APPLICATION OF HIGH SENSITIVITY TROPONIN IN SUSPECTED MYOCARDIAL INFARCTION

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BACK GROUND

- Data regarding high-sensitivity troponin concentrations in patients presenting to the emergency department with symptoms suggestive of myocardial infarction may be useful in determining the probability of myocardial infarction and subsequent 30-day outcomes.

METHODS

In 15 international cohorts of patients presenting to the emergency department with symptoms suggestive of myocardial infarction determined the concentrations of highsensitivity troponin I or high-sensitivity troponin T at presentation and after early or late serial sampling. The diagnostic and prognostic performance of multiple high-sensitivity troponin cutoff combinations was assessed with the use of a derivation–validation design.

METHODS

- Study Design: The Calculation of Myocardial Infarction Risk Probabilities to Manage Patients with Suspicion of Myocardial Infarction (COMPASS-MI) project used individual patient–level data from 15 international cohorts of patients who had suspected myocardial infarction in order to calculate risk probabilities for myocardial infarction with the use of high-sensitivity troponin measurements made at the time of emergency department presentation and, in conjunction with data from 11 population-based cohorts, to estimate long-term risk.

Study Population with Suspected Acute Myocardial Infarction .

- For this population, individual patient– level data from 15 studies prospectively enrolling 23,327 patients who presented to the emergency department with suspected myocardial infarction were combined into one data set,Patients 18 years of age or older were recruited in 13 countries in three geographic regions (Europe, North America, and Australasia).

- Patients with ST-segment elevation myocardial infarction were excluded from this study. Data from 9604 patients from five cohorts available at the time of the first analyses (APACE [Advantageous Predictors of Acute Coronary Syndrome Evaluation], BACC [Biomarkers in Acute Cardiac Care] I, High-STEACS [High-Sensitive Troponin in the Evaluation of Acute Coronary Syndrome], ROMI I [Optimum Troponin Cutoffs for ACS in the ED], and stenoCardia[Study for Evaluation of Newly Onset Chest Pain and Rapid Diagnosis of Myocardial Necrosis]) were used as the derivation data set, and the results were validated in the remaining 13,047 patients.

RESULTS

- Among 22,651 patients (9604 in the derivation data set and 13,047 in the validation data set), the prevalence of myocardial infarction was 15.3%. Lower high-sensitivity troponin concentrations at presentation and smaller absolute changes during serial sampling were associated with a lower likelihood of myocardial infarction and a lower short-term risk of cardiovascular events.

- Overall, 22,651 patients with suspected myocardial infarction in the acute study population were enrolled for the present analysis, after the exclusion of 676 patients with ST-segment elevation myocardial infarction . Evaluation of diagnostic performance was performed in 9604 patientsand validated in 13,047 patients.

The final diagnosis of myocardial infarction was adjudicated in 3455 of 22,651 patients (15.3%). Results of early serial sampling (>45 to 120 minutes) of high-sensitivity troponin I and high-sensitivity troponin T were available in 7833 and 9562 patients, respectively; and the results of late serial sampling (>120 to 210 minutes) in 9905 and 10,950 patients, respectively .

- Patients at low risk for myocardial infarction were likely to have very low concentrations of high-sensitivity troponin I or high-sensitivity troponin T at presentation and small absolute changes on serial sampling, resulting in a high negative predictive value for myocardial infarction ,Patients at high risk for myocardial infarction were likely to have higher concentrations of high-sensitivity troponin I or high-sensitivity troponin T at presentation to the emergency department or a larger absolute change during serial sampling than those at low risk .

CONCLUSIONS

- In addition to the electrocardiogram and clinical symptoms, the serial measurement of cardiac troponin is key in ruling out or diagnosing myocardial infarction,With the development of high-sensitivity troponin assays, rapid triage algorithms have been created to apply these tests safely in clinical practice.

- However, some challenges remain. First, with high-sensitivity troponin tests it is difficult to differentiate between patients who present to the emergency department with acute myocardial infarction and those who have other causes of myocardial injury.

- Second, although it is generally accepted that the initial blood sample for troponin measurement should be obtained immediately on presentation, the appropriate timing of obtaining the second blood sample is a matter of debate, and recommendations vary between 1 hour and 6 hours.

- Third, the long-term prognosis in patients who do not have myocardial infarction but who have persistently elevated high-sensitivity troponin concentrations remains unclear. Comparing outcomes in such patients with those in the general population may increase the understanding of individual risk.

