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Predicting Extent of Coronary Disease: Fuzzy Cluster Analysis vs. Duke Treadmill Score

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We used fuzzy cluster analysis (FCA) to classify 166 positive stress tests as mildly, moderately, or severely abnormal. The method combines ST-segment change with 5 other stress test variables, and then computes a similarity measure to determine how closely each patient's stress test resembles a prototypical mildly, moderately, or severely abnormal stress test. All of the patients had coronary angiography within one month of their stress tests. A Duke treadmill score was also calculated for each patient's stress test: this score is derived from total exercise time, ST-segment change, and the presence or absence of angina. FCA showed better overall correlation with extent of coronary artery disease (CAD) ($r = 0.74$) than the treadmill score ($r = 0.47$). Tests classified as mild by FCA were more strongly associated with single vessel CAD or normal coronaries than treadmill scores of $\geq +5$ (low risk range). For patients with triple vessel CAD, only 44 % had a treadmill score of -11 or less (high risk range), while 76 % were classified as severely abnormal by FCA ($p < 0.01$). For left main CAD, 86 % had severely abnormal tests by FCA compared with 77 % having a score of -11 or less ($P = \text{NS}$). For the combined group with high-grade CAD (left main or triple vessel), 79 % of their tests were classified as severe by FCA compared to 55 % of these tests having a treadmill score of -11 or less ($p < 0.01$). Thus in patients with positive stress tests, FCA better predicts the extent of CAD, especially the presence of triple vessel disease, than the treadmill score. *J Clin Basic Cardiol 2000; 3: 39-41.*

Key words: Fuzzy cluster analysis, stress testing

Several studies have suggested that combining ST-segment changes with other stress test variables improves the predictive and prognostic value of stress testing [1]. One example of this is the Duke treadmill score (combines ST change with treadmill time and the presence/absence of exercise angina) which has been found to be useful in predicting outcomes in both inpatients and outpatients undergoing stress tests [2, 3]. We have shown that fuzzy cluster analysis (FCA), a method of combining six exercise test variables, was useful in predicting the extent of coronary disease in outpatients with positive stress tests [4]. Although the Duke score was developed more as a prognostic tool and the study population was different (only 18 % of the patients had ≥ 1 mm ST depression during exercise) we thought it would be of considerable interest to compare the two methods for predicting the extent of coronary artery disease (CAD), especially severe CAD, in stable outpatients with positive stress tests.

Methods

Study group

Standard Bruce protocol treadmill tests on 1,989 stable outpatients were reviewed. Patients were selected for entry into the study if they had ≥ 0.5 mm of exercise-induced ST-segment depression or 1 mm ST-segment elevation, and if they had undergone cardiac angiography within 4 weeks before or after the stress test. Patients were excluded if they (1) had coronary angioplasty or coronary bypass surgery at any time before the stress test; (2) had known valvular, hypertensive, or congenital heart disease; (3) had left bundle branch block; (4) had significant chronic lung disease or peripheral vascular disease; or (5) were taking β -blockers or digoxin at the time of the stress test. Patients were not excluded if they had ST-segment depression at rest, Q waves, T-wave inversions, or right bundle branch block on the resting electrocardiogram.

As was done in our previous publication [4], ≥ 0.5 mm of exercise-induced ST depression was used as the cutoff value because the fuzzy cluster analysis method (FCA) is designed

to incorporate into the analysis even very minor degrees of abnormality in any particular variable. Also, many patients with less than 1 mm of ST depression were included in the Duke study [2].

One hundred sixty-six patients (144 men and 22 women) aged 32 to 80 years meeting these criteria formed the database. Of these 63 % had typical angina, 22 % had atypical symptoms, 15 % were asymptomatic; 15 % had a previous myocardial infarction. On the day of the test 14 % had taken nitrates, 6 % had taken calcium blockers, and 4 % had taken aspirin. Angiograms showed that 22 patients had left main CAD, 45 had 3-vessel, 41 had 2-vessel, 44 had 1-vessel CAD, and 14 were normal. For purposes of 3-vessel classification, a lesion was considered significant if it was narrowed more than 50 % by visual estimation of the angiographer. Each patient was also assigned a coronary score according to the method of Friesinger [5].

