May 12, 1972

Dr. Naip Tuna Variety Club Heart Hospital University of Minnesota Minneapolis, Minnesota 55455

Dear Naip:

These are useful, thought-provoking and worthwhile data. However, the general pitch I find is unfortunate. It adds unnecessarily to controversy. It appears to support a test which is unphysiologic and non-standardized, when all you really mean is that at work loads comparable to the average obtained with a Master's test, the sensitivity-specificity is similar, in your biased hospital sample.

I would think you should downplay this "argument" and emphasize rather the relationship between ECG response and magnitude of disease. Few will question this demonstration. However, even here you unnecessarily leave many picayunish deficiencies in method and claims that people can shoot at (which I have flone in my running commentary enclosed). The enclosed in 11,000 men, is the only study which shows the independent predictive importance of the exercise test.

Regards,

Henry Blackburn, M.D.

HB/rs

Abstract:

Paragraph 1, second sentence: Meaning unclear. Was sensitivity different? Differences in what?

Paragraph 3: Extrapolation not justified.

Text:

Page 2, paragraph 1: Hardly "universal." Not used by more than 12% of internists in practice!

Paragraph 2: Many might disagree. There are several reasons for using a progressive test which have nothing to do with diagnostic yield. And it is not so much belief that Masters is an inadequate challenge but that it is a non-standard and non-physiologic challenge, as often excessove as inadequate.

Paragraph 3: You make an assumption of "all or none" here: "the minimum degree of coronary narrowing necessary to produce a positive test is not known."

A "positive test" is on a continuum, as is the coronary narrowing, as are the several components of cardiac work. Question this simplistic approach.

Paragraph 4, sentence 1: Question meaning and accuracy. What is based on epidemiological studies? What epidemiological studies. The interpretation has been based largely on insurance population studies, until most recently. What do you mean "normal?" Just say what the studies were.

Rather than criticizing the important work of all your predecessors, why not say, "the advent of coronary arteriography allows consideration of the individual peculiarities . . . etc."

Paragraph 5: b) "mose of response" meaning is unclear here.

Methods:

Are you entirely candid here about where you got the cases with normal arteriograms. You told me it was from sutgical referrals. Informed consent?

Page 4: No discussion of repeat variability of grading, or whether observer was blinded to other variables. I think this is now required for scientific publications. Also you present no evidence of the repeatability or validity of your weighting system. What single monitoring lead? How did it compare to V₅ recorded after? Did you correct for amplitude differences or use same criteria for different lead systems.

In one place you diagnose "abnormality" when upright T waves were inverted and in another you say positive test was a 1 mm. ST depression. Which?

Why did you not make the standard ST measurements and study the continuum of responses? That is: STJ. ST slope. Mid ST amplitude or QX/QT. Your attempt to force diagnosis into positive or negative results inevitably in

1) misclassifications on both sides

2) much loss of information.

Results:

Because resting blood pressure is an important determinant of ST response it would be useful to consider it in the analysis.

Paragraph 2: The difference in what? (resting ECG finding)

Question term "non-myocardial infarction changes."

Tables 2 and 3 potentially valuable but should be more detailed and should include objective criteria in legend. It should state that MI is by ECG criteria and quantify them.

Paragraph 3: You begin to generalize here. "half of patients [in this series] with severe CAD have MI " Qualify such statements!

Table 4: Same leads and criteria? Specify not the same patients.

Page 8: Sensitivity and specificity appear for the first time and are nowhere defined in Methods.

Table7: Begins to get awfully complicated for the (lazy) reader.

Discussion:

Paragraph 1: You are pressing this point too hard. The main use, for purposes of detection (excluding functional evaluation) is to detect "latent," not clinically manifest disease. I don't recall claims that it detected "early" disease, and believe you have inferred this.

What evidence have you that "it is necessary that the diagnosis is made early." In other words, be more circumspect.

I really don't go for the tone throughout of comparing Masters and Treadmill. It appears to support the idea of an outdated, non-standardized, unphysiological test. It would soften this if you, at least in discussion, spoke of work loads attained in the Masters vs. those in a graded test. You should emphasize, if true, that heart rates were similar for those having positive tests. You should emphasize that the Masters is unphysiologic, has no warm-up, and clearly exceeds (overshoots) the "critical" VO₂ in severe CAD (a good argument for a progressive test.

Page 11: The first sentence is disturbing in that is perpetuates your "all or noen" idea. Ischemia is not even "all or none" for the individual, and certainly not for a population.

Paragraph 2: Why disturbing? Name any other test for a chronic disease which is better than 75-80% sensitive?

The point here is that the progressive test does give a significant increased yield of "positive" tests in population studies. Only the correlation with CAD, and the prognosis is uncertain, and we have all admitted this.

Page 13: Have you adequately documented here the relationship to collaterals?

Paragraph 2: Musky. "May be similar," but usually aren't!

Summary:

Page 13: I don't see the necessary relationship between exercise tolerance and positive response.