We therefore sought to develop a tool integrating high-sensitivity troponin concentration at emergency department presentation, the dynamic change in concentration during serial sampling, and the time between the obtaining of samples in order to provide a flexible method to determine the probability of myocardial infarction and 30-day outcomes.

- Concentrations of high-sensitivity troponin I and high-sensitivity troponin T were measured as part of routine clinical care or in batches of samples that had been frozen at −80°C. Detailed times at which blood samples were obtained were documented, and the time frame between the first sample at emergency department presentation and serial resampling was grouped into two categories: early resampling (>45 to 120 minutes) and late resampling (>120 to 210 minutes).

Evaluation of Diagnostic Performance in the Acute Study Population

- To identify the patients at either low or high risk for myocardial infarction, we selected a range of cutoff concentrations of high-sensitivity troponin at presentation (C1, measured in nanograms per liter) and a range of absolute changes (increase or decrease) in the concentrations of highsensitivity troponin on serial sampling (C2, measured in nanograms per liter). The selected cutoff concentrations were chosen to represent a wide range of diagnostic performances.

FOLLOWUP AND CLINICAL END POINTS

- In the acute study population data set, all the patients were followed for at least 1 month to assess death from any cause (except in the HighSTEACS study, in which death from cardiac causes only was recorded) or myocardial infarction. In the APACE, BACC, Heidelberg, ProsPECTUS (Prospektive Kohortenstudie zur Evaluation der Diagnostik und der therapeutischen Strategien in der Chest Pain Unit), and stenoCardia studies, patients were followed for 2 years.

- The shortterm prognostic end point was the composite of subsequent myocardial infarction (excluding the index event) or death from any cause at 30 days. The long-term prognostic end point was the composite of subsequent myocardial infarction (excluding the index event) or death from any cause assessed at 1 year and 2 years

GENERAL POPULATION STUDIES

- For the general population studies, the concentration of high-sensitivity troponin I was centrally measured in batched, stored samples by the Abbott Architect assay. Owing to the low percentage of young and healthy persons with detectable concentrations, high-sensitivity troponin T was not measured in persons in the general population.

Table 2. Baseline Characteristics of All Persons from the General Population and the Matched Patients without Acute Myocardial Infarction (MI) Included in the Prognostic Evaluation.*

Characteristic	Overall General Population (N=71,150)	Matched Patients without Acute MI (N=7682)	Matched Persons from General Population (N=7682)	Standardized Mean Difference
Median age (IQR) — yr	50.9 (41.6–59.7)	61.0 (50.0–72.0)	61.0 (50.0–71.2)	0.0
Male sex — no. (%)	35,048 (49.3)	4989 (64.9)	4989 (64.9)	0.0
Hypertension — no. (%)	29,378 (41.3)	5001 (65.1)	5001 (65.1)	0.0
Dyslipidemia — no. (%)	49,059 (69.0)	3643 (47.4)	3643 (47.4)	0.0
Median body-mass index (IQR)	26.1 (23.5–29.1)	26.6 (24.1–30.0)	27.1 (24.4–30.1)	0.0
Diabetes — no. (%)	3,028 (4.3)	1113 (14.5)	1113 (14.5)	0.0
Daily smoking — no. (%)	19,506 (27.4)	1765 (23.0)	1765 (23.0)	0.0
History of MI or stroke — no./total no. (%)	2,357 (3.3)	1630/7647 (21.3)	368/7682 (4.8)	0.5
Median high-sensitivity troponin I (IQR) — ng/liter†	2.5 (1.5–4.2)	4.0 (2.1–9.0)	3.2 (2.0–5.3)	0.1
Median high-sensitivity troponin T (IQR) — ng/liter‡	NA	7.0 (4.0–14.4)	NA	—

* Details about the definition of the baseline characteristics from the general population are provided in Supplementary Appendix 1. NA denotes not available.
† Data on the high-sensitivity troponin I concentrations were available for 6434 matched patients.
‡ Data on the high-sensitivity troponin T concentrations were available for 6468 matched patients. Owing to the low rate of detectable concentrations in young and healthy persons, high-sensitivity troponin T was not measured in the general population.

STATISTICAL ANALYSIS

- The characteristics of the patients were described according to quartiles for continuous variables and according to absolute and relative frequencies for binary variables. For the evaluation of diagnostic performance, the negative predictive value, sensitivity, positive predictive value, and specificity were calculated for multiple combinations of initial troponin concentrations and serial changes in troponin concentrations (C1 and C2, as described above).

