

## The Clinical Significance of Isocapnic Buffering Phase During Exercise Testing: An Overview

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### Description

During an incremental cardiopulmonary exercise test (CPET), lactic acid begins to accumulate after anaerobic threshold (AT) [1]. Circulating bicarbonate compensates for the lactic acidosis along with increased hyperpnea [2]. Beyond a certain point reaching higher exercise intensity, lactic acid production can no longer be compensated by circulating bicarbonate and thus hyperventilation begins. This point is called the respiratory compensation point (RCP) [3]. The period from AT to RCP is known as isocapnic buffering (IB) phase [2]. In this article, we will review current concepts about the clinical significance of the IB phase.

Most studies regarding the IB phase put emphasis on athletes and healthy individuals. Oshima, Y et al. reported a positive and significant correlation between the duration of IB phase and maximal oxygen consumption ( $\text{VO}_2\text{max}$ ) in young athletes [4]. A correlation between the increase in  $\text{VO}_2\text{max}$  and the increase in IB phase after 6 months of training has also been reported [5]. Mauro Lenti et al. further demonstrated that the duration of IB phase reduces with aging and is higher in trained individuals with better endurance independent of age in cyclists [6]. Some studies, however, showed different results. Chicharro et al. [7] defined IB as the range of  $\text{VO}_2$  and power output from AT to RCP. They found no significant increase in the range of IB throughout the course of a training season in professional cyclists. Another study [8] revealed that in male endurance athletes, short (20-min) but not a longer (90-min) cycling time trial performance had correlation ( $r=0.58$ ,  $p<0.05$ ) with the range of IB, whereas the correlation was weak. They suggested that IB is not representative of endurance performance in time trial in endurance athletes. Nevertheless, according to the above findings, longer IB phase indicates better endurance performance, and after endurance training, IB phase is increased despite aging in athletes.

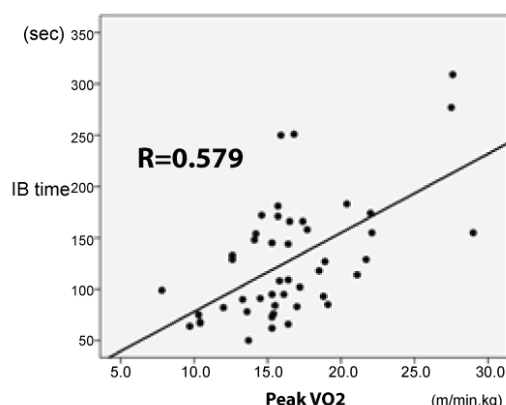
The studies about IB phase in patients with heart diseases are scarce. Masaaki Tanehata et al. [9] reported that in chronic heart failure patients, the period of IB phase is closely related to the slope of  $\text{VO}_2$  as a function of work rate ( $\Delta\text{VO}_2/\Delta\text{WR}$ ), but there is no

correlation between the RCP-AT time and the anaerobic threshold. They suggested that the RCP-AT time is an indicator of aerobic metabolism after AT. However, it is still not clear whether the IB phase could indicate cardiopulmonary function, endurance training effects or prognosis in patients with cardiac diseases.

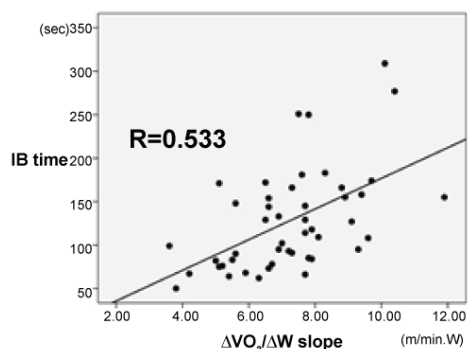
Numerous studies have demonstrated a beneficial effect of exercise training in chronic heart failure (CHF) patients, which is revealed by increased peak  $\text{O}_2$  consumption ( $\text{VO}_2$ ) in CPET after exercise training [10-14], despite limited improvement in left ventricular ejection fraction (LVEF) [15]. On the other hand, ventilatory efficiency ( $\text{VE}/\text{VCO}_2$  slope) [16,17], partial pressure of end tidal  $\text{CO}_2$  ( $\text{PetCO}_2$ ) at AT [18-20] and peak  $\text{VO}_2$  [21,22] all serve as significant prognostic factors in CHF patients according to previous studies. To sum up, the IB phase may be an indicator of cardiopulmonary performance emphasizing on exercise endurance rather than underlying cardiac function (e.g. LVEF), and could also indicate the prognosis in chronic heart failure patients.

Recently, we recruited 47 patients with coronary heart disease (CAD) status post coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) from January 2010 to June 2014 to undergo an incremental cycle ergometer cardiopulmonary exercise test ( $10 \text{ W}\cdot\text{min}^{-1}$ ) and found that there is significant correlation between the IB phase and peak  $\text{VO}_2$  ml/min/kg ( $R=0.579$ ,  $P<0.001$ , Figure 1) and  $\Delta\text{VO}_2/\Delta\text{W}$  slope ( $R=0.533$ ,  $P<0.001$ , Figure 2). The correlation between the IB phase and maximal  $\text{PetCO}_2$  and  $\text{VE}/\text{VCO}_2$  slope is also significant ( $P<0.05$ ). There is no significant correlation between the IB phase and the LVEF of patients. Since the peak  $\text{VO}_2$  represents both central and peripheral cardiopulmonary function, and LVEF only represents central cardiac function, the IB phase may imply the endurance performance in CAD patients derived from peripheral effects regardless of LVEF of patients based on our findings. As  $\Delta\text{VO}_2/\Delta\text{W}$  slope is an indicator of peripheral blood flow [9,23], the significant correlation between the IB phase and  $\Delta\text{VO}_2/\Delta\text{W}$  slope revealed in our study also suggests that the IB phase is an indicator of the peripheral cardiopulmonary function. Besides, since the IB phase is associated with the well-recognized prognostic factors such as  $\text{VE}/\text{VCO}_2$  slope,  $\text{PetCO}_2$  at AT and peak  $\text{VO}_2$ , the IB phase may also infer prognosis of cardiac disease patients. As for the training effects on the IB phase in cardiac disease patients, more longitudinal studies are needed to verify it.

In conclusion, the IB phase could be another useful indicator in cardiac disease patients on the cardiopulmonary function and prognosis. We are anticipating further investigations on the clinical significance of the IB phase in CPET.



**Figure 1:** Correlation between IB time and peak  $\text{VO}_2$ .



**Figure 2:** Correlation between IB time and  $\Delta\text{VO}_2/\Delta\text{W}$  Slope.

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