Original Article

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

Lucky R. Cuenza[1,2*], Emily Mae L. Yap[1], Edgardo Ebba[2]

[1]Department of Adult Cardiology, Philippine Heart Center, East Avenue Quezon City, Manila, Philippines
[2]Section of Cardiac Rehabilitation, Philippine Heart Center, East Avenue Quezon City, Manila, Philippines

Abstract

Introduction: Cardiovascular fitness is an important goal in cardiac rehabilitation (CR) programs and is predictive of outcomes. We sought to determine the utility of a novel clinical treadmill score in determining prognosis of coronary artery disease (CAD) patients after CR.
Methods: Demographic, clinical and exercise data of 262 patients (mean age 55.8 ± 10.1 years) who completed an outpatient CR program were analyzed. The FIT treadmill score was determined prior to program initiation and after completion. Patients were classified according to risk category using the FIT scores after CR completion and were followed up for the occurrence of 10 year all cause mortality.
Results: On median follow up of 10.3 years, 52 patients died. An improvement of the FIT treadmill score by 18.2 points was associated with a 21% reduction in mortality (multivariate-adjusted Hazard Ratio 0.79, 95% CI 0.56-1.08, $P \leq 0.05$). Kaplan-Meier survival curves showed increased occurrence of mortality in the high-risk group. After adjustment for confounders a high-risk FIT score category on exit (HR: 2.7, 95% CI 1.41-5.17, $P \leq 0.05$) was predictive of increased mortality. Both an improvement in the FIT score (AUC=0.81) and the FIT score category on exit (AUC=0.92) had good discrimination in predicting mortality.
Conclusion: The FIT treadmill score is predictive of all cause mortality in patients with CAD undergoing CR. An improvement in the FIT score after CR is associated with improved survival. The FIT score may be a useful prognostic marker of overall cardiovascular fitness and successful outcome for patients who participate in CR programs.

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

Corresponding Author: Lucky R. Cuenza, Email: baldyboy_182001@yahoo.com

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%[4] 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 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

Table 1. Baseline clinical characteristics

| Characteristic (n=262)	Total No. (%) or ±SD
Age	55.8± 10.1
Sex (male)	221 (84.4)
Body mass index	25.1± 3.5
Hypertension	191 (73)
Diabetes	79 (30)
Smoking	138 (52.7)
Dyslipidemia	161 (61.5)
History of previous CABG	231 (88.2)
History of previous PCI	21 (8)
Stable CAD	17 (6.5)
Heart failure	56 (21.3)
Aspirin/Clopidogrel	252 (96.2)
Beta blocker	200 (76.3)
Calcium channel blocker	80 (30.5)
Diuretic	55 (20.9)
Digoxin	68 (25.9)
ACEI/ARB	162 (61.8)
Ejection fraction	58.2 ± 12.5
Double product	23679 ± 5049
Abnormal double product	51(19.5)
Double product reserve	14340 ± 5088
Abnormal double product reserve	40 (15.3)
Abnormal heart rate recovery	75 (28)
PMHR	141.2 ± 18.7 beats per minute
% PMHR	86.1 ± 9.3
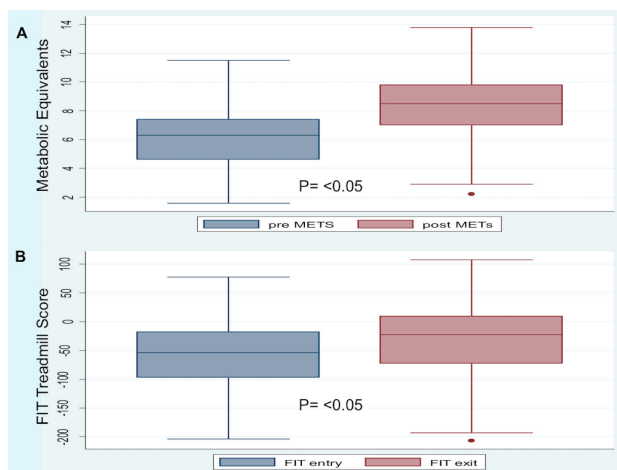
Figure 1. Box plot showing the (A) Metabolic Equivalents (METs) and FIT treadmill scores (B) achieved before and after completion of the Phase 2 cardiac rehabilitation program.

Figure 2. Sensitivity and Specificity curves of the FIT treadmill score in predicting survival.

-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, $P \leq 0.05$). 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 ($P \leq 0.05$).

