations (participants 1, 3, 4, and 5 for the 90-min variation and participants 1, 3, 4, and 10 for the weekly variation). Likewise, 3 healthy individuals were excluded from the calculation of hs-cTnI variations (participants 1, 4, and 9 for the 90-min variation and participants 3, 4, and 10 for the weekly variation).

**STATISTICS**

For the duplicate measurements, a maximum of 3 results within each series were identified as analytical outliers as defined by Burnett (31), and therefore excluded. Six results for the HD cohort were excluded from the calculation of 90-min hs-cTnI variation (4 of these were in patient 16, who was consequently excluded from the calculation; see online Supplemental Table 1). Based on the criteria of Reed et al. (32), 1 healthy individual (number 18) was excluded from all calculations.

Simple linear regression was used to identify trends that could indicate that a non–steady-state situation was present. The measurements at 90-min intervals exhibited a significant trend: declining concentrations were seen in 17/18 HD patients and 14/15 healthy individuals for the hs-cTnT assay, and in 11/14 HD patients for the hs-cTnI assay. The trend was calculated as a percentage from the first result, and a regression line was estimated on the basis of the mean decrease in the values (Fig. 1). The homogeneity of the slopes was tested using an F-test, in which the variation among regression coefficients was compared with the weighted mean variation (33). The data were adjusted according to the B value of the relevant regression equations, and an adjusted “steady state” was achieved. A declining trend was not seen either in the data describing the 90-min variation of hs-cTnI in the healthy individuals (Fig. 1) or in any of the data series describing the weekly variations.

The residuals of the data did not conform to a gaussian distribution, and the data were therefore transformed into natural logarithms. As suggested by Fraser and Harris (27), the variance homogeneity in the analytical and within-person variances were tested for each data series (log-transformed data; healthy individuals and HD patients for both assays) using the Cochran and Bartlett tests. Patients exhibiting nonhomogeneity were identified by plotting the cumulative fractions of the ranked individual variation results (consisting of both CVi and CVa) on a Rankin scale as a function of the within-person variation of hs cardiac troponin (1 curve per series), and patients or healthy individuals were excluded until homogeneity of variance was achieved (data not shown) (34). For hs-cTnT, homogeneity of variance was achieved in both series describing the 90-min variation without excluding any individual, although 1 healthy individual (number 5) and 1 HD patient (number 10) were excluded from the calculation of the weekly biological variation (see online Supplemental Table 1). For hs-cTnI, variance homogeneity was achieved after excluding 2 HD patients from the calculations of the 90-min biological variation (patients 17 and 19). One HD patient (patient 18) and 1 healthy individual (participant 5) were excluded from calculations of the weekly biological variation (see online Supplemental Table 1).

**CALCULATION OF CVa, CVi, CVb, RCV, AND II**

The CVa, CVi, and CVb values for hs-cTnT and hs-cTnI were calculated on log-transformed data separately for healthy individuals and HD patients, using nested ANOVA. The numbers of HD patients and healthy individuals included in the calculations are given in Table 2. The SDs were retransformed into CVa, CVi, and CVb using the following formula:

$$CV_i = \sqrt[100]{exp(\sigma^2 - 1)}$$

where $\sigma$ is the estimated SD for the ln-transformed data and $CV_i$ is the adjoining retransformed CV. The RCV values (with 95% CIs) were retransformed as
described by Fokkema et al. (35) using the following formulae:

\[
\text{RCV}_{\text{pos}} = \{\exp[1.96 \times 2^{1/2} \times (\sigma_a^2 + \sigma_i^2)^{1/2}] - 1\} \times 100
\]

and

\[
\text{RCV}_{\text{neg}} = \{-1.96 \times 2^{1/2} \times (\sigma_a^2 + \sigma_i^2)^{1/2}\} - 1\} \times 100,
\]

where \(\sigma_a\) is the analytic SD and \(\sigma_i\) is the within-person SD of the logarithmic data.

