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The pattern and timing of breathing during incremental exercise: a normative study

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ABSTRACT: Clinical evaluation of the pattern and timing of breathing during submaximal exercise can be valuable for the identification of the mechanical ventilatory consequences of different disease processes and for assessing the efficacy of certain interventions.

Sedentary individuals (60 male/60 female, aged 20–80 yrs) were randomly selected from >8,000 subjects and submitted to ramp incremental cycle ergometry. Tidal volume (*V*T)/ resting inspiratory capacity, respiratory frequency, total respiratory time (*T*tot), inspiratory time (*T*I), expiratory time (*T*E), duty cycle (*T*I/*T*tot) and mean inspiratory flow (*V*T/*T*I) were analysed at selected submaximal ventilatory intensities.

Senescence and female sex were associated with a more tachypnoeic breathing pattern during isoventilation. The decline in *T*tot was proportional to the *T*I and *T*E reductions, *i.e.* *T*I/*T*tot was remarkably constant across age strata, independent of sex. The pattern, but not timing, of breathing was also influenced by weight and height; a set of demographically and anthropometrically based prediction equations are therefore presented.

These data provide a frame of reference for assessing the normality of some clinically useful indices of the pattern and timing of breathing during incremental cycle ergometry in sedentary males and females aged 20–80 yrs.

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The increased metabolic demands associated with dynamic exercise determine a range of integrated cardiorespiratory adjustments for maintaining the homeostasis of the internal milieu [1]. The ventilatory apparatus (lungs and chest wall) is centrally involved in these responses since it provides the functional and structural basis for external gas exchange. The general characteristics of the ventilatory response to progressive exercise are well known; several studies have provided reference values for judging the adequacy of the system functioning under these special circumstances [2–5].

It has long been recognised that pulmonary ventilation, at least during moderate dynamic exercise, closely follows carbon dioxide output ($V'\mathrm{CO}_2$). At higher work rates, however, ventilation increases out of proportion with $V'\mathrm{CO}_2$, mainly to compensate for the ongoing lacticacidaemia [1]. In this context, it is intuitive to assume that a given ventilatory output could result from a wide variation in the combined determinants of "air pumping" capacity, namely amplitude (tidal volume (*V*T)) and frequency (respiratory frequency (*f*R)). Similar considerations might be applied to the timing components of the breath, such as inspiratory and expiratory time (*T*I and *T*E, respectively) and the duty cycle, *i.e.* the fraction of the breathing cycle (*T*tot) during which inspiration takes place (*T*I/*T*tot) [6, 7].

Several physiological mechanisms might modulate the pattern and timing components of exercise hyperpnoea, the most obvious being age and sex. For instance, ageing is associated with a decline in chest compliance and lung elastance, reduced ventilatory efficiency and poorer respiratory muscle performance [8]. Conversely, females exhibit smaller lung volumes and reduced inspiratory and expiratory flow rates [9]. There is growing evidence that these responses could be clinically useful for: 1) assessing mechanisms of exercise impairment [10, 11], with prognostic implications [12]; 2) helping in the identification of mechanical ventilatory abnormalities [13, 14]; and 3) unravelling the effects of interventions, such as pulmonary rehabilitation [15] and lung volume-reduction surgery [16].

Surprisingly, this relevant aspect of the ventilatory response has been overlooked in previous normative investigations [2–5]. For instance, the few studies that have given reference values provided them at maximum exercise [4], or described only V_T at one or two submaximal intensities [17, 18]. Other experimental studies involved a small number of subjects [19, 20] or narrow age ranges [21–24]. The present authors are not aware of any normative study that has looked comprehensively at the pattern and timing of breathing at several ventilatory intensities during rapidly incremental exercise in a large number of sedentary subjects of broad age range.

The present objective was, therefore, to establish a frame of reference for assessing the normalcy of the pattern and timing of breathing at selected submaximal ventilatory stresses. For this purpose, a randomly selected sample of 120 sedentary males and females, aged 20–80 yrs, who were submitted to a standard rapidly incremental cycle ergometer test to the limit of tolerance, was evaluated.

Methods

Study design and subjects

This study was performed on a random sample of ancillary staff (clerical and manual workers) from a large university population using a controlled prospective design. The subjects were chosen randomly by electronic selection from this total population (n=8,226); a total of 120 individuals (60 males, 60 females), evenly distributed in age groups (20–39, 40–59 and 60–80 yrs), were evaluated (table 1). No subject had had any previous experience with cardiopulmonary exercise tests. Reference values for pulmonary gas exchange, ventilatory and cardiovascular variables obtained using this sample have been presented elsewhere [5, 25].

