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## PRE-OPERATIVE CARDIOPULMONARY EXERCISE TESTING FOR A SEVERELY MALNOURISHED LUNG CANCER RESECTION SURGERY CANDIDATE

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### ABSTRACT

**Tardie GB, Dorsey DA.** Pre-Operative Cardiopulmonary Exercise Testing For A Severely Malnourished Lung Cancer Resection Surgery Candidate. *JEPonline*. 2005;8(1)34-43. A male 58 year old patient with mixed lung disease, celiac sprue, and left lower lobe tumor was referred for pre-operative lung cancer evaluation due to concern by the surgical team over the patient's underweight status. A 10 Watt/min incremental cardiopulmonary exercise test was performed to assess functional capacity. Peak  $\dot{V}O_2$  and split lung function scan were utilized to assess predicted post-operative status. The underweight status of the patient required adjustment of predicted values to accurately reflect the patient's true functional capacity. Peak  $\dot{V}O_2$  of > 1000 mL/min, 23.1 mL/kg/min, and 60% predicted provide a reasonable prognosis.

**Key Words:** Emphysema, Celiac Disease, COPD, Risk Stratification

## INTRODUCTION

Scarcely one short decade ago, clinical exercise testing was simplistically limited to the detection of cardiovascular disease through the presence of an abnormal resting or exercise ECG. This mode of exercise testing lacked the diagnostic capability to offer insight into underlying cardiovascular, ventilatory or neuromuscular mechanisms for exertional intolerance. However, the widespread availability of computerized metabolic measurement systems has permitted broadened use of exercise testing. More recently, this includes expanded utilization of clinical exercise testing as a tool to stratify, based on surgical risk, potential surgical candidates for lung cancer resection surgery and heart transplantation surgery. Clinical data suggest that patients whose pre-operative values for maximal oxygen uptake ( $\text{VO}_2$ ) fall below 15 mL/kg/min experience less favorable post-surgical outcomes, as do patients whose peak  $\text{VO}_2$  values fall below 60% predicted (1,2).

The use of cardiopulmonary exercise testing as an assessment tool for pre-operative risk is based on the ability of the test to evaluate the capacity of the heart, lungs, and vasculature to deliver oxygen to the body. The use of peak  $\text{VO}_2$  as a predictor of surgical outcome is supported by clinical data which suggest that patients whose pre-operative values for maximal oxygen uptake ( $\text{VO}_2$ ) fall below 15 mL/kg/min experience less favorable post-surgical outcomes (1), as do patients whose peak  $\text{VO}_2$  values fall below 60% predicted (2,3).

Since oxygen utilization is heavily dependent on body weight, it is a fundamental physiological principle that an individual with a large body mass will demonstrate a greater oxygen requirements than individuals with lesser body mass. Therefore, functional capacity expressed in terms of mL oxygen per kg of body weight negates the impact of body mass, essentially providing a unit of measurement "standardized" for weight. As a result, the use of surgical criteria based on relative oxygen consumption per kilogram unit of body weight does account for differences in body weight of surgical candidates.

However, some authors choose an alternative method of assessing risk, and base their risk assessments on attainment by the patient of a given percentage of their predicted maximal aerobic capacity (2,3,4). Unfortunately, this approach has disadvantages as well. This is particularly true when a percentage of predicted peak oxygen consumption is selected as the clinical benchmark for risk stratification for patients who are severely underweight. Such cases present a challenge in the selection of appropriate reference values.

In the testing of tall, underweight individuals, such as those affected by cachexia, the selection of reference norms based on actual body weight artifactually increases the relative  $\text{VO}_2$  and provides a deceptively positive representation of the patient's medical status and as such, falsely favors a positive surgical outcome. Conversely, intuitively correcting by the selecting a predicted peak  $\text{VO}_2$  reference value based on *predicted* body weight can dramatically reduce the reported functional capacity (% predicted  $\text{VO}_2$ ) and exert misleadingly negative impact on prognosis for a favorable outcome. Thus, the selection of reference values that present a more precise depiction of the patient status is essential, as a  $\text{VO}_2$  peak greater than 60% predicted is a significant benchmark indicative of a more favorable surgical outcome (2,3,5).

