


The Academic Life of a Noninvasive Test

We are disappointed that Lachterman et al did not find the simple ST/HR index to improve the discriminating power of the exercise electrocardiogram. While we welcome criticism of our work, we believe that our method is valid and that the differences between our studies can be explained by the cumulative effects on test performance of their selection of rather unusual normal subjects and one or more methodologic problems in their analysis of the data. The issues of methodologic detail transcend the "academic life cycle of a noninvasive test," and we can actually duplicate their seemingly negative findings by serial incorporation of these flaws into reanalysis of our original data.

We grant the well-recognized effect of population on test performance, but we disagree with the assertion that catheterized patients without demonstrable coronary disease comprise a clinically useful normal population for assessing test performance, particularly when 26% of these "normals" had a history of prior infarction and many had typical angina, and often abnormal exercise tests, leading to angiography. Such patients commonly have important myopathic disease and occasionally have small-vessel coronary disease. The lower test specificity that we reported in our catheterized patients without coronary obstruction is quite comparable with findings in the "normal" subjects from Long Beach. Had we used our similarly "normal" catheterized patients, instead of our referred clinical normals, as representative of subjects without coronary disease, the receiver operating characteristic (ROC) curve for the delta ST/HR index would have been shifted downward and rightward; at the specificity of 73% used for comparison of methods by Lachterman et al, test sensitivity for the heart rate–adjusted index falls from 97% to 81%, but remains considerably higher than the performance of standard criteria even under these unusual conditions.

A more important area of disagreement lies not in Bayesian polemic, but in a major error in the methodologic implementation of the heart rate–adjusted index used by Lachterman et al. By measuring ST depression at the J-point (rather than at 60 or 80 msec after the J-point), Lachterman et al inadvertently eliminate the discriminatory power that is present in the ST/HR index. We can further reanalyze our data to show how this seemingly minor methodologic problem (substitution of J-point depression for ST depression measured 60 msec after the J-point) seriously degrades test performance of the heart rate–adjusted index. By applying this different measurement to recalulation of the ST/HR index in our previously reported patients and in our catheterized "normal" subjects, the ROC curve shifts even farther downward and rightward and we reproduce from our original data the poor test performance reported by Lachterman et al. At the same matched specificity of 73%, sensitivity of the ST/HR index now falls to only 60% under these cumulative conditions, similar to the outcome of their study. The area under this final ROC curve is nearly identical with that reported for their patients (0.69 versus 0.66), but it is significantly less than the area under the curve using J + 60 msec measurements, even when catheterized "normals" comprise our reference population (0.84, p < 0.001). Accordingly, Lachterman et al do not show that the delta ST/HR index works poorly in their population, but rather that flawed application of this method does not work. This is a critical distinction.

Even with artifactually poor ROC curve performance of the ST/HR index that results from these methodologic factors, however, partition values along these otherwise similar curves differ substantially. We remain perplexed by the poor sensitivity found by Lachterman et al for our ST/HR index partition of 1.6 \( \mu V/\text{beat} \times \text{min}^{-1} \); Because positive standard tests have at least 100 \( \mu V \) of horizontal or downsloping ST depression, the simple rate-adjusted index should exceed 1.6 for these cases, except where the heart rate change exceeds 62 beats/min, at a very minimum, or considerably more when ST depression is greater. Given the frequent occurrence of substantial amounts of upsloping ST depression in patients whose tests are not defined as positive by standard criteria and the low peak heart rates shown by Lachterman et al in Table 3, we are surprised that an abnormal ST/HR index was not found in more patients with coronary disease. Differences in extent of disease and differences in exercise protocol might have some effect; while we have found CM5 to be the most sensitive lead for use with heart rate–adjusted methods and this was not used in their study. Although we note that any magnitude of upsloping ST depression was "assigned the value 0" by Lachterman et al for the construction of ROC curves for standard test criteria, we trust that these assigned values were not used instead of measured ST depression in retrospective calculation of the data. This would result in erroneous ST/HR index values of 0 for many patients and would reduce apparent sensitivity of the heart rate–adjusted method. Alternatively, if these findings were obtained from a data base that rounded small values of ST depression downward, much of the discriminatory power of the delta ST/HR index would also be lost.

It should also be recognized that the simple delta ST/HR index, which these data address, is not identical with the more complex but more accurate ST/HR slope and performance of the simple index cannot be extrapolated to performance of the linear regression method without detailed evaluation and careful attention to methodology. The methodologic problems outlined above also affect performance of the ST/HR index used by Lachterman et al for the identification of anatomically extensive disease, but in fact we have shown that it is the ST/HR slope, not the simple index, that works better than the standard test for this purpose. We make no claims of test perfection for heart rate–adjusted methods in exercise testing, and we must again emphasize that performance of these methods will vary with patient selection, technical implementation, and purpose, and cannot be extrapolated to untested populations without critical evaluation. These methods should be used in an appropriate clinical context to ask clinically useful questions. Applied in this way, these methods appear to improve the value of the exercise electrocardiogram.

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References

1. Lachterman B, Lehmann KG, Detrano R, Neutel J, Froelicher VF: Comparison of ST segment/heart rate index to standard ST

Reply

We share the disappointment of Kligfield and Okin with our results. The ST/HR index has an intuitive appeal, and our hope was to validate their findings.

Out of respect for their work, we would not want to let our singular analysis of one data set convince us of our conclusion. Subsequent doubling of the presented data set by adding patients, stratifying by β-blocker administration or prior myocardial infarction, all resulted in the same findings.

More recently, we have used computer analysis to facilitate measurement. This has enabled us to use ST 0 (J-junction) or ST 60 and to sum ST deviation in multiple leads. Once again, we come to the same conclusion: the ST/HR index does not offer improved diagnostic accuracy compared with standard criteria.

We would advise clinicians not to replace standard, proven criteria with a measurement whose performance has not been definitively demonstrated to be an improvement. In fact, we are concerned that the major problem with most comparison studies is that they have not applied careful visual ST analysis. We are convinced the best results with exercise testing are obtained by measuring the ST displacement at J-junction (ST 0) and considering the ST response to be abnormal only when there is 1 mm or more of depression below the isoelectric line and slope is horizontal or downward. Also, excluding a high percentage of tests as equivocal, as done by Kligfield and colleagues, does not seem appropriate.

We encourage the Cornell group and others to continue the exciting work of proposing new methods of analyzing the exercise test. We believe that such research will lead to improvement of this important testing modality. However, it is especially important to validate new techniques before their widespread application. This is particularly important as the exercise test is being increasingly used by noncardiologists.

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Reference

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