After selection, subjects were contacted and the purpose of the study explained. If they refused to participate, the reasons for nonparticipation were established using a questionnaire, which also determined previous and current health, leisure and sports habits, and anthropometric measurements (height and weight). Thus care was taken to avoiding selecting a population of participants who had a different profile from that of nonparticipants. Further selection was always performed if a subject refused to participate or was excluded (see below); this continued until the desired number of subjects (120) had been obtained.

Subjects who had a medical history or physical or laboratory findings of cardiac, respiratory, haematological (haemoglobin <14 g·dL^{-1} in males and <12 g·dL^{-1} in females), metabolic or neuromuscular disease were excluded from the study. Although normal pulmonary function data (table 1) and the absence of respiratory symptoms were required for entry into the study sample, subjects who had a current or past history of smoking of <25 pack-yrs were not excluded. Underweight subjects (body mass index (BMI) <18.5) or those who were grade III overweight (BMI >40) were excluded, as were subjects who engaged in intense athletic activity (>8 h·week^{-1} activity involving large group muscles). The distribution of reasons for exclusion (n=213) were as follows: systemic arterial hypertension (n=54), cardiac disease (n=36), previous severe illness (n=33), respiratory disease (n=27), osteomuscular disorder (n=18), diabetes mellitus (n=11), use of drugs (n=8), underweight (n=7), overweight (n=11) and athleticism (n=8). In summary, a total of 333 subjects were screened to establish the study group of 120 subjects. Informed consent (as approved by the Institutional Medical Ethics Committee) was obtained from all subjects.

Level of regular physical activity

The BAECKE *et al.* [26] questionnaire for epidemiological studies was used to detail and quantify information regarding occupation, sports activities and leisure habits. Subjects rated their usual physical activity using a scale of 1–5 (5 typically representing the most active) with eight questions about

Table 1. – Population characteristics according to sex and age

	Males			Females		
	20–39 yrs	40–59 yrs	60–80 yrs	20–39 yrs	40–59 yrs	60–80 yrs
Anthropometric						
Height cm	171.2±5.3**	166.5±6.7	167.4±6.2	160.3±6.7$^{**,\#\#}$	156.9±5.8$^{\#\#}$	155.2±6.2$^{\#\#}$
Weight kg	72.8±10.7	77.0±15.2	73.7±8.5	63.9±13.8$^{\#\#}$	63.4±10.7$^{\#\#}$	62.8±8.5$^{\#\#}$
BMI kg·m^{-2}	25.2±3.3	27.1±5.2	25.9±3.1	27.5±8.2	26.3±3.6	26.0±3.5
Resting functional						
FVC % pred	93.3±10.5	104.5±8.7	96.3±7.9	90.5±8.1	98.5±10.1	101.7±12.9
FEV1 % pred	89.7±7.5	93.1±5.9	90.5±8.1	92.5±10.3	87.9±5.7	98.1±12.0
FEV1/FVC	0.80±0.06	0.77±0.04	0.75±0.05	0.83±0.04	0.78±0.04	0.75±0.04
TLC % pred	108.3±14.2	95.2±12.5	102.9±11.9	90.8±18.1	110.1±10.3	105.3±15.8
$D_{L,CO}$ % pred	98.3±18.6	105.2±15.5	89.9±12.9	100.8±20.1	111.1±21.8	106.4±17.8
MIP cmH_2O	133.3±19.4**	117.4±25.5	92.5±24.3	93.6±11.4**	84.4±9.1$^{\#\#}$	75.7±4.8$^{\#\#}$
MVV L·min^{-1}	168.5±25.6**	140.4±30.3	120.7±23.2	124.2±12.1$^{**,\#\#}$	110.9±14.3$^{\#\#}$	94.6±18.6$^{\#\#}$
Peak exercise						
Work-rate W	185±32**	143±30	105±19	116±19$^{**,\#\#}$	93±17$^{\#\#}$	61±15$^{\#\#}$
$V'O_2$ mL·min^{-1}	2621±366**	2085±345	1585±210	1679±228$^{**,\#\#}$	1319±143$^{\#\#}$	1052±116$^{\#\#}$
RER	1.21±0.08	1.18±0.06	1.17±0.10	1.16±0.08	1.15±0.09	1.12±0.10
f_C beats·min^{-1}	187±10**	169±11	149±17	182±12**	174±11	148±17
% pred	99.3±3.1	95.0±3.5	101.3±3.5	97.7±3.5	101.1±3.4	102.5±2.2
$V'_{E,max}$ L·min^{-1}	119.6±28.3**	98.7±22.2	76.7±11.7	75.8±13.7$^{**,\#\#}$	67.3±11.2$^{\#\#}$	50.1±10.0$^{\#\#}$
$V'_{E,max}$/MVV	0.69±0.12	0.69±0.11	0.67±0.13	0.60±0.11$^{\#\#}$	0.60±0.11$^{\#\#}$	0.56±0.12$^{\#\#}$

