Dear Timothy Shipley,

We would like to thank the suggestions of the reviewers, certainly relevant points. In response we revised the manuscript and with this cover letter we show a point-by-point response to the concerns.

It was reported “the authors should consider a more expanded discussion of the particular challenges facing Brazil and the specific community they study with regard to the resources of the healthcare system relative to the disease burden provide incidence and prevalence of CAD in Brazil with associated morbidity and mortality data, current financial expenditure, and a brief discussion on risk factor prevalence and resources allocated for CVD prevention.” We set “The prevalence of heart disease in the age group between 35 and 49 years of age is approximately 3.7% in Brazil [17].” “Irrational use of diagnostic complementary methods directly impacts in healthcare spending. The cost of cardiovascular disease is significant in Brazil, with an expense of about 1.74% of Gross National Product [17]. In 2012, 497,242 treadmill exercise stress tests have been
performed in the Brazilian public health system, with a cost of more than $ 7 million US dollars. With our results in mind, nearly 243 thousand exams could be considered inappropriate in the Brazilian wide perspective, representing an unnecessary expense of more than $ 3 million dollars in 2012 [18].” (lines 244, 245, 256-261).

The reviewer pointed out about the details of the health system: “In addition a more detailed description and comparison of the public and private healthcare systems in the discussion section would be helpful to better delineate why this is the only independent risk factor for inappropriate testing-financial incentives, patient demands.” We add new information to the discussion, making clearer understanding of the important role of the health system as a risk factor for inappropriate testing. “In Brazil coexist two healthcare systems: the public and the private. The evident imbalance between the funding expenses for private and public health in a developing country as Brazil leads to an unequal health policy. In December 2013 there were 2109 offices specialized in the public system, while in the private network had 8937 specialized consultation room[15]. It reflects in the higher availability of health services in the private healthcare system, compared to the scarce resources in the public system. Although covering only 24% of the population, about 54% of the spent in the Brazilian healthcare in 2011 was in the private system. The public health system covers the majority of the Brazilian population, investing around 512 dollars per person per year [4;16].” (lines: 231-239).

We make the “minor essential revisions”. We corrected terms “treadmill test” as “treadmill exercise stress test”. We used term "diagnostic evaluations" in place of "tests" and "exams". We changed comma (,) in tables to decimal points (.). It was requested “detailed references and evidence for the appropriateness criteria for CAD evaluation by treadmill exercise stress testing based on ACC/AHA established guidelines.” I believe this to be one of the most important points to understand the study. “There is no specific guideline on appropriate use criteria for treadmill exercise stress test. But based on the evidence on screening in asymptomatic and assessment in those stable patients with CAD, but also in probabilistic concept of using the method according to the probability of coronary artery disease, we defined the inappropriate diagnostic evaluation parameters. Treadmill exercise stress tests were then rated as inappropriate if they presented one of the following two criteria: (1) patients asymptomatic for CAD; (2) symptomatic patients with low or high pretest probability of CAD. Treadmill exercise stress test in individuals above 70 years of age with chest pain was rated as appropriate, as well as those patients symptomatic with known CAD. Individuals younger than 30 years were classified as the likelihood of CAD according to age group 30-39 years in the criteria of Diamond-Forrester.” (lines 126-138). “Studies evaluating appropriateness criteria in the use of treadmill exercise stress tests for diagnosis of obstructive CAD are still sparse in the literature. However, evidences show that asymptomatic individuals do not benefit from active screening for obstructive CAD [9-12]. Additionally, mandatory myocardial stress testing in patients with known CAD did not reduce major CV outcomes [1,13,14]. Similarly, individuals in both low and high pre-test probability
for obstructive CAD do not benefit from treadmill test screening, as results may not substantially affect the likelihood of disease. Therefore, the main utility of the exercise test in the diagnosis of obstructive CAD lies in symptomatic patients with intermediate pretest probability.” (lines 215-226).

The reviewer mentioned “It is not clear why a single regression analysis was not conducted to determine the independent variables related to inappropriate use treadmill exercise stress test explain in detail the advantages of the statistical models used. Greater precision, reduced errors, better for smaller sample sizes.” We used three logistic regression models to represent the associating parameters derived from the univariate analysis. The models also reflect the thinking of the doctor, who may consider in the prescription of diagnostic evaluation, the cardiovascular risk of your patient or even the risk factors alone or the amount of them. “The model 1 is adjusted for clinical variables (hypertension, dyslipidemia and diabetes); model 2 for the number of risk factors and the model 3 is associated with cardiovascular risk. These associations were also described by odds ratios and 95% CI. Variables that remained in the final model with P <0.05 were defined as independent predictors. The calibration of the models was assessed by testing Hosmer-Lemeshow.” “In model 1, among the clinical variables only hypertension was shown to be inversely associated with inappropriate use of the treadmill exercise stress test. In Model 2 and Model 3 revealed no significant association between the number of risk factors or cardiovascular risk with inappropriate indications for treadmill exercise stress test (Table 3). In second moment, we adjusted the model 1 for age, only in order to verify that the inverse association of hypertension with inappropriate testing was mediated by these patients being younger. In fact, hypertension lost statistical significance in this model, while additional network of health remained strongly associated (when adjusting for age, OR=3.5; P=0.003). Therefore, patient being in the private health care system was the only important significant covariate in the models, with OR=4.3 (P<0.001) for private healthcare system, according to the model adjusted for clinical conditions. The P value of the Hosmer-Lemeshow test for all models was > 0.05 indicating a good calibration.” (lines 185-203).

We commented about the limitations of the study: “There are limitations regarding the generalization of our study. In fact, It is a small sample and the results may represent the local reality of a center in Northeastern Brazil. Further research assessing different populations in other health centers may reinforce our findings and broaden the discussion of this important topic.” (lines 272-275).

The authors hope to have assessed all the suggestions made. As mentioned before we approach a serious problem in health care: the overuse of a complementary method. In fact we believe this manuscript “Prevalence and Factors Associated with Inappropriate Use of Treadmill Exercise Stress Test for Coronary Artery Disease” is suitable for publication in BMC Cardiovascular Disorders because it remarks the inappropriate use of the treadmill exercise stress test in the clinical practice.

All authors have read and approved this review version of the manuscript.

With best wishes,
Antônio Marconi Leandro da Silva, M.D, MSc
University of São Francisco Valley –UNIVASF, Petrolina, Brazil.