vidual 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 TnI 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 (TnI-Ultra, Siemens Medical Solutions Diagnostics SrL) for measurement of cardiac troponin I (cTnI). The chemiluminescent TnI-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 Bortolo Hospital in Vicenza.

The limit of detection (limit of the blank) for the TnI-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 cTnI was absent; a mean cTnI concentration of 0.006 μg/L was found. The total imprecision (CV%) of the TnI-Ultra method, assessed according to the NCCLS EP5-A protocol over 20 consecutive working days, was 11.6%, 5.6%, and 4.4% for 3 plasma samples with cTnI concentrations of 0.05, 0.25, and 2.68 μg/L, respectively. From plots of CV vs log-transformed values of cTnI concentration in the range 0.006–0.20 μg/L, the cTnI concentrations that corresponded to 10% CV were 0.064 μg/L for ADVIA Centaur 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 concent was obtained by all individuals and patients before testing, and the study protocol was approved by the local ethics committee. The measured cTnI 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 TnI-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 cTnI concentration), and so an arbitrary concentration of 0.001 μg/L was attributed to these samples. A highly significant correlation was found between cTnI values and age ($R = 0.268$, $P < 0.0001$ by Spearman rank correlation coefficient test). Moreover, a significant difference was found between the cTnI 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 cTnI (as a dependent variable after log transformation of original values) by using a stepwise multiple regression analysis (log cTnI = −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 cTnI values measured by ADVIA TnI-Ultra with the Centaur CP® platform and the Access AccuTnI™ method on the UniCell® 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 TnI-Ultra method showed higher cTnI values than the Access AccuTnI

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 mean concentration of rheumatoid 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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Midtrimester Amniotic Fluid Adiponectin in Normal Pregnancy

To the Editor:

Adiponectin is an adipose tissue–derived protein with important metabolic effects and a strong correlation with insulin sensitivity. In pregnancy there is a progressive increase of insulin resistance, whereas plasma adiponectin concentrations decrease in the 2nd half of gestation *(1)*. In contrast, cord plasma adiponectin concentrations increase throughout gestation *(2)*. Nothing is known about the concentration, origin, or role of amniotic fluid adiponectin, particularly in relation to amniotic insulin. Therefore we evaluated adiponectin and insulin concentrations in the midtrimester amniotic fluid of women with normal pregnancies.

Beginning January 1, 2006, we selected the first 50 pregnant women who underwent a midtrimester amniocentesis for prenatal diagnosis (15–18 weeks gestation) and were found to have a normal pregnancy, defined as an uncomplicated pregnancy with full-term delivery of an infant of adequate size for gestational age. The study was approved by the institutional review board, and all women gave written informed consent.

Amniotic fluid samples were obtained by transabdominal amniocentesis and collected in 15 mL dry tubes. All samples were free of blood contamination, as estimated by microscopic inspection. The samples were immediately centrifuged for 10 min at 3000*g* and stored at –70 °C. Plasma EDTA samples were centrifuged for 15 min at 1000*g* within 30 min of collection and stored at –70 °C. Plasma samples required 200-fold dilution before assay. The adiponectin concentration was measured by immunoenzymatic assay (R&D Systems). The intra- and interassay imprecision (CVs) for adiponectin at a concentration of 15.0 μg/L were 3.5% and 5.5%, respectively. The intra- and interassay imprecision values (CVs) for insulin at a concentration of 4.0 mIU/L were 3.3% and 5.6%, respectively.

Amniotic and plasma adiponectin and amniotic insulin concentrations are presented as the median and the 25th–75th percentile range; all other variables are presented as the mean (SD). The Mann–Whitney *U*-test was used to compare continuous variables between the 2 groups. Univariate correlations between amniotic fluid adiponectin and all the other variables were assessed using the Spearman test. The statistical analysis was performed using SPSS 13.0 (SPSS Inc.). All tests were 2-sided; a P value <0.05 was considered statistically significant.

The clinical characteristics of pregnant women are reported in Table 1. Median adiponectin amniotic fluid values were 26.8 (13.9–37.3) μg/L, but when we dichotomized for sex, there was a significant difference ($P = 0.01$) between female 34.8 (18.2–48.7) μg/L and male fetuses 18.2 (13.4–26.8) μg/L. Univariate analysis