Data are presented as mean±SD (n=20 for each group). BMI: body mass index; FVC: forced vital capacity; FEV1: forced expiratory volume in one second; TLC: total lung capacity; $D_{L,CO}$: lung diffusion capacity for carbon monoxide; MIP: maximal inspiratory pressure; MVV: maximal voluntary ventilation; $V'O_2$: oxygen uptake; RER: respiratory exchange ratio; f_C: cardiac frequency; $V'_{E,max}$: maximal minute ventilation; % pred: percentage of the predicted value. **: $p<0.01$ *versus* other age groups within sex; $^{\#\#}$: $p<0.01$ *versus* males.

occupation, four about sport activities and four about habitual leisure habits. Results were expressed as the sum of the scores. According to this questionnaire, 102 (85%) subjects were considered sedentary with a total score of <8; of these, 70 subjects had scores of 6–8 and 32 of <6. The remaining 18 (15%) subjects had scores of >8 and were considered more active but still nontrained subjects. No subject used cycling for daily transportation or during routine leisure activities.

Pulmonary function tests

Spirometric tests were performed using a CPF-System (Medical Graphics Corp., St Paul, MN, USA), with flow measurement carried out using a calibrated pneumotachograph (Fleisch No. 3; Hans-Rudolph, Inc., Kansas City, MO, USA). The subjects completed at least three acceptable maximal forced expiratory manoeuvres; technical procedures, acceptability and reproducibility criteria were those recommended by the American Thoracic Society [27]. Forced vital capacity and forced expiratory volume in one second were recorded at body temperature and ambient pressure, and saturated with water vapour (BTPS). Values were compared with those predicted by KNUDSON *et al.* [28]. Maximal voluntary ventilation was established as the largest volume that subjects could breathe into and out of their lungs during a 12-s interval with maximal voluntary effort. At least two acceptable manoeuvres were obtained (with $\leqslant$10% difference between them) and, after flow integration, the highest value was recorded by extrapolating the 12-s accumulated volume to 1 min (at BTPS).

Static lung volumes were determined by breath-by-breath open-circuit nitrogen wash-out, using a PF-DX System (Medical Graphics Corp.) connected to a dedicated microcomputer. Personnel, technique, procedures and calibration were standardised [29, 30]. The recorded total lung capacity (TLC; at BTPS) was the mean of at least three acceptable measurements which were within 10% of the largest value. Values were compared with those predicted by STOCKS and QUANJER [30]. Carbon monoxide diffusing capacity of the lung was measured by a modified Krogh technique (single-breath) using a computer-based automated system (PF-DX System). At least two tests were performed with results within 10% or 3 mL $CO \cdot min^{-1} \cdot mmHg^{-1}$; absolute values were reported at standard temperature and pressure, dry (STPD). Values were compared with those predicted by KNUDSON *et al.* [31].

Maximal inspiratory pressure was obtained at functional residual capacity, with subjects wearing nose clips and with a rigid plastic flanged mouthpiece in place. Subjects were connected to a manual shutter apparatus and the pressures measured using a calibrated manometer with an aneroid-type gauge (±300 cmH_2O). Inspiratory effort was sustained for $\geqslant$1 s; subjects performed three to five acceptable and reproducible manoeuvres ($\leqslant$10% difference between values), with the value recorded being the highest unless it derived from the last effort [29].

Cardiopulmonary exercise testing

The exercise tests were carried out on an electromagnetically-braked cycle ergometer (CPE 2000; Medical Graphics Corp.), with gas exchange and ventilatory variables being analysed breath-by-breath using a calibrated computer-based exercise system (MGC-CPX System; Medical Graphics Corp.). Using this system, a breath is defined as the interval between onset and end of CO_2 wash-out and oxygen (O_2) wash-in; breaths with a total volume of $\leqslant$150 mL are automatically discarded. The CO_2 and O_2 analysers were calibrated before and after each test using a two-point measure: a calibration gas (5% CO_2, 12% O_2, balance nitrogen) and a reference gas (room air after ambient temperature and pressure, saturated, to STPD correction). A Fleisch No. 3 pneumotachograph was also calibrated with a 3-L syringe using different flow profiles. Periodically, the overall output data system was validated against a respiratory gas exchange simulator that allows a range of metabolic rates to be established (0.2–5.0 $L \cdot min^{-1}$), with a resulting accuracy of ±2%; this validation, however, does not take into consideration issues such as humidity and temperature. During the exercise tests, only two investigators were allowed in the laboratory, and room temperature and humidity were controlled by air conditioning. All tests were performed in the same laboratory at an altitude of 680 m above sea level (São Paulo, Brazil), barometric pressure of 91.1–93.0 kPa (685–699 mmHg) and ambient temperature of 18–20°C.