When there is a systematic increase or decrease in the results, a constant (i.e., the \(\beta\) value of the systematic change) should be added to the RCV (27, 36). The present data revealed a significant constant decline (i.e., 90-min variation for hs-cTnT in healthy individuals, hs-cTnT in HD patients, and hs-cTnI in HD patients). The \(\beta\) values for data recalculated as percentages were added to the RCV values (retransformed into percentage values) for calculation of the asymmetric RCV using the following formulae:

\[
\text{asymmetric RCV}_{\text{pos}} = \beta \text{ value} + \{\exp[1.96 \times 2^{1/2} \times (\sigma_a^2 + \sigma_i^2)^{1/2}] - 1\} \times 100
\]

and

\[
\text{asymmetric RCV}_{\text{neg}} = \beta \text{ value} + \{-1.96 \times 2^{1/2} \times (\sigma_a^2 + \sigma_i^2)^{1/2}\} - 1\} \times 100.
\]

The II was calculated using the retransformed data as follows (27, 37):

---

**Fig. 1.** During the sampling period (i.e., 0830–1430) a regular decline was seen in the hs cardiac troponin concentration of HD patients (A, B). For healthy individuals, this decline was seen for the hs-cTnT assay (C) but not for the hs-cTnI assay (D). The HD patients were sampled on a day when they did not receive HD treatment.
<table>
<thead>
<tr>
<th></th>
<th>90 min</th>
<th>Weekly</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HD patients</td>
<td>Healthy individuals</td>
</tr>
<tr>
<td></td>
<td>hs-cTnT (n = 18)</td>
<td>hs-cTnI (n = 15)</td>
</tr>
<tr>
<td></td>
<td>hs-cTnI (n = 15)</td>
<td>hs-cTnI (n = 17)</td>
</tr>
<tr>
<td></td>
<td>hs-cTnI (n = 14)</td>
<td>hs-cTnI (n = 15)</td>
</tr>
<tr>
<td>Concentration, mean (range), ng/L</td>
<td>86.1 (19.2–227.3)</td>
<td>41.5 (5.5–160.1)</td>
</tr>
<tr>
<td>CVa, mean (95% CI), %</td>
<td>1.4 (1.1–1.7)</td>
<td>6.2 (5.2–7.4)</td>
</tr>
<tr>
<td>CVi, mean (95% CI), %</td>
<td>1.9 (1.4–2.4)</td>
<td>3.3 (0.0–5.5)</td>
</tr>
<tr>
<td>CVb, mean (95% CI), %</td>
<td>110.0 (73.3–213.6)</td>
<td>148.1 (102.0–514.7)</td>
</tr>
<tr>
<td>90-min decline, β value, %</td>
<td>−1.5</td>
<td>−1.2</td>
</tr>
<tr>
<td>RCV, %</td>
<td>−6/7</td>
<td>−17/22</td>
</tr>
<tr>
<td>Asymmetric RCV, 90 min, %</td>
<td>−8/5</td>
<td>−18/21</td>
</tr>
<tr>
<td>Asymmetric RCV, 6 h, %</td>
<td>−12/1</td>
<td>−22/17</td>
</tr>
<tr>
<td>II</td>
<td>0.02</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*a Original data.

*b NA, not applicable.

+* Before addition of the decline.
Results

The patient characteristics are given in Table 1. Nephrosclerosis and glomerulonephritis were the main causes of renal disease in approximately one-half and one-third of the HD patients, respectively. Figs. 2 and 3 show the ranges of hs cardiac troponin concentrations for the individuals. The mean hs-cTnT concentration in the HD cohort was much higher than the 99th percentile (see Materials and Methods) defined in healthy individuals. Meanwhile, for the hs-cTnI assay, a lower mean value closer to the 99th percentile (see Materials and Methods) was seen in the HD cohort. The mean concentrations of hs cardiac troponin varied considerably for each participant (Table 2). Furthermore, the absolute concentration changes in individual patients were quite large. For example, during a 3-h observation period, the ranges of δ values for hs-cTnT and hs-cTnI were 1.0–16.5 and 1.1–20.0 ng/L (both uncorrected data), respectively. The largest absolute changes were seen for the patients with the highest baseline hs cardiac troponin concentrations. Table 2 lists the analytical and biological variation data. Quite similar CVi values were found for the healthy individuals and the HD patients, and the higher RCV values observed for the healthy individuals were attributable to the higher CVa values seen at low hs cardiac troponin concentrations. The CVa and CVi values were highest for the hs-cTnl assay. The declining hs cardiac troponin concentrations (original data recalculated as percentages) observed between 0830 and 1430 are shown in Fig. 1, and the 90-min decline is presented in Table 2. Table 2 also

\[ II = \sqrt{(\text{CVa}^2 + \text{CVi}^2)/\text{CVb}} \]