The purpose of this case report will be to examine the selection of reference values, and detail the roles of split perfusion scanning, pulmonary function testing, and cardiopulmonary exercise testing in the assessment of surgical complications and post-operative prognosis of a candidate for lung cancer resection surgery.

## CASE REPORT

### History

A 58-year-old African-American male with non-small cell lung cancer was referred to our human performance laboratory for pre-operative evaluation to determine his suitability for lung cancer resection surgery. He initially presented with chronic abdominal pain to the emergency room and was found to have a 4 cm basilar mass in the left lung (Figure 1). Additional symptoms included poor exercise tolerance and anorexia. A subsequent evaluation with fine-needle aspiration indicated the presence of non-small cell lung cancer with squamous features. His past medical history was significant for celiac sprue, anemia, diabetes, and heavy smoking (50 pack-years). His medications included naproxen sodium, morphine, and insulin. The remainder of his exam was essentially normal. Given his low body weight (52.16 kg) and abnormal pulmonary function tests, the surgery service was reluctant to perform curative lung resection until he had a functional assessment of his performance status via cardiopulmonary exercise testing (CPET).

### Physical Examination

Ht. 72" (182 cm); Wt. 115 lb. (52.16kg); Ideal Body Weight: 183 lb. (83 kg). Vital signs were normal. The patient was a thin, underweight male in mild discomfort. Physical examination was significant only for diminished bilateral breath sounds. Cardiac exam was normal, and there was no evidence of lymphadenopathy, focal bony tenderness, neurologic findings, extremity clubbing or edema.

### Laboratory Findings

A split lung perfusion (or V/Q) scan was performed, to quantify blood flow (i.e., lung function). The patient was injected with technetium per standard protocol [4.4 microcuries of T<sub>c</sub>-99M] and images of the lung were obtained in the anterior and posterior projection. Geometric mean uptake was then determined, with left geometric mean reported as 41%, and right geometric mean 59%. The split perfusion study and the predicted post-operative (PPO) values are reported in Tables 1 and 2.

Spirometry and plethysmography was performed in part to determine PPO values based on the split perfusion scan. Pulmonary function testing suggested a patient with mixed lung disease: obstructive-restrictive ventilatory impairment, no significant changes post-bronchodilator, severe reduction in D<sub>L</sub>CO, and evidence of hyperinflation. Baseline pulmonary function and plethysmography values are reported in Table 3.



**Figure 1. Computed tomography illustrating a lower left lobe mass with extensive bibasilar fibrosis**

**Table 1. Split Lung Perfusion Values (distribution of perfusion to each lung/lobe).**

<b>Right Lung</b>	<b>59%</b>	<b>Left Lung</b>	<b>41%</b>
<b>RUL</b>	16%	<b>LUL</b>	41%
<b>RML</b>	14%		
<b>RLL</b>	70%	<b>LLL</b>	59%

**Table 2. Predicted Post Operative (PPO) Values.**

		<b>% Pred</b>
<b>FEV<sub>1</sub></b>	1.81 L	53%
<b>FVC</b>	2.08 L	48%
<b>D<sub>L</sub>CO</b>	6.06	20%
<b>VO<sub>2</sub> Peak</b>	0.908 L	46%

absolute and percent predicted value calculated based on 4 segment removal, assuming homogenous distribution of emphysema: NHANES III Black pulmonary Norms, Hansen Cycling Norms

