Reviewer’s report

Title: Prognostic value of cardiopulmonary exercise testing in patients with systemic sclerosis

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Reviewer: Harrison Farber

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In this submission, Ewert et al. have retrospectively assessed CPETs in 210 patients with scleroderma (SSc) from six centers. After examining multiple different metrics, the authors found that peak VO2 (<64.5% of predicted) and VE/VCO2-slope >35 were predictive of prognosis in these patients. These are interesting observations, but raise several questions.

1) What is the appropriate control group for this population? It is clear that SSc patients fare much worse than the general population - CPET metrics are not necessary to know this. One could argue that in SSc patients with ILD, this should be patients with similar degrees of ILD (but w/o scleroderma) or in SSc-PH/PAH patients, a like group without SSc. In the group used in this submission it is not mentioned whether the groups were matched by sex (since SSc patients are predominantly female).

2) In the patients who underwent RHC (a minority), what was the reason for the RHC - were there any specific criteria that led to RHC? And what percentage had left-heart disease during the CPET (since it is becoming more apparent that SSc is a likely risk factor for development of diastolic dysfunction)? In the group who had PAH at RHC, were they treated and, if so, did this change prognosis? Lastly, were there differences in the predictive value of the metrics in patients who underwent RHC vs. those that did not?

3) Likewise, only a minority of patients underwent 6MWT. Was there a reason that some patients did and the majority did not? And, if so, how were these patients different? Were there differences in the predictive value of the metrics in patients who underwent 6MWT vs. those that did not?

4) CREST is no longer considered a separate group by most Rheumatologists - it is a subgroup of limited SSc.

5) The literature on the prognosis of patients with SSc-ILD is very controversial - there are much data to suggest that ILD is detrimental and much data suggesting that is is not predictive - this discussion should be better balanced. The difference between the older and newer literature may be aggressive treatment of the ILD with cyclophosphamide, mycophenolate, etc.

6) Ultimately, are the authors suggesting that all patients with SSc should undergo CPET? This would be difficult (impractical) to say the least and there are many SSc patients who cannot or will not ride a bike. Lastly, even if this were ever possible, it would have to be shown that changing these values with treatment altered the outcomes in these patients. In other words, what is the clinical utility of this findings above what is already known about scleroderma patients?
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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