Fuzzy cluster analysis and treadmill score

The details of fuzzy cluster analysis (FCA) are described in our previous report [4]. In brief, a fuzzy set is created for each of six stress test variables (ST-segment change, difference between resting systolic and peak exercise systolic blood pressure, total treadmill time, peak exercise heart rate as a percentage of 100 % predicted maximum for age, time to onset of angina, and duration of repolarization abnormalities) with the degree of membership ranging from 0.1 (mildest abnormality) to 1.0 (most severe abnormality). The degree of membership is thus a measure of the strength of association of any variable with its fuzzy set. Ranges for prototypical mildly, moderately, and severely abnormal tests are defined. For each patient's stress test, the membership functions for each of the six variables are incorporated into a weighted algorithm which generates a similarity measure to compute how closely the patient's test resembles a prototypical mildly, moderately, or severely abnormal stress test.

The Duke treadmill score is calculated as follows: duration of exercise in minutes - ($5 \times$ the maximal net ST-segment

deviation during or after exercise, in millimeters) – (4 x the treadmill angina index) [2]. The treadmill angina index has a value of 0 if the patient had no angina during exercise, 1 if the patient had nonlimiting angina, and 2 if angina was the reason for stopping exercise. A score of $\geq +5$ is considered low risk, a score of -10 to $+4$ is considered moderate risk, while a score of < -11 is considered high risk.

Statistical analysis

Data between groups were compared by analysis of variance and by means of an unpaired t test. Data within a single group were compared by means of a paired t test. All correlations were determined by calculation of Pearson’s coefficient of correlation. A chi-square analysis was used to assess potential differences in proportions among groups. All tests were 2-tailed, and a p value < 0.05 was considered statistically significant.

Results

Fuzzy cluster analysis (FCA) showed better overall correlation (Figure 1) with coronary score ($r = 0.74$) than did the treadmill score ($r = 0.47$). For tests classified as mild by FCA and tests in the $\geq +5$ treadmill score group, no patient had left main or triple vessel CAD. However, 40 % of patients in the $\geq +5$ group had double vessel CAD compared with 15 % in the mild FCA group ($p < 0.05$). For patients with normal coronaries, 13 of these 14 patients were classified as mild by FCA (93 %) while only 3 of the 14 (21 %) were in the low risk $\geq +5$ treadmill score group.

For patients with triple vessel CAD, 76 % of their tests were classified as severe by FCA, while only 44 % of these tests had a treadmill score of < -11 (high risk) ($p < 0.001$). Although patients with left main disease had 86 % of their

tests classified as severe by FCA compared to 77 % of these tests having a treadmill score of < -11 , this difference was not statistically significant. For the combined group with high-grade CAD (left main and triple vessel patients), 79 % of their tests were classified as severe by FCA compared to 55 % of these tests having a treadmill score of < -11 ($p < 0.01$).

Tests with a treadmill score of -10 to $+4$ and tests classified as moderate by FCA had a wide range of CAD (Table 1). Patients with normal coronaries comprised 11 % of the -10 to $+4$ treadmill score group, but only about 2 % of the moderate FCA group ($p < 0.05$).

Because the number of women in this study was small (22), it is very difficult to make a meaningful comparison between the two methods for women patients with positive stress tests. However, for these 22 patients FCA did show a better overall correlation with coronary score ($r = 0.77$) than did the treadmill score (0.69). Interestingly, all five of the women patients with triple vessel disease were classified as severe by FCA, while four of these five had a treadmill score of -10 to $+4$ (moderate risk range).

Table 1. Distribution of Coronary Artery Disease in the Fuzzy Cluster Analysis and Treadmill Score Groups

	Number of Coronary Arteries Narrowed 50 %				
	Normal (n=14)	1 (n=44)	2 (n=41)	3 (n=45)	4* (n=22)
Mild (FCA)	13	21	6	0	0
+5 (Duke)	3	3	4	0	0
Moderate (FCA)	1	20	19	11	3
-10 to +4 (Duke)	11	34	26	25	5
Severe (FCA)	0	3	16	34	19
-11 (Duke)	0	7	11	20	17

*Includes left main disease alone or together with any combination of 1-, 2-, or 3-vessel disease.