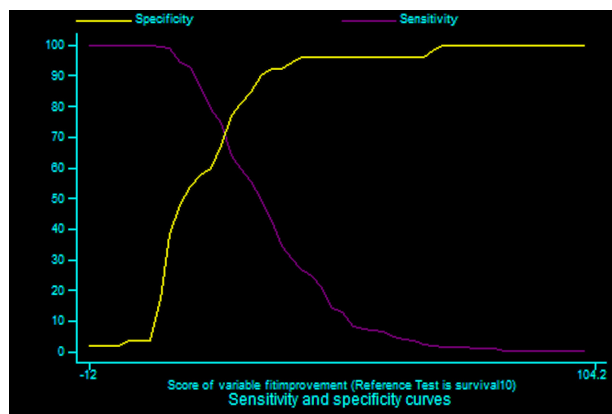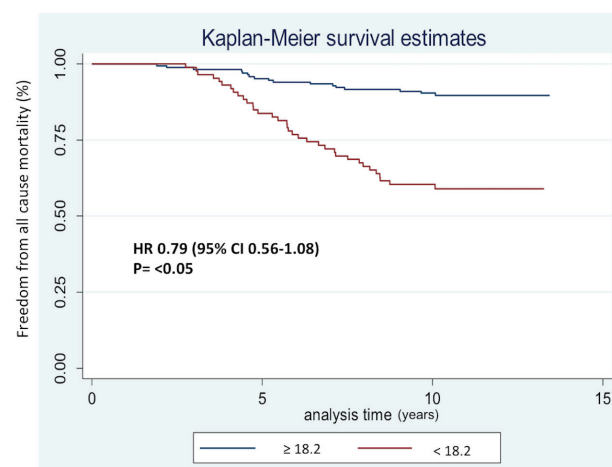The receiver operator characteristics curves are shown

Figure 3. Kaplan Meier survival curves according to improvement of the FIT score on Exit. The cut off of 18.2 points in improvement in the FIT score was used. HR, hazard risk; CI, confidence interval.
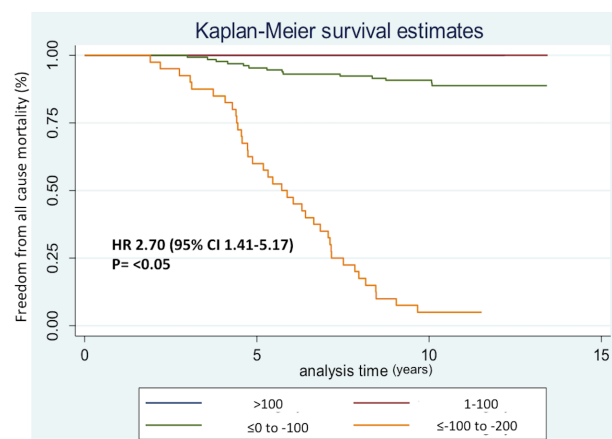

Figure 4. Kaplan Meier survival curves according to the FIT score Category on Exit. FIT exit category FIT score >100=very low risk. FIT score 1-100=low risk. FIT score ≤0 to -100= moderate risk. FIT score ≤-100 to -200= high risk. HR, hazard risk; CI, confidence interval.

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
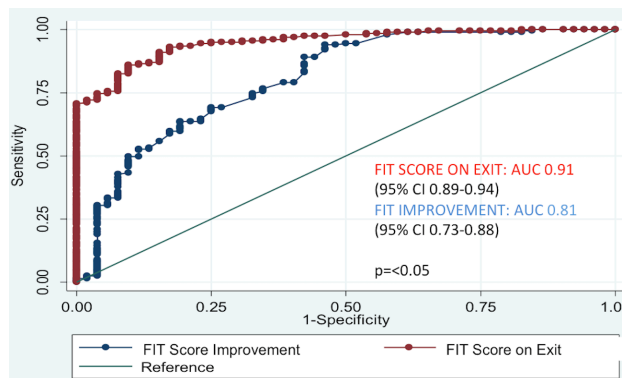
Figure 5. Comparison of area under the curve (AUC) of FIT score on EXIT and improvement in the FIT score in predicting mortality (CI, confidence interval).

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.[4] 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.[5] 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.[6] 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.[7] 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.[8] 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.[9]

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.[10] 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.[11]

There have been numerous proposed measures in assessing outcomes in CR.[12] 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.[13] It has been consistently shown that fitness level is the most powerful predictor of mortality[14,15] with prognostic power that is independent of age, gender, ejection fraction and all other traditional cardiovascular risk factors.[16] The predictive power of cardiorespiratory fitness is independent of CAD and revascularization status.[17]

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.[18] Patients with a high risk FIT score category undergoing CR can be

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.[19] 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[20] 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.[21] 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.

References

1. Mampuya WM. Cardiac rehabilitation past, present and future: an overview. **Cardiovasc Diagn Ther** 2012;2(1):38-49. doi: 10.3978/j.issn.2223-3652.2012.01.02.

2. Silva AK, Barbosa MP, Bernardo AF, Vanderlei FM, Pacagnelli FL, Vanderlei LC. Cardiac risk stratification in cardiac rehabilitation programs: a review of protocols. **Rev Bras Cir Cardiovasc** 2014;29(2):255-65. doi: 10.5935/1678-9741.20140067.