**Table 3: Pulmonary Function Testing and Plethysmography**

		% Pred			% Pred			% Pred
<b>FVC</b>	2.74	<b>(63%)</b>	<b>TLC</b>	5.46	<b>( 84%)</b>	<b>RV</b>	2.69	<b>(132%)</b>
<b>FEV<sub>1</sub></b>	2.39	<b>(70%)</b>	<b>FRC</b>	4.30	<b>(126%)</b>	<b>RV/TLC</b>	49%	
<b>FEV<sub>1</sub>/FVC</b>	87		<b>IC</b>	1.16		<b>D<sub>L</sub>CO<sub>adj</sub></b>	8.0	<b>( 27%)</b>

absolute and percent predicted value: NHANES III, Black norms

Combining the quantitative split perfusion study and pulmonary function test results, as well as peak aerobic capacity provides the basis for calculating the PPO. Overall, the predicted post-operative lung function suggested that the patient could tolerate resection of his left lower lung lobe (PPO FEV<sub>1</sub>=1.85). Based on these data, the patient was scheduled for a CPET in the human performance laboratory to assess his exercise tolerance and cardiovascular function with the intent of determining the patient's ability to tolerate left lower lobectomy.

### Cardiopulmonary Exercise Testing

A 10 Watt /min incremental exercise test (IET) was performed according to the guidelines of the American Thoracic Society (6) to a peak workload of 70 watts (Table 4).

**Table 4: Maximal, Symptom Limited, Incremental Exercise Test: 10 Watts/min.**

		<b>Hansen VO<sub>2</sub> (Actual Body Weight) 52.16kg</b>		<b>Wasserman: Underweight (Mean of Actual and Predicted Body Weight) 67.97kg</b>		<b>Hansen Predicted Weight VO<sub>2</sub> 83.77kg</b>	
	Peak	Pred.	% Pred	Pred.	% Pred	Pred.	% Pred
<b>Time</b>	9:00						
<b>Power (Watts)</b>	70	109	(64%)	142	(49%)	185	(38%)
<b>VO<sub>2</sub> (L/min)</b>	1198	1515	(79%)	1982	(60%)	2444	(49%)
<b>VO<sub>2</sub> (ml/kg/min)</b>	23.1	36.0*	(64%)				
<b>?VO<sub>2</sub>?WR</b>	10.59	8.7-11.9					
<b>VT (VO<sub>2</sub> L/min)</b>	0.842	>0.604L >40% Pred. VO <sub>2</sub>	(56%)	>0.792L >40% Pred. VO <sub>2</sub>	(42%)	>1.02L >40% Pred. VO <sub>2</sub>	(33%)
<b>HR (beats/min)</b>	160	160	(100%)				
<b>O<sub>2</sub> Pulse (ml/beat)</b>	7.49	9.43	(79%)	12.38	(61%)	15.99	(47%)
<b>BP (mmHg)</b>	188/82						
<b>V<sub>E</sub></b>	78.9		120.4				
<b>V<sub>E</sub>/MVV<sub>meas</sub></b>	78.9/114		(69%)				
<b>f (br/min)</b>	45		<60				
<b>V<sub>E</sub>/VCO<sub>2</sub> (at VT)</b>	40		(N<34)				
<b>RER</b>	1.43						