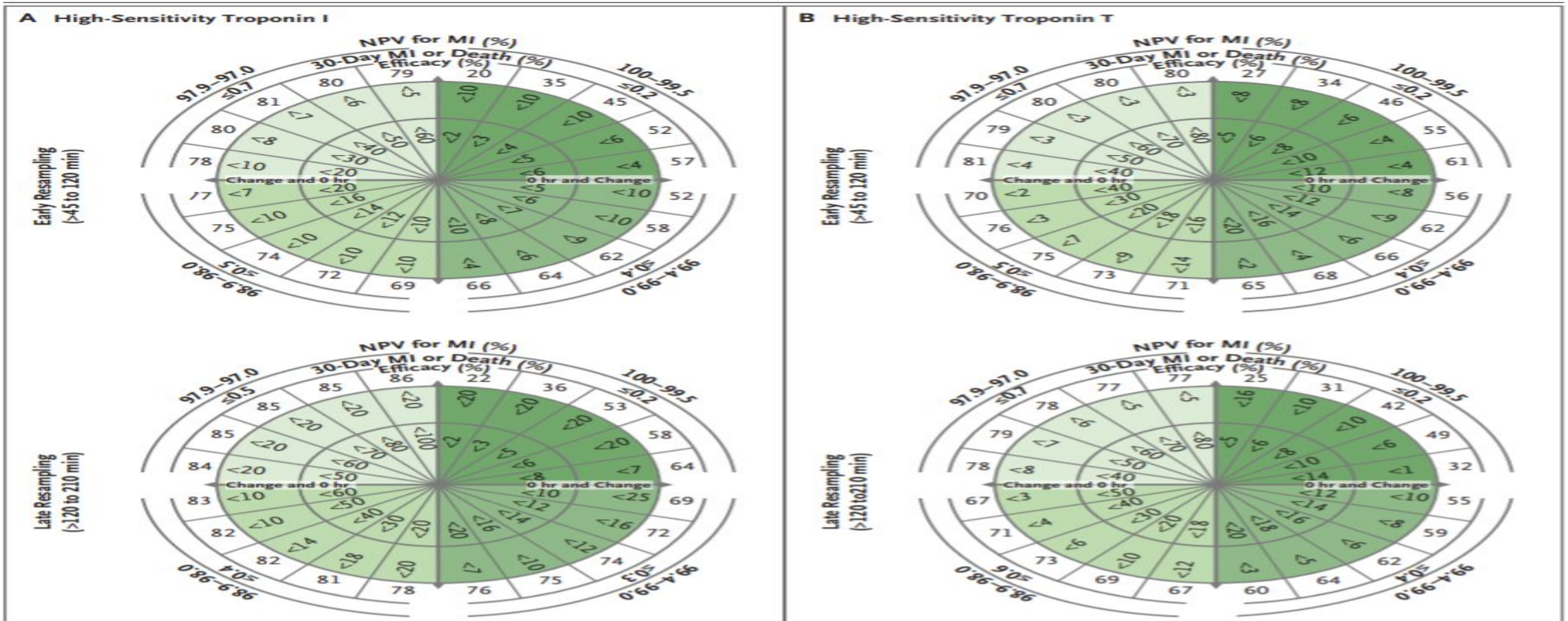

Figure 1. Risk-Assessment Tool for Defining Low Risk of Myocardial Infarction (MI) on the Basis of High-Sensitivity Troponin Cutoff Concentrations.

Panel A shows data during early resampling (top) and late resampling (bottom) of the high-sensitivity troponin I concentration, and Panel B during early resampling (top) and late resampling (bottom) of the high-sensitivity troponin T concentration. To use these diagrams, select the figure panel corresponding to the high-sensitivity troponin assay used (troponin I or troponin T) and determine whether the second blood sample for troponin measurement was obtained early after the first sample (>45 to 120 minutes) or late (>120 to 210 minutes). Then select the cutoff concentration for the initial high-sensitivity troponin measurement (time 0; values in nanograms per liter) from the innermost circle of the panel, and the cutoff concentration for the change (increase or decrease; values in nanograms per liter) in the high-sensitivity troponin concentration on resampling from the second circle. The third circle shows the efficacy of this troponin combination (the proportion of patients who will be designated to have low risk if both values are below the cutoff). The fourth circle shows the 30-day risk of MI or death (excluding the index event) with this troponin combination. The outermost circle shows the negative predictive value (NPV) of this troponin combination for MI. All calculations were based on the overall data set including patients with suspected acute MI and were not adjusted for multiple testing. For simplicity, the values shown in this figure are presented without 95% confidence intervals. Full lists of data according to each increment of high-sensitivity troponin I or high-sensitivity troponin T together with 95% confidence intervals are provided in Supplementary Appendix 2. An interactive risk calculator is provided in Supplementary Appendix 3 and at www.compass-mi.com.