3. Adams BJ, Carr JG, Ozonoff A, Lauer MS, Balady GJ. Effect of exercise training in supervised cardiac rehabilitation programs on prognostic variables from the exercise tolerance test. **Am J Cardiol** 2008;101:1403-7. doi: 10.1016/j.amjcard.2008.01.016.

4. Ahmed HM, Al-Mallah MH, Mcevoy JW, Nasir K, Blumenthal R, Jones SR, et al. Maximal Exercise testing variables and 10-year survival: fitness risk score derivation from the FIT project. **Mayo Clin Proc** 2015;90(3):346-55. doi: 10.1016/j.mayocp.2014.12.013

5. Franklin BA, McCullough PA. Cardiorespiratory fitness: an independent and additive marker of risk stratification and health outcomes. **Mayo Clin Proc** 2009;84(9):776-9.

6. Kavanagh T, Mertens DJ, Hamm LF, Beyene J, Kennedy J, Corey P, et al. Prediction of long-term prognosis in 12 169 men referred for cardiac rehabilitation. **Circulation** 2002;106(6):666-71.

7. Dutcher JR, Kahn J, Grines C, Franklin B. Comparison of left ventricular ejection fraction and exercise capacity as predictors of two- and five-year mortality following acute myocardial infarction. **Am J Cardiol** 2007;99:436-41.

8. Tabet J, Meurin P, Beauvis F, Weber H, Renaud N, Thabut G, et al. Absence of exercise capacity improvement after exercise training program: a strong prognostic factor in patients with chronic heart failure. **Circ Heart Fail** 2008;1(4):220-6. doi: 10.1161/CIRCHEARTFAILURE.108.775460.

9. Martin BJ, Arena R, Haykowsky MJ, Hauer T, Austford LD, Knudtson M. Cardiovascular fitness and mortality after contemporary cardiac rehabilitation. **Mayo Clin Proc** 2013;88(5):455-63. doi: 10.1016/j.mayocp.2013.02.013.

10. Lawler P, Filion K, Eisenberg M. Efficacy of exercise-

based cardiac rehabilitation post–myocardial infarction a systematic review and meta-analysis of randomized controlled trials. **Am Heart J** 2011;162(4):571-584.e2. doi: 10.1016/j.ahj.2011.07.017.

11. Shenoy C, Patel M. Improved fitness as a measure of success of cardiac rehabilitation: Do those who get fitter live longer? **Int J Cardiol** 2013;167(3):903-4. doi: 10.1016/j.ijcard.2011.11.044.

12. Sanderson B, Southard D, Oldridge N. AACPVR consensus statement outcomes evaluation in cardiac rehabilitation/ secondary prevention programs: improving patient care and program effectiveness. **J Cardiopulm Rehabil** 2004;24(2):68-79.

13. Rodrigues P, Santos M, Sousa MJ, Brochado B, Anjo D, Barreira A, et al. Cardiac rehabilitation after an acute coronary syndrome: the impact in elderly patients. **Cardiology** 2015;131(3):177-85. doi: 10.1159/000381824.

14. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. **N Engl J Med** 2002;346(11):793-801.

15. Gulati M, Pandey DK, Arnsdorf MF, Lauderdale DS, Thisted RA, Wicklund RH, et al. Exercise capacity and the risk of death in women. The St James Women Take Heart Project. **Circulation** 2003;108(13):1554-9.

16. Myers J. Physical activity: the missing prescription. **Eur J Cardiovasc Prev Rehabil** 2005;12(2):85-6. doi: 10.1097/01.hjr.0000161884.01893.ba.

17. Hung RK, Al-Mallah MH, McEvoy JW, Whelton SP, Blumenthal RS, Nasir K, et al. Prognostic value of exercise capacity in patients with: the FIT (Henry Ford ExercIse Testing) project. **Mayo Clin Proc** 2014;89(12):1644-54. doi: 10.1016/j.mayocp.2014.07.011.

18. Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Asnumi M, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. **JAMA** 2009;301(19):2024-35. doi: 10.1001/jama.2009.681.

19. Haljan-Tilaki K. Receiver operating characteristic (ROC) curve analysis for medical diagnostic test evaluation. **Caspian J Intern Med** 2013;4(2):627-35.

20. Savage P, Rengo J, Menzies K, Ades P. cardiac rehabilitation after heart valve surgery: comparison with coronary artery bypass graft patients. **J Cardiopulm Rehabil Prev** 2015;35(4):231-7. doi: 10.1097/HCR.0000000000000104.

21. Blair SN, Kohl HW 3rd, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. Changes in physical fitness and all-cause mortality: a prospective study of healthy and unhealthy men. **JAMA** 1995;273(14):1093-8.