? American Heart Association

**Exercise Stop: Leg Fatigue ( 4)**  
**Dyspnea ( 4)**

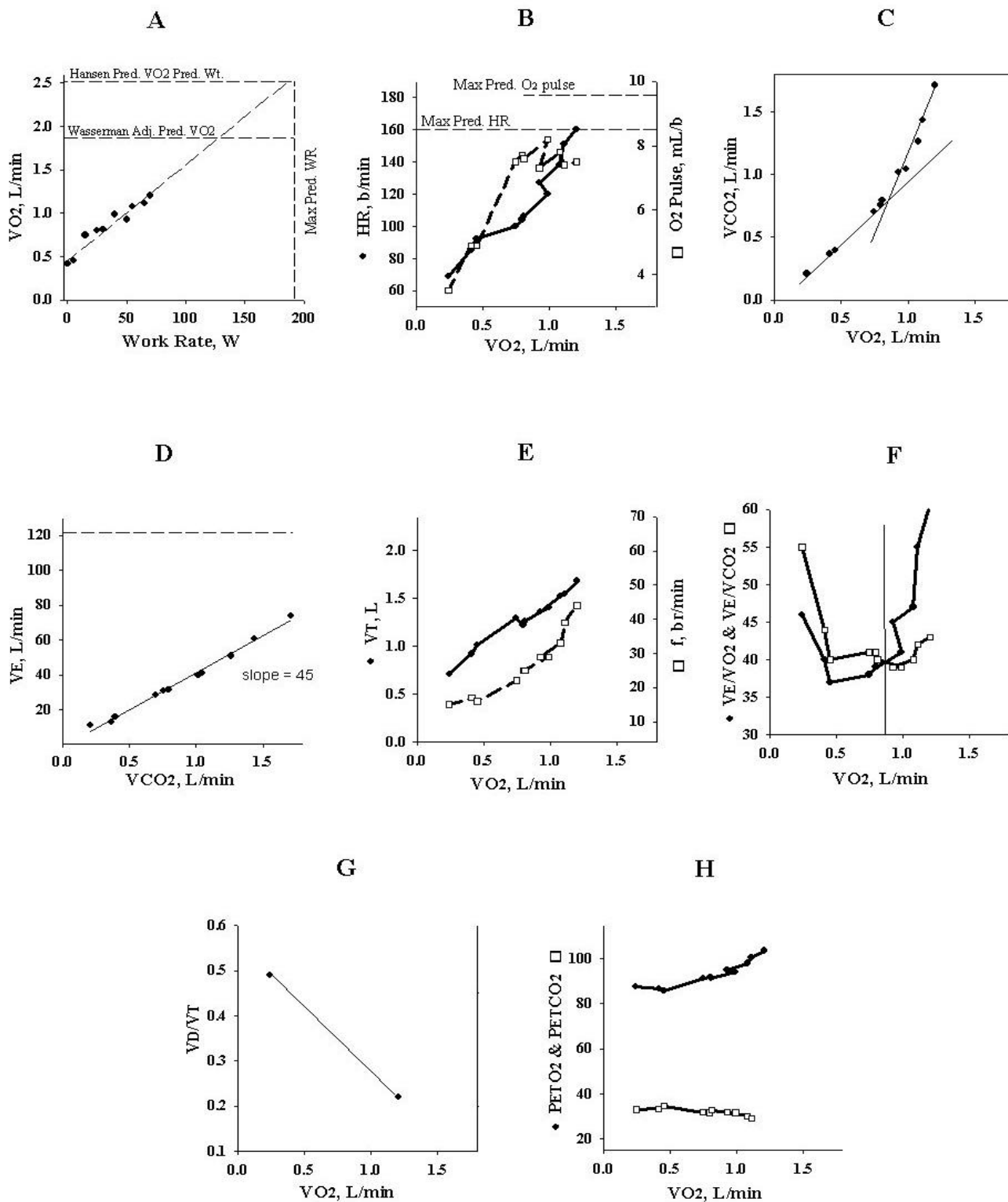


Figure 2. Cardiopulmonary exercise testing panel graphic display illustrate in part the impact of reference values on the predicted  $\dot{V}O_2$ . A.  $\dot{V}O_2$  measured and predicted, B. Heart rate and  $O_2$  pulse responses, C. V-slope determination of the ventilation threshold (VT), D. VE vs.  $\dot{V}CO_2$  response, E. Tidal volume and breathing frequency responses to  $\dot{V}O_2$ , F. VT determined by  $VE/\dot{V}O_2$  and  $VE/\dot{V}CO_2$ , G.  $VD/VT$  to  $\dot{V}O_2$ , H. End-tidal partial pressures for  $O_2$  and  $CO_2$  vs.  $\dot{V}O_2$ .

