The primary task of the cardiopulmonary system is to provide blood flow and oxygen in quantities sufficient to support the individual’s metabolic needs. The cardiopulmonary system is maximally stressed when an individual’s metabolic rate is increased, a condition that occurs most commonly during physical activity or exercise. Cardiopulmonary exercise testing (CPX) quantitatively assesses a patient’s capacity to adapt to the hemodynamic demands of exercise. Those who are found to have a cardiopulmonary system incapable of supporting normal amounts of exercise are likely to be less resilient, more vulnerable to illnesses, and more predisposed to health complications when confronting the inevitable challenges of life. A weakened cardiopulmonary system is also likely to be more susceptible to further damage or injury. It is therefore not surprising that data from CPX has been found to carry powerful and important prognostic implications.

Indeed, past studies have found that the peak oxygen consumption (VO₂) is one of the best predictors of morbidity or mortality in a variety of cardiovascular conditions including congestive heart failure, pulmonary hypertension, tetralogy of Fallot, transposition of the great arteries, and Fontan circulations. The article by Inuzuka et al is the latest contribution to this literature. These investigators have collected a large and diverse cohort of patients with congenital heart disease and have used novel, sophisticated statistical analyses to further establish the clinical value of CPX in this patient population. Their study found that peak VO₂ and heart rate reserve data can be used to generate estimates of 5-year survival across a wide spectrum of adults with congenital heart disease (CHD). This information will certainly inform and enhance clinical decision making in this unique group of patients. It is interesting to note that a previous study examining the relationship between CPX data and mortality in Fontan patients also found peak VO₂ and chronotropic incompetence to be powerful independent predictors of increased mortality.

There are a number of anomalies in Inuzuka et al’s article that must be noted, however. Almost regardless of diagnosis, the percentage of predicted peak VO₂ of the patients included in their study was surprisingly low, below levels typically found in reports from other tertiary care centers. For instance, the median peak VO₂ for patients with simple lesions (who should have peak VO₂ approaching 100% of predicted) was only 70% of predicted, and one-fourth of the patients had peak VO₂ <54% predicted. The respiratory exchange ratio (RER) at peak exercise was also inappropriately low. It averaged only 1.07±0.13, suggesting that a large fraction (perhaps a majority) of the patients did not approach their cardiovascular limit and/or expend an adequate effort (an RER >1.09 has been suggested as a threshold indicative of a good effort). A number of factors may account for these anomalies. However, the most plausible and likely explanation is that many of Inuzuka et al’s patients terminated exercise before reaching their cardiovascular limit. This may constitute a serious shortcoming for a study that seeks to evaluate the prognostic value of peak exercise data, for it permits factors unrelated to a subject’s cardiovascular health (eg, the patient’s level of motivation on the day of the CPX test) to contaminate the data and analyses. As one might expect, the prognostic power of peak VO₂ and heart rate reserve were significantly reduced in patients whose peak RER was <1.00. When these patients were excluded from the analyses, the CPX variables identified as prognostic markers remained unchanged. Indeed, it is likely that the prognostic power of the CPX data was even stronger when patients with low peak RER were excluded. More importantly, as the authors suggest, these considerations imply that it would be inappropriate and potentially misleading to use Inuzuka et al’s data to draw conclusions concerning an individual patient’s prognosis if the patient did not achieve an adequate RER on his/her CPX test.

Another surprising finding from Inuzuka et al’s article was the relatively weak prognostic power of the minute ventilation/carbon dioxide production relationship (VE/VO₂ slope). The VE/VO₂ slope has been found to be one of the most powerful independent predictors of mortality in patients with CHF, pulmonary hypertension, and tetralogy of Fallot. Its relationship to mortality in these conditions is probably due to the fact that the slope elevation is largely a consequence of, and proportional to pulmonary blood flow maldistribution (resulting in ventilation/perfusion mismatch and inefficient gas exchange) that develops as a consequence of pulmonary capillary wedge pressure elevation (in patients with CHF), progressive pulmonary vascular disease (in patients with...
pulmonary hypertension),\(^3\) and pulmonary artery stenoses (in patients with tetralogy of Fallot).\(^10\) Similar considerations may account for the strong association between VE/V\(\text{CO}_2\) slope elevation and mortality in patients who have undergone atrial repairs of transposition of the great arteries.\(^3\) However, the VE/V\(\text{CO}_2\) slope has not been related to prognosis among patients with Fontan physiology.\(^6\) This observation is explained by the fact that the slope elevation commonly encountered among Fontan patients is probably related, to a large extent, to pulmonary blood flow maldistribution (and ventilation/perfusion mismatch) secondary to the absence of a pulmonary ventricle and the consequent lack of normal pulmonary artery pulsatility. This condition is common to all Fontan patients. Therefore, in contrast to the aforementioned conditions, among Fontan patients the VE/V\(\text{CO}_2\) slope elevation is not proportional to disease progression/severity and does not carry strong prognostic significance. The inclusion of Fontan patients within their study population may therefore underlie Inuzuka et al’s anomalous findings regarding the prognostic value of the VE/V\(\text{CO}_2\) slope.

The data from Inuzuka et al’s study raise 2 important questions. First, would interventions that improve patients peak V\(\text{O}_2\) effectively improve their 5-year survival? Cardiologists and surgeons are adept at using medical and surgical techniques to optimize a CHD patient’s anatomy/physiology and reduce the impact of his/her residual hemodynamic lesions to the lowest level possible by the use of current technology. In contrast, however, exercise/rehabilitation programs are underutilized in the CHD population. These programs have been found to improve peak V\(\text{O}_2\) in patients with CHD.\(^11,12\) They also improve the peak V\(\text{O}_2\) and prognosis of patients with acquired heart disease.\(^13\) Similar benefits may also accrue to the growing adult CHD population. Second, would interventions that improve the heart rate reserve of patients with CHD (eg, a lower threshold for pacemaker implantation and/or more physiological pacing algorithms for patients with pacemakers) improve their survival? Patients with pacemakers were excluded from Inuzuka et al’s heart rate reserve analyses, and their data therefore do not provide insights into this issue. Additional studies examining this question may be interesting and worthwhile.

### Disclosures

None.

### References


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Cardiopulmonary Exercise Testing in Adults with Congenital Heart Disease: Can We Prognosticate and Improve Prognosis?

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