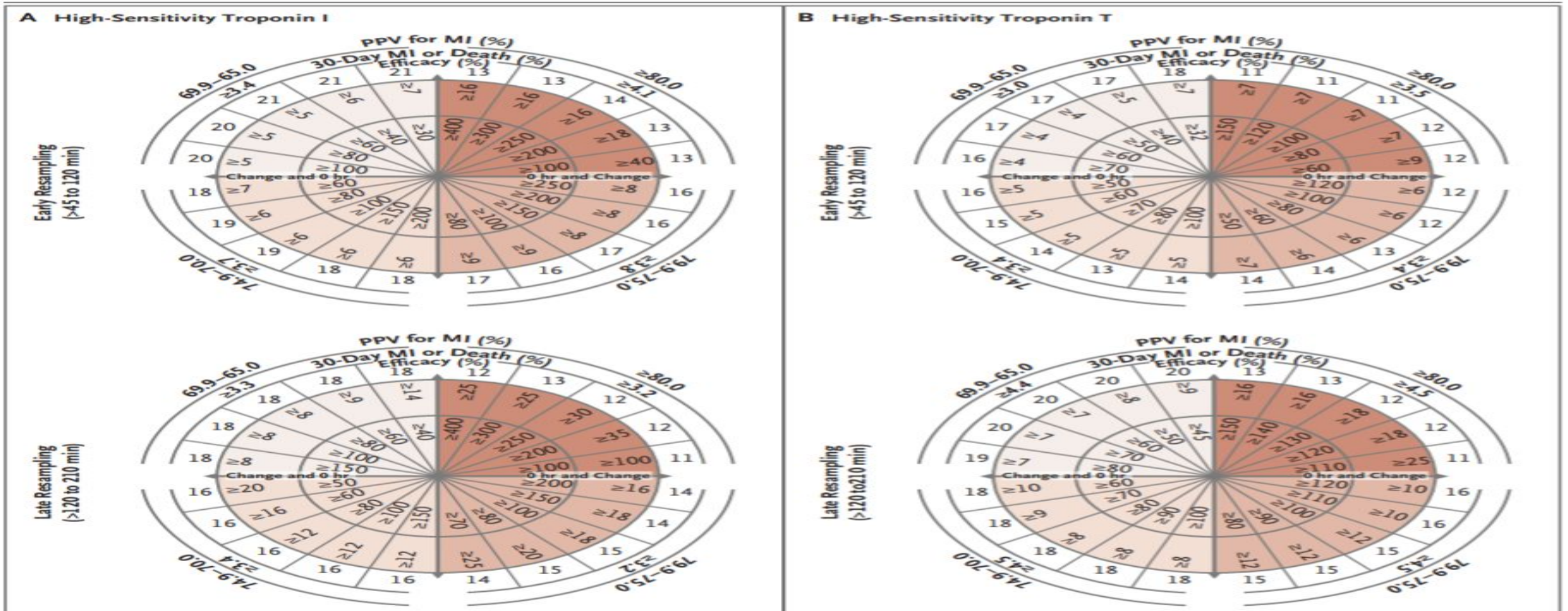

Figure 2. Risk-Assessment Tool for Defining High Risk of MI on the Basis of High-Sensitivity Troponin Cutoff Concentrations.

Panel A shows the data during early resampling (top) and late resampling (bottom) of the high-sensitivity troponin I concentration, and Panel B during early resampling (top) and late resampling (bottom) of the high-sensitivity troponin T concentration. To use these diagrams, select the figure panel corresponding to the high-sensitivity troponin assay used (troponin I or troponin T) and determine whether the second blood sample for troponin measurement was obtained early after the first sample (>45 to 120 minutes) or late (>120 to 210 minutes). Then select the cutoff concentration for the initial high-sensitivity troponin measurement (time 0; values in nanograms per liter) from the innermost circle of the figure panel, and the cutoff concentration for the change (increase or decrease; values in nanograms per liter) in high-sensitivity troponin on resampling from the second circle. The third circle shows the efficacy of this troponin combination (the proportion of patients who will be designated to have high risk if either value is greater than or equal to the cutoff). The fourth circle shows the 30-day risk of MI or death (excluding the index event) with this troponin combination. The outermost circle shows the positive predictive value (PPV) of this troponin combination for myocardial infarction. All calculations were based on the overall data set including patients with suspected MI and were not adjusted for multiple testing. For simplicity, the values shown in this figure are presented without 95% confidence intervals. Full lists of data according to each increment of high-sensitivity troponin I or high-sensitivity troponin T together with 95% confidence intervals are provided in Supplementary Appendix 2. An interactive risk calculator is provided in Supplementary Appendix 3 and at www.compass-mi.com.