Constant work (CW) exercise at 55 Watts (75% of peak IET workload) was performed after a one-hour recovery interval. A dyspnea score of 4 was reported at peak exercise. The test was terminated due to leg fatigue with a Borg score of 4. The patient exhibited outstanding effort with a peak heart rate of 160 (100 % predicted). No wheezing, or dizziness was reported. The patient reported leg fatigue that resolved approximately 15 minutes post-exercise. There was a significant reduction in aerobic capacity  $VO_2 = 23.1$  mL/kg/min (64 % predicted). When calculated based on ideal body weight,  $VO_2$  peak was further reduced to 47 % predicted. There was a normal  $VO_2$  to work rate relationship (10.59) (Figure 2).  $VO_2$  predicted values were corrected using the Wasserman method (predicted  $VO_2$  for underweight patients) (7). The patient demonstrated normal baseline ECG and normal heart rate and normal blood pressure responses with occasional premature ventricular contractions during exercise and recovery. The ventilation threshold was abnormal: 0.842 L/min (33% predicted). Ventilatory responses revealed normal ventilatory reserve ( $V_E/MVV$ ) at peak exercise ( $78.9/114 = 69$  % predicted). However, the patient did exhibit inefficient ventilation: Increased  $V_E/VCO_2$  (40 at ventilation threshold as determined by the dual criteria method: V-Slope and Ventilatory Equivalents) and throughout exercise was most probably due to dynamic hyperinflation, and possibly V/Q abnormalities. Resting acid base balance was borderline normal; with questionable metabolic alkalosis and mild resting hypoxemia ( $PaCO_2 = 43.0$  mmHg,  $pH = 7.426$ ,  $PaO_2 = 63.8$  mmHg,  $HCO_3 = 27.7$  mmol/L,  $P(A-O)_2 = 12.0$  mmHg). Arterial blood sampling at peak exercise was not successful within an appropriate time interval.

### Calculation Of Predicted Post-Operative $VO_2$

Based on the extent of planned resection it is important to determine the remaining post-operative function. A post-operative predicted  $VO_2$  of less than 10 mL/kg/min is associated with virtually a 100% mortality rate (2). One may be tempted to simply subtract  $1/5^{th}$  of the pre-operative values to factor out the resected lobe from lung mass. However in heterogenous lung disease, such as emphysema, lung mass linearity to whole body  $VO_2$  cannot be assumed. Lung resection surgery results in some compensation for a loss of lung mass by increasing the function (inflation and perfusion) of the remaining lung so that total lung  $VE/Q$  is not as impaired as predicted. However, it is an inexact science due to the reason previously cited. In order to account for the post-surgical loss of the mass of affected lobe, several methods have been proposed for use in determining PPO status. Technitium -99 macroaggregates perfusion scans (split function studies) are widely employed for this purpose. This technique permits the determination of the contribution of each lobe of the lung based on actual perfusion, to functional capacity, and the ability to factor out segments to determine post-operative function. In the case of this patient; subsequent to the completion of the CPET, predicted post-operative values were completed for  $VO_2$ . The uptake values provided in the split lung perfusion study scan were used in this process and are reported in Table 2. The method of calculation was as follows:

Based on 41 % uptake in the left lung, and 59 % in the right lung, peak  $VO_2$  was partitioned to the contribution of each lung. The total partition for the left lung was then multiplied by 0.41 to account for the loss of the 59 % contribution of the left lower lobe. Thus the total post-lobectomy contribution of the left lung would be 41 % of the pre-operative total. This value was added to the partitioned value for the right lung to arrive at the predicted post-operative values. Calculations used to obtain these values are reported in Table 5.

### Determination Of Predicted Peak $VO_2$

Using the nomogram in Figure 3 (7), points were plotted on the horizontal axis corresponding to the patient's height and actual weight. A vertical line was drawn halfway between these two points extending to the diagonal line that indicated the patient's age. From this intersection, a horizontal line was drawn that extended to the vertical axis and revealed the predicted peak  $VO_2$  in L/min.

