individual variation in warfarin dosage. Prospective studies that incorporate both gene testing and a variety of ethnic, clinical, pharmacological, and environmental variables, along with age, sex, and body weight, will be required to demonstrate the real safety, cost-effectiveness, and feasibility of individualized dosing regimens according to the statistical models for warfarin dose calculation.

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Evaluation of Analytical Performance of the Siemens ADVIA Tnl Ultra Immunoassay

To the Editor:
In light of recommendations on the quality (1) and clinical use (2) of troponin assays, we evaluated the analytical performance of the ADVIA Centaur and ADVIA CP® platforms (Tnl-Ultra, Siemens Medical Solutions Diagnostics SrL) for measurement of cardiac troponin I (cTnl). The chemiluminescent Tnl-Ultra method uses 2 monoclonal capture antibodies directed to epitopes at amino acids 41–49 and 87–91 and a tracer polyclonal goat antibody labeled with acridinium ester, directed against amino acids 27–40 (1, 3, 4).

Two clinical laboratories participated in the study: the CNR Institute of Physiology in Pisa and the San Barto
tolo Hospital in Vicenza.

The limit of detection (limit of the blank) for the Tnl-Ultra method was calculated as the concentration corresponding to a signal of 3 SD above the mean of 60 replicates (obtained in 4 different runs and pooled together) for the calibrator in which cTnl was absent; a mean cTnl concentration of 0.006 µg/L was found. The total im
precision (CV%) of the Tnl-Ultra method, assessed according to the NCCLS EP-5-A protocol over 20 consecutive working days, was 11.6%, 5.6%, and 4.4% for 3 plasma samples with cTnl concentrations of 0.05, 0.25, and 2.68 µg/L, respectively. From plots of CV vs log-transformed values of cTnl concentration in the range 0.006–0.20 µg/L, the cTnl concentrations that corresponded to 10% CV were 0.064 µg/L for ADVIA Cen
taur CP® and 0.07 µg/L for ADVIA Centaur.

Blood samples, collected in polypropylene tubes with lithium heparin, were used in the study, according to the routine protocol adopted by both clinical laboratories. The 2 laboratories enrolled a white population including 418 apparently healthy adult individuals (204 men and 214 women) with a mean (SD) age of 50.7 (16.6) years, range 16–89 years; the mean (SD) age in women was 52.6 (17.5) years and in men 48.7 (15.5) years. The presence of cardiac or other acute or chronic diseases was excluded by clinical examination and laboratory tests. Informed consent was obtained by all individuals and patients before testing, and the study protocol was approved by the local ethics committee. The measured cTnl values approximated a log-normal distribution with a calculated 99th percentile of 0.087 µg/L; therefore, the ratio of 10% CV concentration to 99th percentile limit for the Tnl-Ultra method was 0.067: 0.087 = 0.77 (1). In 82 samples, including 81 females and only 1 male, we found values <0.004 µg/L (i.e., undetectable cTnl concentration), and so an arbitrary concentration of 0.001 µg/L was attributed to these samples. A highly significant correlation was found between cTnl values and age (R = 0.268, P <0.0001 by Spearman rank correlation coefficient test). Moreover, a significant difference was found between the cTnl values found in men and women, respectively [mean (SD) 0.015 (0.018) µg/L, median 0.012 µg/L, range 0–0.196 µg/L, n = 204 for men; 0.009 (0.014) µg/L, 0.008 µg/L, 0–0.130 µg/L, n = 214 for women; P <0.0001 by Mann–Whitney U-test]. We found that both sex (as a dummy independent variable with F = 1 and M = 2) and age (as a continuous independent variable) independently contributed to the regression with cTnl (as a dependent variable after log transformation of original values) by using a stepwise multiple regression analysis (log cTnl = −3.164 + 0.456 sex + 0.007 age; P <0.0001, F-value = 71.962, R = 0.508, n = 416).

A close linear relationship was found between cTnl values measured by ADVIA Tnl-Ultra with the Centaur CP® platform and the Access AccuTnl® method on the Uni
Cell® DxI 800 platform (Beckman Coulter) in 318 plasma samples of 155 apparently healthy individuals and 163 cardiac patients (ADVIA = 0.016 + 1.272 Access; R = 0.936). The Tnl-Ultra method showed higher cTnl values than the Access AccuTnl
method (on average by 22.0%; \( P < 0.0001 \) by Wilcoxon signed-rank test) and based on the 99th percentile values for each assay, 9 discordances were found between assays for values within the reference interval vs increased values.

The ADVIA TnI-Ultra method showed no interference from dilutions with plasma samples that contained high concentration of triglycerides (6.6 g/L, final dilution 1:128; \( y = -0.044 + 0.14x, n = 8, R = 0.99 \)) or hemoglobin (1.47 g/L, final dilution 1:4996; \( y = 0.04 + 0.060x, n = 13, R = 0.99 \)). No apparent positive interference was seen in 58 patients with symptomatic rheumatoid arthritis [10 men and 48 women, mean (SD) age 60.8 (10.2) years] with a factor of 189.6 kIU/L (range 40–1280 kIU/L), because the mean (SD) cTnI concentration was not increased 0.017 (0.023) μg/L.

The present study indicates that the ADVIA TnI-Ultra method meets the quality specifications recommended by NACB and IFCC Committee for the Standardization of Cardiac Damage (5).

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