Excel 2010 and SPSS version 20.0 were used for the statistical analysis.
gives the RCV and asymmetric RCV values that were applicable for different time frames. The greatest hs-cTnT asymmetric RCV values including the 6-h decline for the healthy individuals and HD patients ranged from −34% to +22% and from −12% to +1%, respectively. Among the healthy individuals, there was no systematic change during the 6-h observation period for the hs-cTnI measurements, and the 90-min RCV value ranged from 39% to 64%. The 6-h asymmetric hs-cTnI RCV for the HD patients ranged from 22% to 17%. Owing to CVb being larger than CVi, the II value was low. The difference in II found for the 2 assays was explained mainly by the higher CVa seen for the hs-cTnI assay, at both low and higher hs cardiac troponin concentrations.

Fig. 4 shows the hs-cTnT and hs-cTnI changes for the 4 patients who were excluded from the calculations of the weekly CV values due to cardiac events. Quite similar hs cardiac troponin concentrations were observed for both assays during an event, with the exception of patient 16. Importantly, the change in hs cardiac troponin concentration was greater than the calculated weekly RCV values in those patients with definite cardiac events (see Materials and Methods); patient 3 exhibited a +146% (hs-cTnT)/+405% (hs-cTnI) increase, patient 8 exhibited a +121% (hs-cTnT)/−74% (hs-cTnI) change, and patient 16 exhibited an increase of +175% (hs-cTnT)/+1251% (hs-cTnI) in the first sample after the clinical event. Patient 13 had unspecific symptoms that developed over a period of weeks, and in the week after the initial symptoms the hs-cTnT concentration increased by +35%, which is above the calculated hs-cTnT RCV value of +26%. However, the similar hs-cTnI increase of +37% was not higher than the estimated RCV value of +53%.
Discussion

The main interpretation of the findings of this study is that in an HD population and in healthy individuals it is expected that the hs-cTnT change in clinically stable individuals should be lower than the suggested diagnostic criterion for MI of 20% and 50%, respectively, when 2 measurements are performed within an interval from 90 min to 6 h (15). In HD patients the use of an absolute \( \delta \) value of 7–9 ng/L (6, 13, 14) will increase the risk of false-positive results, since the hs-cTnT variation in patients with a stable hs cardiac troponin significantly exceeds this cutoff. For the hs-cTnI assay (Abbott Diagnostics) the normal variation due to CVa and CVi may overlap with the suggested diagnostic \( \delta \) values of 20% and 50% in HD patients and healthy individuals, respectively. The use of these \( \delta \) values could therefore lead to higher rates of false-positive diagnoses in these populations. If only increasing hs cardiac troponin values are considered relevant, the RCV value should be calculated using a 1-sided test. This would give hs-cTnI RCV values of 18% (HD patients) and 52% (healthy individuals), both of which are still within the borderline ranges compared to the suggested diagnostic cutoffs. The low II seen in the 90-min variation data suggests that \( \delta \) values could be used as the only diagnostic criterion for MI, and the use of diagnostic cutoffs (i.e., the 99th percentile) might be omitted, assuming that the analytical variation is sufficiently low.

A limitation of the current study is the exclusion of a relatively large number of HD patients owing to clinical events. This was an expected outcome of the well-known high morbidity related to HD treatment (1).
Furthermore, a large number of healthy individuals were excluded owing to nonmeasurable hs cardiac troponin concentrations, reducing the number of patients that could be included in the final calculations. However, the number of included participants is comparable to that in previous studies of the biological variation of hs-cTn, which have typically included 12–25 individuals (16, 17, 19, 21–23). The uncertainties regarding our calculations are reflected in the CIs given for all CV values.