**Table 5. Predicted Post-Operative Calculations**

<b>VO<sub>2</sub></b>	<b>FVC</b>
$1.198 * .59 = 0.7068 \text{ L}$	$2.74 * .59 = 1.62 \text{ L}$
$1.198 * .41 = 0.491 \text{ L}$	$2.74 * .41 = 1.12 \text{ L}$
$0.491 * .41 = 0.2013 \text{ L}$	$1.12 * .41 = 0.461 \text{ L}$
$0.2013 \text{ L} + 0.7068 \text{ L} = 0.9081 \text{ L} \text{ (46 \%)}$	$0.461 \text{ L} + 1.62 \text{ L} = 2.08 \text{ L} \text{ (48 \%)}$
<b>FEV<sub>1</sub></b>	<b>D<sub>L</sub>CO</b>
$2.39 * .59 = 1.41 \text{ L}$	$8.0 * .59 = 4.72$
$2.39 * .41 = 0.98 \text{ L}$	$8.0 * .41 = 3.28$
$0.98 * .41 = 0.402 \text{ L}$	$3.28 * .41 = 1.34$
$0.402 \text{ L} + 1.41 = 1.81 \text{ L} \text{ (53 \%)}$	$1.34 \text{ L} + 4.72 = 6.06 \text{ (20 \%)}$

*% data refer to % post-surgical predicted reference value*

### Final Working Diagnosis

The CPET was interpreted as an abnormal exercise test, with moderate reduction in aerobic capacity (VO<sub>2</sub>) in part due to deconditioning. There was an abnormal breathing pattern consistent with hyperventilation. Cardiovascular factors likely contributed to exercise limitation. Deconditioning and loss of skeletal muscle due to malnourishment were also likely contributors to exercise intolerance.

This test was performed on a high-risk patient for lung re-sectional surgery with co-morbid conditions (celiac disease, consequent malnourishment, deconditioning) and continued smoking. The predicted post-operative values were based on a left lower lobectomy with a four-segment removal. For pre-operative evaluation, a VO<sub>2</sub> greater than 60 % predicted is consistent with more favorable surgical outcome (2,3,5). The peak VO<sub>2</sub> of 63 % predicted portends reasonable prognosis. Additionally, the patient attained a peak VO<sub>2</sub> of 1198 ml/min; 23.1 ml/kg/min which also provides evidence for a lowered risk (1,8,9,11). Thus, the addition of VO<sub>2</sub> peak to D<sub>L</sub>CO and FEV<sub>1</sub> and PPO values further supports a reasonable outcome. However, selection of appropriate reference values for underweight patients is a confounding factor in test sensitivity.

### Treatments And Outcomes

For this patient, continued use of pulmonary medications was recommended. The patient was also advised to stop smoking. Lobectomy was selected as the surgical intervention, with a four-segment removal from right upper lobe, as previously reported. Post-operative pulmonary rehabilitation is recommended with a post-operative CPET within three months of surgery. The patient underwent video-assisted thorascopic surgery (VATS) with curative intent.

### DISCUSSION

The referral of this particular patient for CPET was based on the need to address concerns expressed by the surgical colleagues due to the effects of celiac sprue, regarding the ability of the patient to tolerate surgery with minimal likelihood of morbidity or mortality.

The suggestion that an adjustment in the predicted peak VO<sub>2</sub> values for underweight patients has been addressed for some time. Initially this correction was accomplished by decreasing predicted peak VO<sub>2</sub> in direct proportion to the increase in body weight (7). However, due to the likelihood that there will be reductions in muscle mass as well as fat in underweight individuals, it is now suggested to calculate the mean of actual body weight and ideal body weight for determination of predicted peak VO<sub>2</sub> in the underweight patient (7). This adjustment is an acknowledgment of the detrimental impact of underweight on peak aerobic capacity.

