Assessment of the prognostic utility of the FIT treadmill score in coronary artery disease patients undergoing cardiac rehabilitation

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Introduction
While there is overwhelming evidence that comprehensive cardiac rehabilitation (CR) and its multidisciplinary components of exercise, behavioral and lifestyle interventions are associated with a reduction in both cardiac mortality and total mortality,1 there is a lack of studies that focus on the risk stratification of these patients. Available risk stratification models such as that of the American Association of Cardiovascular and Pulmonary Rehabilitation and the American Heart Association are used to determine risks involved in the initiation and exercise participation in the program.2 Other studies focused on singular markers predictive of risk such as ejection fraction, exercise capacity and heart rate recovery.3 Studies regarding the effect of these prognostic markers on long term outcomes are scarce. Similar to the risk scoring systems for primary prevention it would be ideal to have a risk stratification system for patients who underwent CR to be able to quantify their residual risk after an event and after participation with the program.

Researchers from John Hopkins hospital developed the FIT treadmill score in 2015 and they were able to derive a formula using variables derived from a standard stress test that enables the clinician to predict a patient’s ten-year risk of all cause mortality.4 The score has not been validated for use in different patient populations. Potentially it can be a useful tool for determination of fitness, playing a role in illustrating the spectrum of risk in patients after undergoing CR.

Materials and Methods
This retrospective cohort study is based on patients with coronary artery disease (CAD) seen at the Philippine...
Heart Center who underwent and completed the outpatient Phase II comprehensive CR program. Relevant information was derived through review of department records from 2001 to 2006 along with our institutional electronic data (Medtrak). Using this data patients were prospectively followed up through clinic or telephone calls from the time of completion of the program for up to ten years for all cause mortality (both cardiovascular and non cardiovascular cause). Follow up was done by an individual who was blinded to the study objectives and outcomes.

**Fit treadmill score**

The FIT treadmill score is a risk score that was derived to predict a person’s ten-year risk of mortality. The formula uses the patient’s age, gender, fitness level (measured via metabolic equivalents (METs) achieved in an exercise test), and peak maximal heart rate (PMHR) reached during exercise and their estimated risk is calculated. The computation of the FIT treadmill score is as follows: PMHR + 12 x METs – 4 x age (+ 43 if female). Patient scores were calculated at the start of the program and on completion and the exit scores were used to determine risk stratification. In the original study from which the equation was logistically derived a score of greater than or equal to 100 means a patient has 2% risk of death in ten years. On the other end of the spectrum a score of -100 to -200 entails a risk of 38%. Our population was classified in quartiles of risk based on the FIT treadmill score after completion of Phase 2 CR and we reclassified risk assessment based on the FIT treadmill score with ≥100 as very low risk, a score of 1-100 is classified as low risk, ≤0 to -100 is intermediate risk and ≤-100 to -200 was classified as high risk.

**Statistical analysis**

Quantitative variables were summarized and presented as mean and standard deviation, while qualitative variables were tabulated and presented as frequency and percent distribution. Paired t test was used to determine a significant change in parameters pre- and post-cardiac rehab completion. A sensitivity and specificity analysis was done to determine the cut off value of the change in FIT score in predicting survival. Survival curves were estimated by the Kaplan-Meier method and hazard ratios (HRs) with 95% confidence intervals (CI), and P-values for the change in FIT score and FIT score category were analyzed using the multivariate Cox proportional hazard model. The discriminatory ability of the FIT treadmill score was determined with receiver operator characteristics (ROC) curve analysis. The level of significance was set at <0.05. Data analysis was done using STATA SE version 13 (Stata Corp LP, Texas)

**Results**

There were 459 patients in our original cohort. We excluded 134 (29.1%) patients because they were referred for CR for reasons other than CAD such as valvular and congenital heart disease. We then excluded 45 (13.8%) as they did not have all the variables needed to calculate the FIT score due to missing exercise stress test and data. Another 12 (4.2%) patients were excluded as we could not ascertain their 10 year outcome status by 2016. Thus, a total of 262 patients were eligible for analysis. The different baseline characteristics of the patients are listed in Table 1. The patients’ mean age were 55.8 ± 10.1, most were male and hypertensive (84% and 73% respectively) 231(88.2%) underwent coronary artery bypass graft, 21 (8%) had percutaneous coronary intervention and 17(6.5%) were referred for stable CAD. Fifty-six (21.3%) had concomitant heart failure. The mean ejection fraction was 58.2 ± 12.5. On entry patients’ mean METs achieved was 6.2 ± 2.0 prior to initiation of CR and 8.3 ± 2.2 after Phase 2 with a mean improvement of 2.1 ±1.2. The mean FIT score was -56.9 ± 59.5 on entry and -30.9 ±63.3 on exit, respectively, with a mean improvement of 26.1 ±16.2 points (Figure 1). Both changes in the two parameters were statistically significant (P<0.05)

With regards to risk category, on program entry there were 38 (14.5%) who had an entry FIT score of 1-100 (low risk), 164 (62.6%) had an entry FIT score in the 0 to -100 range.
-99 range (moderate risk) and 60 (22.9%) were classified as high risk. As expected, participation in CR resulted in improvement of risk stratification based on the FIT score, with 3 patients achieving very low risk status (exit FIT score >100), and a decrease in the number of patients belonging in the moderate risk (49.6%) and high risk (15.2%) compared to previous classification, respectively. There were 14 deaths (5%) in the moderate risk group and 38 (14.5%) in the high risk group.