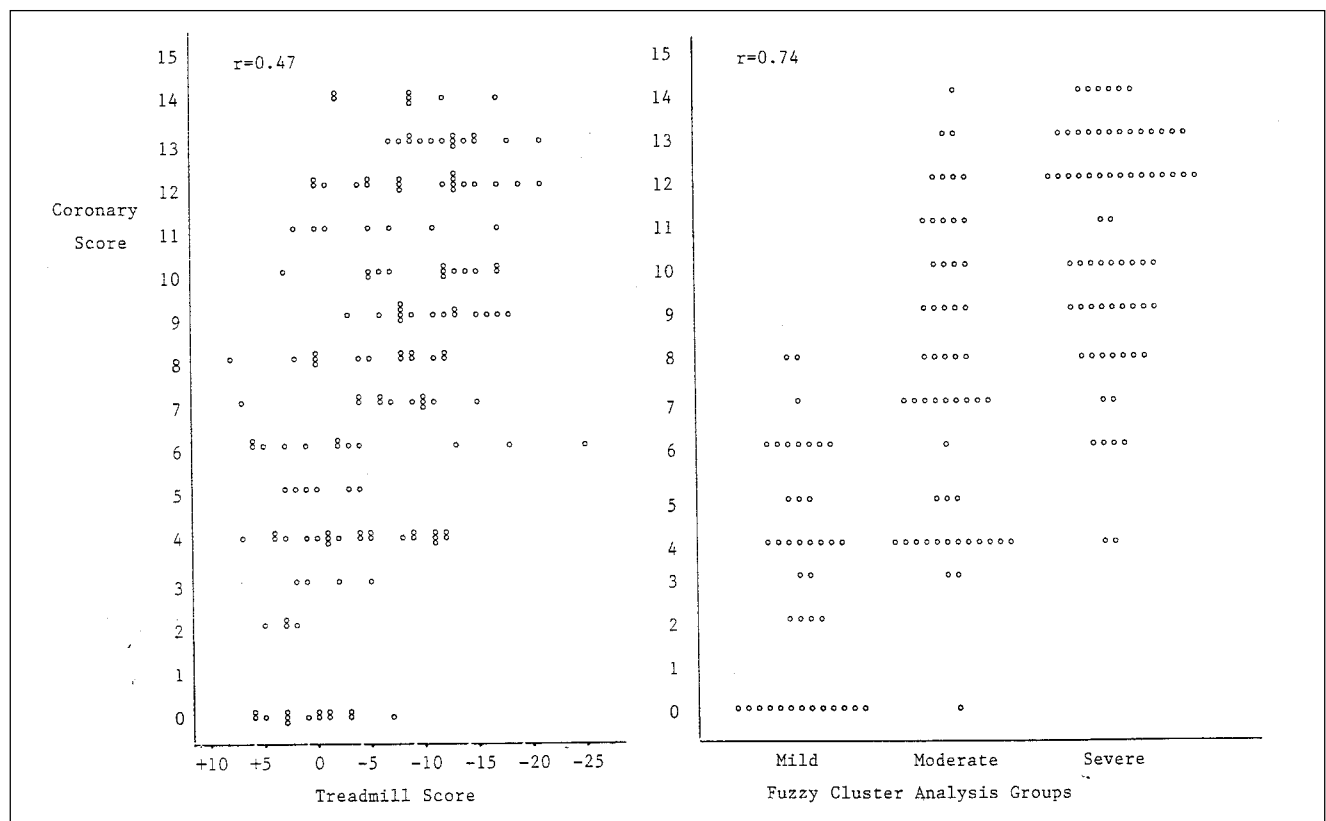


Figure 1. Coronary artery score plotted against treadmill score and fuzzy cluster analysis groups

Discussion

In this study, FCA better predicted overall extent of CAD than the treadmill score. Especially of interest is that tests classified as severe by FCA were strongly associated with high-grade (triple vessel or left main) CAD, whereas 45 % of patients with high-grade CAD did not have treadmill scores of < -11 (high risk range). Tests classified as mild by FCA were more strongly associated with single vessel CAD or normal coronaries than treadmill scores of $\geq +5$ (low risk range).

Several factors may help to explain these results. FCA uses six stress test variables while the treadmill score uses three. Several studies have shown that variables not included in the treadmill score (blood pressure response, duration of repolarization abnormalities, and peak heart rate) have some predictive value regarding the extent of CAD in patients with positive stress tests [6–9]. Moreover, FCA incorporates a graded degree of abnormality for each variable so that each variable, even if in the normal range, adds some useful information in determining how abnormal each stress test is. Also, for exercise-induced angina, FCA defines exactly how many minutes into the test the angina occurred, while the treadmill angina index uses a less well defined presence/absence of limiting/nonlimiting angina which may vary greatly between tests.

Again it should be noted that the treadmill score was developed as a prognostic tool rather than to predict extent of CAD. The population examined in the Duke study was different: of the 613 outpatients tested only 18 % had ≥ 1 mm of ST depression during the exercise test [2].

Despite these considerations, we believe that FCA can be very useful to clinicians in managing patients with positive stress tests. Patients with severely abnormal tests by FCA may be strongly considered for angiography, even if their treadmill score is in the moderate risk range. For mildly abnormal tests by FCA, the clinician may feel comfortable that continued medical therapy is appropriate. For moderately abnormal tests by FCA, stress echocardiography or nuclear stress testing may help to delineate which patients in this group have higher degrees of CAD.

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