Ventilatory equivalents of CO2 for the diagnosis of idiopathic hyperventilation syndrome

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BACKGROUND

The *idiopathic hyperventilation syndrome* (HVS), is one of the respiratory patterns referring to breathing dysfunction, when any other organic respiratory disease has been ruled out (1). It is common to suspect a HVS during the course of a maximal cardiopulmonary exercise test (CPET), when subjects ventilate excessively during the entire CPET. End-points of the CPET have also been suggested for the diagnosis of HVS with little information on their predictive properties (2)(3)(4)(5).

We aimed to explore the predictive properties of CPET outcomes for diagnosis of HVS.

METHODS

From medical records, we retrospectively investigated an ergocycle CPET of 14 subjects diagnosed as HVS positive (HVS+) on the basis of a positive hyperventilation provocation test (HVTest) and a significant score at the Nijmegen questionnaire (≥ 23/64)(6). Cases (HVS+) were matched with controls (HVS-) for gender (24 women, 4 men), age (46 *Yrs* ±14 *Yrs*), height (165 *cm* ±9 *cm*), weight (65 *kg* ±11 *kg*) and BMI (21 *kg/m2*±4 *kg/m2*). The 28 subjects underwent a spirometry which was within the expected values. For each outcome that showed a relevant difference between groups, ROC curve is drawn with Area Under Curve (AUC) and the cut-off with the best Sensitivity and Specificity is identified.

RESULTS

CPET outcomes	HVS- (n=14)	HVS+ (n=14)	Comparison	Predictive properties
At peak exercise	*mean±SD*	*mean±SD*	*p-value*	*AUC [IC95%] Cut-off (Sen/Sp)*
RER	1,21±0,15	1,17±0,19	0,530†	-
VO_2/kg *(ml/min/kg)*	22,5 ± 6,9	18,7 ± 8,0	0,185¥	-
VO_2 *(% predicted)*	89 ±23	68 ± 18	0,023† *	-
Load *(watts)*	120 ± 54	78 ± 54	0,035¥ *	0,74 [0,53 ; 0,94] 78,0 (0,86 ; 0,71)
$EqCO_2$	32 ± 4	38 ± 8	0,002† ***	0,83 [0,67 ; 0,98] 34,7 (0,71 ; 0,86)
$P_{ET}CO_2$ *(mmHg)*	36 ± 5	32 ± 5	0,023† *	0,75 [0,56 ; 0,93] 33,2 (0,71 ; 0,71)
$PECO_2$ *(mmHg)*	27 ± 4	23 ± 4	0,014¥ *	0,78 [0,59 ; 0,96] 24,3 (0,77 ; 0,71)

CPET outcomes	HVS- (n=14)	HVS+ (n=14)	Comparison	Predictive properties
At ventilatory threshold (VT_1)	*mean±SD*	*mean±SD*	*p-value*	*AUC [IC95%] Cut-off (Sen/Sp)*
VO_2/kg *(ml/min/kg)*	14,3 ± 3,7	12,8 ± 4,2	0,357†	-
$EqCO_2$	29 ± 2	34 ± 5	0,009† ***	0,78 [0,55 ; 1,00] 33,2 (0,70 ; 1,00)
EqO_2	28 ± 3	32 ± 7	0,043† *	0,68 [0,43 ; 0,93] 28,7 (0,70 ; 0,69)
V_D / V_T	21 ± 6	24 ± 2	0,029¥ *	0,76 [0,56 ; 0,95] 22,5 (0,82 ; 0,71)
$PECO_2$ *(mmHg)*	28 ± 3	24 ± 4	0,017† *	0,79 [0,59 ; 0,99] 26,7 (0,77 ; 0,82)

† *Parametric test* ¥ *Non parametric test*

RER: Respiratory Exchange Ratio ; VO_2 maximal oxygen consumption; $EqCO_2$: carbon dioxide equivalent; $PetCO_2$: end-tidal CO_2 pressure; $PECO_2$: mean partial pressure of exhaled CO_2; EqO_2 : oxygen equivalent; V_D / V_T: ratio of dead-space ventilation (V_D) to tidal ventilation (V_T).

At ventilatory threshold (VT_1), the best predictive properties appear in favour of $PECO_2$. Excellent properties of the more commonly reported $EqCO_2$ was retained. At maximal exercise, the best predictive properties appears for $EqCO_2$.

DISCUSSION

According to Wasserman, the $EqCO_2$ of female controls (HVS-) at VT_1 is 26,7 ± 2,6(7). In 1993, Kinnula et al. compared HVS- to HVS+ and found that an $EqCO_2$ > 35 allows the identification of HVS+ with excellent Sen/Sp (0.91/1.00)(2). Ionescu et al. recently confirmed this cut-off of $EqCO_2$ and introduced two additional criteria for diagnosing HVS+ : *(1)* a $PetCO_2$ <30 mmHg at rest and at exercise; *(2)* an erratic ventilatory response to load intensity (in terms of BR and/or Vt)(5). Brat et al. found that the $EqCO_2$ in HVS+ at peak exercise ranged from 35 to 43, without further clarification on the predictive values for the HVS+(3). Having selected the HVS+ and HVS- in our sample on more rigorous criteria (HVTest and Nijmegen questionnaire), in order to maximise the true positives and true negatives, we observed some comparable results, with the $EqCO_2$ showing the best predictive properties for diagnosis HVS.

While rigorous criteria were used to select HVS+ and HVS- to maximise the true positives and true negatives, we observe at peak exercise results suggesting differences in physical condition between groups. The $EqCO_2$ at VT_1 shows the best predictive properties for HVS diagnosis, independent of the fitness level.

CONCLUSION

Patients with HVS have specific exercise responses :

(1) As previously described, EqCO2 at peak exercise > 34,7 identifies HVS+, however with some nuances on Sp (0,71/0,86)

(2) EqCO2 at VT > 33,2 identifies HVS+ with maximum specificity (Sen/Sp=0,70/1,00)

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