Sensitivity and specificity analysis curves (Figure 2) show that improvement of the FIT score with a cutoff of 18.21 points has a 74.63% sensitivity (CI 68.03%-80.49%) and 67.31% specificity (CI 52.89%-79.67%) in predicting 10-year survival. Using this cutoff, Kaplan-Meier survival curves (mean follow up of 10.3 years) showed that patients whose FIT treadmill score did not improve had a 5-year survival rate of 77% and 10 year survival rate of around 59% respectively. In contrast those whose FIT treadmill score improved by at least 18.2 points had a 5 and 10-year survival rate of 94% and 90%, respectively (Figure 3). After adjustment for confounders (beta blocker use, left ventricular ejection fraction, smoking history, heart failure, gender and FIT category on entry) Cox proportional hazards analysis showed that improvement of the FIT score using the specified cut off value is associated with a 21% improvement in survival (Hazard Ratio 0.79, 95% CI 0.56-1.08, P≤ 0.05). Survival estimates were also analyzed using the FIT score category on exit (Figure 4). Patients belonging to the intermediate risk group (FIT score ≤0 to -100) after Phase 2 CR showed an 88% 10-year survival rate. In contrast, patients belonging to the high-risk group (FIT score ≤-100 to -200) had a 48% survival rate in 5 years, which progressively decreased to around <10% survival in 10 years. A high-risk FIT score category on exit (HR: 2.70, 95% CI 1.41-5.17) is also associated with increased mortality (P≤ 0.05).

The receiver operator characteristics curves are shown in Figure 5. The improvement in the FIT score with area under the curve (AUC) of 0.81 (CI 0.73-0.88) and the FIT score on exit (AUC: 0.91, CI: 0.89-0.94) both have excellent
It should be noted that in the FIT cohort patients with prognostic association is also depicted in the survival curves clearly statistically significant probability of survival. The inverse points increase in the FIT score was associated with a strong prognostic significance. Secondly, the degree of improvement in the FIT score is also strongly associated with improved survival. The determination of a cutoff point of 18.21 points based on the crossover point of sensitivity and specificity curves was done so that we have a quantitative measure of change in the FIT score that predicted prognosis. When using the cutoff of 18.21 points increase in the FIT score was associated with a statistically significant probability of survival. The inverse association is also depicted in the survival curves clearly showing a higher likelihood of mortality for patients who failed to reach this cutoff. Tabet et al noted that a lack of

predictive ability, with the Exit FIT score category having a better discriminatory ability than the improvement in FIT Score (P \leq 0.05).

**Discussion**

In our study, there was no mortality in the very low risk (>100) and low risk category (FIT score 1-100). In comparison for the original FIT study patients with a score greater than 100 had 98% survival, those with a score of 1 to 100 had 97% survival, those with a score of ≤0 to -100 had 89% survival, and those with a score less than -100 had 62% survival at a median follow-up of 10 years. It should be noted that in the FIT cohort patients with established CAD were excluded in contrast to our CR patients already undergoing secondary prevention.

A high risk category (≤-100 to -200) was predictive for the occurrence of all cause mortality. This emphasizes the importance of cardiovascular fitness in predicting outcomes. Kavanagh et al reported in patients referred for CR that a higher exercise capacity was associated with decreased mortality even when controlling for traditional cardiovascular risk factors. In patients with acute myocardial infarction who underwent percutaneous catheter intervention, exercise capacity was shown to be an independent and better predictor of 2 and 5 year mortality than left ventricular ejection fraction. The FIT score which makes use of important exercise variables provides a measure of cardiorespiratory fitness with strong prognostic significance. Secondly, the degree of improvement in the FIT score is also strongly associated with improved survival. The determination of a cutoff point of 18.21 points based on the crossover point of sensitivity and specificity curves was done so that we have a quantitative measure of change in the FIT score that predicted prognosis. When using the cutoff of 18.21 points increase in the FIT score was associated with a statistically significant probability of survival. The inverse association is also depicted in the survival curves clearly showing a higher likelihood of mortality for patients who failed to reach this cutoff. Tabet et al noted that a lack of improvement in exercise capacity after an exercise training program has a strong prognostic value for adverse events. Conversely, after participating in a CR program, there is a strong association between increase in fitness and decreased mortality with a 30% reduction in mortality per METs increase in cardiorespiratory fitness during CR especially in patients with low fitness levels.