Thus, adjustment of predicted peak  $\text{VO}_2$  values in situations where an underweight patient's suitability and/or eligibility for surgery are at issue, will reduce the scenario of a poor surgical candidate undergoing surgery.

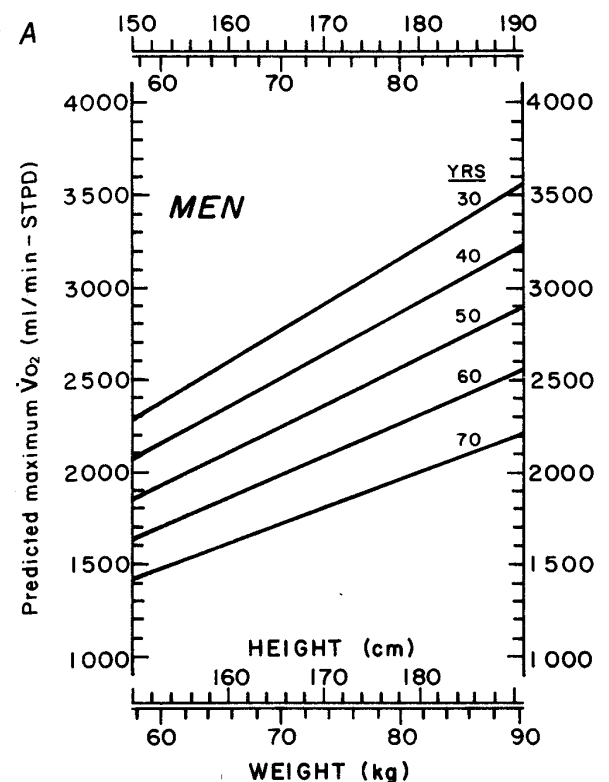
### Peak $\text{VO}_2$ As An Indicator Of Mortality Or Risk

The literature provides some degree of guidance for the application of peak  $\text{VO}_2$  measurement in the pre-operative assessment and selection of patients with severely symptomatic disease who may benefit from surgery, with an acceptable level of surgical risk. When used in conjunction with split lung perfusion scan, peak  $\text{VO}_2$  can prove a reasonable risk stratification tool, and provide prognostic data for the determination of post-operative status (12).

The use of cardiopulmonary function tests, spirometry and split function scans as predictors of post surgical outcomes has been studied in patients undergoing lung cancer resection surgery (13). It has been suggested that PPO  $\text{VO}_2$  may be an effective indicator of immediate surgical risk, though it may not be useful in predicting long-term disability. In patients whose post operative predicted  $\text{FEV}_1$  (PPO  $\text{FEV}_1$ ) was less than 40 %, exercise testing was conducted; if  $\text{VO}_2$  was between 10 ml/kg/min and 20 ml/kg/min, a split lung function test was performed. The pre-operative guidance offered in the algorithm utilized by (14) suggest the same guideline of > 40 % PPO  $\text{FEV}_1$  with the addition of PPO  $\text{D}_L\text{CO}$  also > 40% as a threshold for selection to undergo lung resection surgery. Likewise, a peak  $\text{VO}_2$  of > 15 mL/kg/min was considered a threshold at which surgical intervention can be undertaken. In the case of this particular patient, though his PPO  $\text{FEV}_1$  was > 40 % (54%), his weight status prompted the recommendation of cardiopulmonary exercise testing.

The issue then became the selection of appropriate reference values that would accurately reflect the patient's medical status. When using actual body weight of 52.16 kg, the predicted maximal  $\text{VO}_2$  using the Hansen cycling equation (15);  $\text{Predicted } \text{VO}_2 = (50.72 - (0.372 * \text{age})) / 1000$  was calculated as 1.51 L/min. The peak oxygen uptake attained in the CPET was 1.198 L/min, representing 79 % of the predicted maximal value. Since the lower 95 % confidence interval = 84 %, using actual body weight describes the patient as having a mildly reduced  $\text{VO}_2$ .