Before the exercise tests, inspiratory capacity (IC) was determined by getting the subject to breathe normally for at least five breaths and then inhale maximally from the resting expiratory level. The value recorded was the mean of two reproducible values (<5% difference). The exercise test consisted of the following: 1) 2 min at rest; 2) 3 min with "zero" workload, obtained through an electrical system which moves the ergometer flywheel at 60 rpm; 3) an incremental phase; and 4) a 4-min recovery period. Patients wore a nose clip and breathed through a mouthpiece connected to a T-shaped low-resistance nonrebreathing valve (Series 2700; Hans-Rudolph, Inc., Kansas City, MO, USA). Inspiratory and expiratory resistances were 0.5–0.6 and 1.0–1.1 cmH_2O at 50 $L \cdot min^{-1}$ and 100 $L \cdot min^{-1}$ ventilation, respectively. The total dead space of the breathing apparatus (valve and mouthpiece) was 115 mL; this value was entered in the system software for corrected calculation of the variables.

The power (work-rate) was continuously increased in a linear "ramp" pattern (10–25 $W \cdot min^{-1}$ in females and 15–30 $W \cdot min^{-1}$ in males); the incremental rate was individually selected in such a way that the ramp duration was >8 and <12 min (mean±SD 10.3±1.1 min) in all subjects [32]. Participants were free to choose the pedalling frequency provided that it was not <40 rpm. The following data were obtained breath-by-breath and expressed as 15-s averages: pulmonary O_2 uptake ($V'O_2$); minute ventilation ($V'E$); V_T; f_R; T_{tot}; T_I; T_E; T_I/T_{tot}; and mean inspiratory flow (V_T/T_I). Cardiac electrical activity and cardiac frequency (in beats per minute) were recorded continuously (ECG-3^{TM}; Funbec, São Paulo, Brazil).

$V'O_2$ at the lactate threshold (LT) was estimated using the gas exchange method and visually inspecting the inflection point of $V'CO_2$ expressed as a function of $V'O_2$ (modified V-slope) [33] and by the ventilatory method, when $V'E/V'O_2$ and end-tidal oxygen tension increased while $V'E/V'CO_2$ and end-tidal carbon dioxide tension remained stable. The respiratory compensation point (RCP) was defined as the ventilatory level at which $V'E$ started to change out of proportion with $V'CO_2$, *i.e.* at which a systematic increase in $V'E/V'CO_2$ accompanied by inflexion of the $V'E$ response expressed as a function of $V'CO_2$ occurred.

Data analysis

After confirmation of normal distribution, data are reported as mean±SD; they were analysed at absolute and relative isoventilation (see Results section). One-way analysis of variance and t-tests were used to determine differences among age groups and between sexes, respectively. Backward stepwise multiple linear regression was carried out using the technique of least squares minimisation with inclusion of exercise responses as dependent variables and age, weight, height and their interactions with sex (assuming sex as the "dummy variable") as independent variables. The probability of a type I error was established as 0.05 for all tests.

Results

General response characteristics

The following patterns of response as a function of V'_E were more commonly found, irrespective of sex and age: 1) a curvilinear increase in V_T as a fraction of IC (fig. 1a); 2) a progressive increase in f_R, which was more prominent near V_T stabilisation (fig. 1c); 3) a linear decrease in T_I but a curvilinear decline in T_E (fig. 2a and c); 4) a relatively constant T_I/T_{tot} (fig. 2e); and 5) a linear increase in V_T/T_I (fig. 2g).

Data were pooled only after confirmation that there was no systematic influence of regular physical activity pattern, baseline lung function (table 1) and rate of power increment on the variables of interest ($p>0.05$).