CR is a multidisciplinary approach that involves risk factor modification, behavioral education, and nutritional counseling in addition to exercise training. It is expected that participation in exercise based CR has favorable effects on cardiovascular risk factors, including smoking, blood pressure, body weight, and lipid profile along with significant reductions in mortality and adverse events. Improvements in cardiopulmonary fitness are tightly coupled to the exercise training component of CR and it has been suggested that improvements in cardiorespiratory fitness will have the most prognostic value, making it a potential quantifiable biomarker in assessing response to CR.

There have been numerous proposed measures in assessing outcomes in CR. Most studies have analyzed individual qualitative components of the exercise test such as improvement in functional capacity, PMHR, heart rate recovery and improvement of metabolic profiles. It has been consistently shown that fitness level is the most powerful predictor of mortality with prognostic power that is independent of age, gender, ejection fraction and all other traditional cardiovascular risk factors. The predictive power of cardiorespiratory fitness is independent of CAD and revascularization status.

The novelty of the FIT treadmill score is that it provides a quantitative measure of cardiovascular fitness. It is easy to compute and determine. Additionally it would appear that among the advantages of the FIT treadmill score is the fact that it does not rely on symptoms, is not confounded by electrocardiographic changes and it factors in gender and age to the equation for prediction of risk. Finally, the FIT treadmill score emphasizes fitness and exercise performance to predict long-term survival rather than risk during exercise participation or predicting obstructive CAD. In the original FIT study patients in the intermediate and high risk category had a mortality rate of 11% and 38% respectively. Participation in the CR program can lead to improvement of the FIT score, which presumably led to a lower mortality rate in our study (5% and 14.5% for intermediate and high risk groups, respectively). No mortality was observed in the low risk and very low risk classification. CR promotes better adherence to medications, exercise, lifestyle and risk factor modification and this can expected to reflect in the FIT score as well, and there is available evidence that quantitative improvements in cardiorespiratory fitness have favorable and considerable effects on established cardiovascular risk factors and mortality. Patients with a high risk FIT score category undergoing CR can be

![Figure 5. Comparison of area under the curve (AUC) of FIT score on EXIT and improvement in the FIT score in predicting mortality (CL, confidence interval).](image-url)
targeted to improve their FIT score with a goal to increase exercise capacity and improve their outcomes. This study has certain limitations. First this was a single center study with a relatively small sample size of predominantly male population (only 15.6% comprised of women) that was retrospective in nature and inherent to potential biases. The applied methodology is comparable to other prospective validation and population studies. The authors took into account all follow up status with blinded prospective follow up and excluded all missing data to get the most accurate representation of the sample. Though the percentage of people lost to follow up is small (4.2%), the authors recognize this limitation. While the use of cutoff values and hazard ratios are informative from a clinical standpoint in informing patients, there are still issues in bias and confounding. Even after adjustment it should be noted that our findings are mostly hypothesis generating and needs to be verified by larger multicenter validation studies. Secondly, the study was limited to patients with CAD who underwent CR subject to selection bias. We did not include patients with other forms of heart disease (congenital, valvular). Further studies will be needed to confirm our findings externally although there is ample evidence to suggest that CR will equally benefit these patients and this may be expected to reflect in the FIT score. Lastly, the FIT score was calculated using METs derived from our institutional protocol (modified Naughton) that has less incremental increases in speed and grade, compared to the Bruce protocol. The original investigators of the FIT study used the Bruce protocol, which may have differential effects on different exercise parameters. Many of our patients are elderly and previously have undergone coronary artery bypass or percutaneous catheter interventions and may have been likely unable to perform the Bruce protocol. The modified Naughton protocol is a submaximal test which primary measures exercise capacity making it suitable for less fit patients.

To the best of our knowledge since its derivation, this is the first study that explored the potential prognostic utility of the FIT treadmill score in patients who underwent CR. We are unaware of studies where the FIT treadmill score has been applied prospectively in real time, but such studies would be useful to further confirm the prognostic value of the score in different patient populations. The FIT treadmill score is quickly calculated, easily attainable from a standard exercise test and has excellent discriminative ability for long term mortality. It has been shown that poor cardiovascular fitness is a modifiable risk factor, and improvements in fitness over time have been demonstrated to improve prognosis. The FIT treadmill score can potentially be used as a reliable metric in assessing response to CR to improve cardiovascular fitness and prognosis.

Conclusion
The FIT treadmill score predicts long term mortality in patients with CAD after undergoing CR. An improvement in the FIT treadmill score is associated with improved survival. It can be potentially utilized as simple tool for risk stratification of patients that may be used as gauge of overall cardiovascular fitness and a marker of a successful outcome of patients participating in a CR program.

Ethical approval
Our local Institutional and Ethics Review Board approved this study (ethics number PHC.IERB.01.15.42).

Competing interests
All authors declare no competing financial interests exist.

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