However, in examining the predicted values for this patient using the Hansen predicted weight equation (15):  $\text{Predicted } \text{VO}_2 = ((0.79 * \text{height in cm}) - 60.7 * (50.72 - (0.372 * \text{age})) / 1000$ , we obtain a



**Figure 3.** Illustrates a nomogram developed by Wasserman (7) to correct for the predicted  $\text{VO}_2$  of an underweight patient. The average between actual and predicted body weight is plotted on the x-axis and a vertical line drawn upward to intersect with the diagonal line denoting the age of the patient. A horizontal line is then drawn from that point to the Y-axis to determine the compensated predicted  $\text{VO}_2$ . This adjustment for the underweight patient can also be accomplished by inserting the mean of actual and predicted body weight in the following Hansen equation (15):  $\text{Predicted } \text{VO}_2 = (50.72 - (0.372 * \text{Age}) * \text{Weight}) / 1000$  (used with permission Lippincott, Williams, Wilkins)

predicted peak  $\text{VO}_2$  of 2.559 L/min. Therefore the peak  $\text{VO}_2$  of 1.198 L/min represents 47 % using this his predicted peak value using this equation.

We then performed a calculation of the patient's predicted  $\text{VO}_2$  based on the Wasserman (7) nomogram illustrated in Figure 3. The patient's height was plotted at 182 cm. The patient's actual body weight was plotted, and the midpoint between these two points (height and actual body weight) was plotted. A line was drawn from this mid-point as a vertical line extended to just above the diagonal indicator for 60 years of age. A horizontal line was then projected to the vertical axis indicating predicted  $\text{VO}_2$  peak. This produced a predicted  $\text{VO}_2$  value was determined as approximately 1.9 L/min. Thus, this patient's percent of predicted maximal aerobic capacity was estimated as 63 % using this method. The same consideration for body weight was necessary in the determination of predicted peak work rate; since the peak work attained was 70 Watts, which was 38 % of predicted when based on the predicted weight, but was 64 % when based on actual body weight.

In the case of this patient, the use of data based on a percent of a predicted value, reference values to determine prognosis was complicated by his extremely cachectic state. This was of concern to the medical staff as the peak  $\text{VO}_2$  data may have lead to misclassification of the patient relative to his suitability for lung cancer resection surgery.

Research appears warranted that produces normative values for exercise that accurately reflect normal maximal oxygen uptake values of an un-diseased population of individuals significantly below their ideal body weight.

## CONCLUSION

The use of cardiopulmonary exercise testing provides a valuable diagnostic tool in the preoperative assessment of candidates for lung resection candidates and in conjunction with split lung perfusion studies provides an accurate index of risk when based on peak oxygen uptake. The use of aerobic capacity in the risk stratification process appears to be a good independent indicator of surgical risk, and represents the single best parameter to evaluate both the pulmonary as well as cardiovascular reserves(12). Although  $\text{VO}_2$  has been shown to be a dependable predictor of postoperative outcomes, several recommendations are expressed in a percent of a predicted value. However, in the case of underweight patients, the use of standard predicted values based on actual body weight may result in misleading risk stratification profile; possibly portraying patient status more favorably than is reality. Likewise, the use of reference values based on predicted body weight may mistakenly exclude a patient.

## KEY POINTS

1. Underweight patients who are surgical candidates present a special challenge in determining appropriate reference values; in the underweight patient, the mean of actual and ideal body weights can provide a more reasonable estimate of peak oxygen consumption.
2. The use of peak aerobic capacity in the risk stratification process appears to be a good independent indicator of surgical risk. When used in conjunction with split lung perfusion (V/Q) scan to calculate post-operative predictive values, additional empirical evidence in the forecast of surgical risk and for postoperative functional impairment

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