One main strength of this study is the use of 2 distinct assays and the inclusion of 2 cohorts (i.e., both healthy and diseased). To the best of our knowledge, comparison of the biological variation of 2 hs cardiac troponin assays in 2 populations known to have widely different baseline hs cardiac troponin concentrations and cardiovascular morbidities has not been performed previously. Despite the differing cohort characteristics, remarkably similar hs-cTnT or hs-cTnI CVi values were found in the 2 groups. It is therefore likely that similar CVi values can also be expected for patients with baseline hs cardiac troponin values that lie between these 2 diverging examples.

The 90-min CVi values seen in our study are lower than those reported previously; that is, 1- to 4-h hs-cTnT CVi values that ranged from 6% to 58% and hs-cTnI CVi values that ranged from 14% to 24% (16–19, 21–23). A recent study measured CVi for hs-cTnT and hs-cTnI (Abbott Diagnostics) at 4-h intervals (17); those values are comparable to the weekly values found in the current study. Different handling of nonmeasurable results or analytical outliers, or the use of CVa values in the calculations that were obtained outside the study situation, may lead to discrepancies. In the current study, CVa was determined from duplicate hs cardiac troponin measurements performed in a single run. This method gives the lowest possible CVa value and was chosen to minimize the interference of CVa in the calculations of CVi and CVb (38). The same CVa was used for the calculation of the RCV, and it must be emphasized that each laboratory should use its own CVa value—preferably the one that relates to the time interval that they are investigating (e.g., week-to-week variations) and is applicable to the hs cardiac troponin concentration in the population studied—when calculating the RCV. Another reason for the low CVi values in the current study is that the adjustment of the data to establish a steady state provides lower values compared to the noncorrected data used in other studies. However, the 90-min asymmetric RCV value (i.e., including CVa and CVi, and adding the β value corresponding to the systematic decline) was similar to the RCV values found in some studies (17, 21, 23) and lower than those found in others (16, 18, 19, 22).

An important novel finding of the current study was the significant declines in hs-cTnT (both populations) and hs-cTnl (HD patients) concentrations seen between 08:30 and 14:30. A definite trend was not found in hs-cTnl in healthy individuals, possibly because CVa in this group was much higher than the biological variation. Diurnal variation is indeed a common finding for many biological constituents (39, 40), and we assume that the declining values seen in the current study represent a part (i.e., 6 h) of the diurnal variation of hs-cTn. In principle, the calculated RCV found in our study is valid only between 08:30 and 14:30, because the magnitude and direction of diurnal variation assumed during the 24-h cycle is unknown. However, the difference between the RCV value and the asymmetric RCV value was moderate, implying that the clinical relevance of defining the 24-h asymmetric RCV profile in a future study may be limited.

A previous study using the fourth-generation cTnT assay explored the weekly variations of cTnT in HD patients (25) and found that 95% of all of the variance from the patients’ median values was 63%. However, the statistical methods and handling of the nonmeasurable results (35%) was poorly described. The weekly hs-cTnT CVi values found in the current study are comparable to the long-term CVi shown in stable coronary disease and chronic heart failure (i.e., 7%–11% for the hs-cTnT assay) (17, 26), but smaller than those demonstrated by others (i.e., 30%–94% for the hs-cTnT assay and 24%–80% for the hs-cTnl assay) (16, 19, 22). In the current study, all patients who experienced definite clinical events exhibited a change in the hs-cTnT concentrations beyond the calculated RCV value, indicating that the RCV values may be useful for monitoring clinical changes. Patient 8 exhibited declining hs-cTnl values and increasing hs-cTnT concentrations after the event, which may be explained by the different half-lives of the 2 proteins.

Conclusion

Clinically stable HD patients and healthy individuals exhibited similar CVi values in the different hs cardiac troponin assays, and differences in RCV values and II between the cohorts and assays can be explained mainly by differences in CVa. The 90-min hs-cTnT RCV in stable healthy individuals and CKD patients treated with HD were lower than the suggested diagnostic δ values of 50% and 20%, respectively (15), while RCV for the hs-cTnl assay overlapped with the suggested δ criterion, thus increasing the risk of false-positive diagnoses if these δ values are used.
Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

References