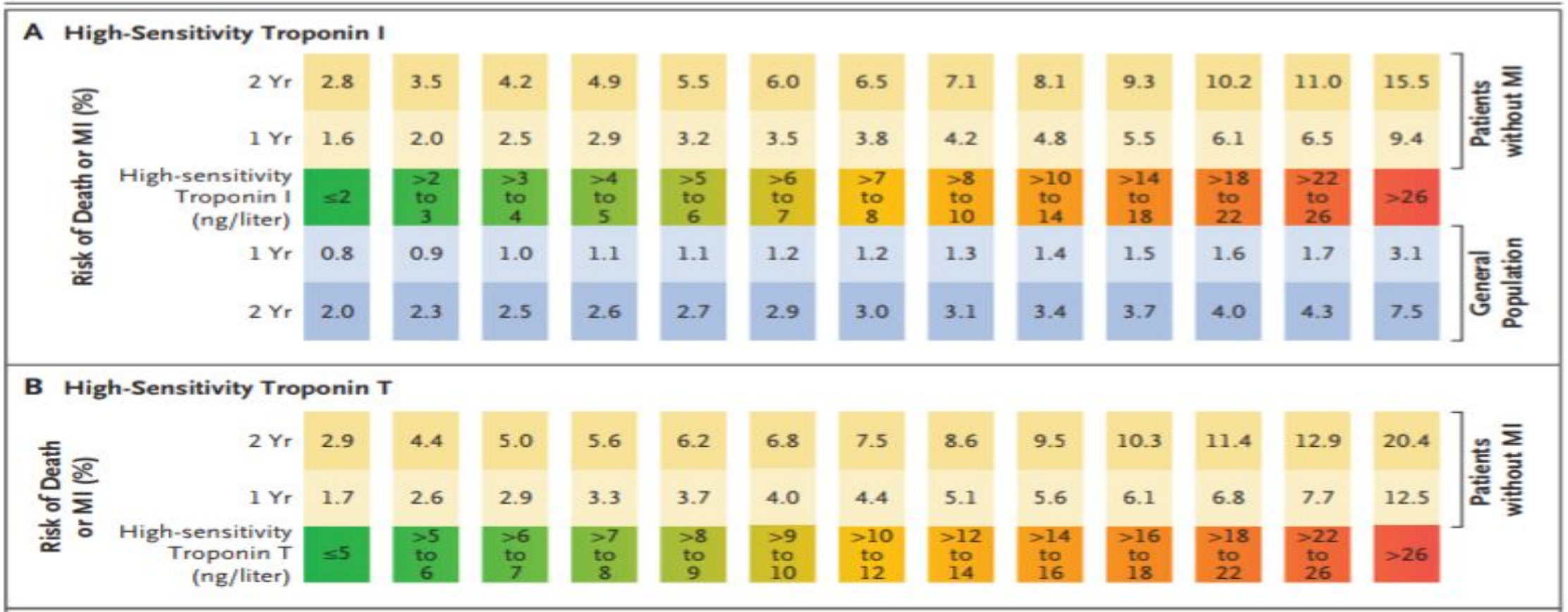

Figure 3. Long-Term Risk–Prediction Charts.

Shown is the estimated risk of death or MI within 1 or 2 years among patients who presented to the emergency department with symptoms suggestive of acute MI in whom MI was ruled out. Data are shown for increasing concentrations (measured in nanograms per liter) of high-sensitivity troponin I (Panel A) and high-sensitivity troponin T (Panel B). In Panel B, comparison is made between patients in the acute study population and persons from the general population; patients were matched for age, sex, presence or absence of hypertension, presence or absence of diabetes, smoking status, and presence or absence of dyslipidemia. Owing to the low rate of detectable concentrations in young and healthy persons, high-sensitivity troponin T was not measured in the general population. No adjustment for multiple testing was performed. For simplicity, these risk estimates are presented without 95% confidence intervals. Full lists of data with 95% confidence intervals are provided in Table S7 in Supplementary Appendix 1.

MY VIEWS

- After reading this journal I came to know there was a strong association between high sensitivity troponin and acute myocardial infarction.
- Patients with acute MI has 3 times increased risk of death as compared to general population those who has troponin concentration >10 -14 ng/lit.

THANK YOU