Breathing pattern at absolute isoventilation

As expected, owing to the large differences in body dimensions (table 1), males exhibited significantly higher

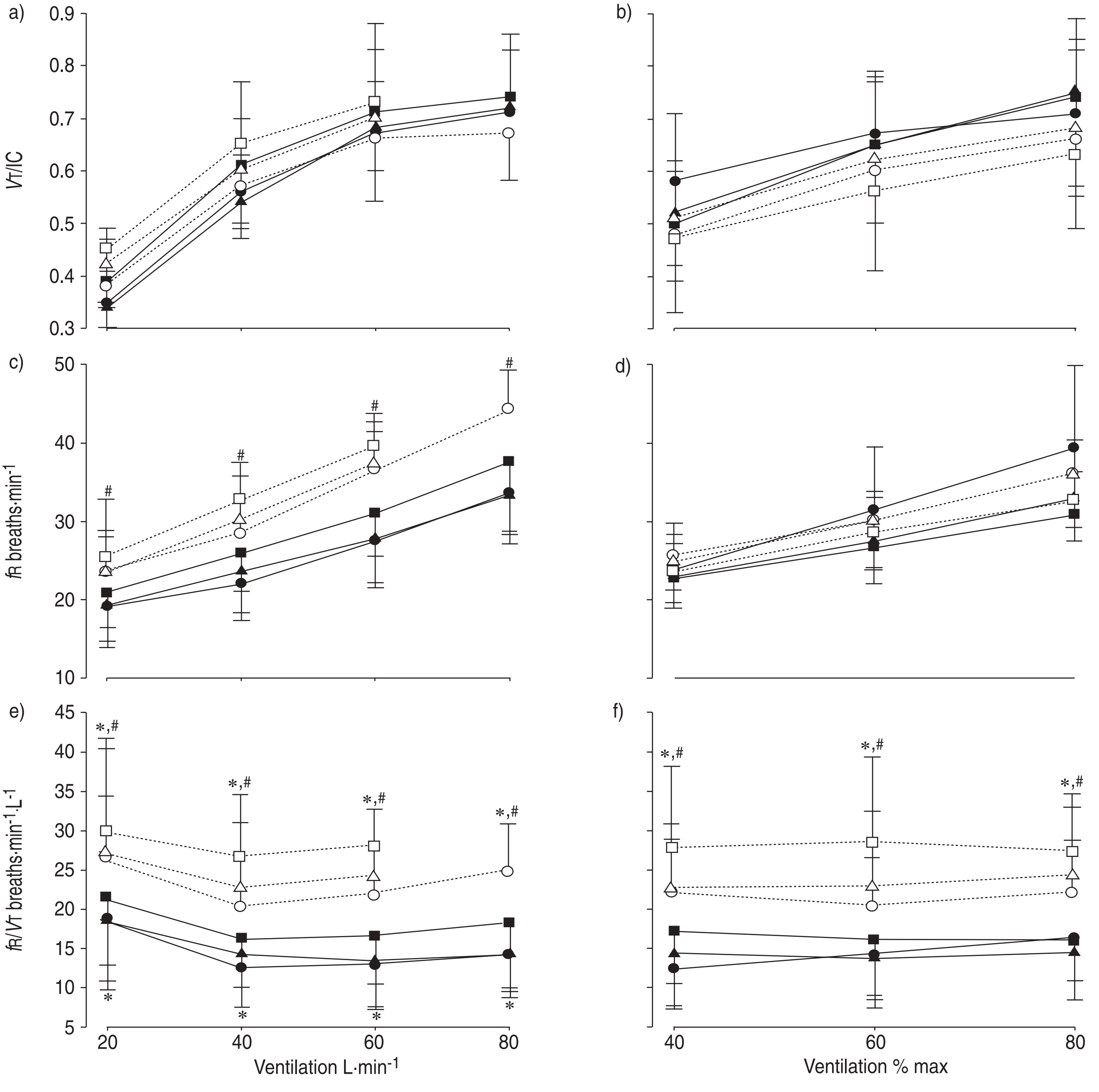

Fig. 1. – Breathing pattern during incremental exercise expressed as a function of absolute (a, c and e) and relative (b, d and f) ventilatory response in males (——) and females (·········) aged 20–39 (●, ○), 40–59 (▲, △) and 60–80 yrs (■, □). Vertical bars represent SD. Note that, in the female group, only the youngest subjects reached ventilation at 80 $L \cdot min^{-1}$. V_T: tidal volume; IC: inspiratory capacity; f_R: respiratory frequency; % max: percentage of maximal attained. *: $p<0.05$ *versus* other age groups within sex; #: $p<0.05$ *versus* males of same age.

resting ICs than females ($p<0.01$). In addition, older subjects exhibited lower ICs than their younger counterparts within both sexes: 3.67±0.53 *versus* 2.61±0.50 L at 20–39 yrs, 3.18±0.58 *versus* 2.36±0.30 L at 40–59 yrs, and 2.85±0.66 *versus* 2.07±0.38 L at 60–80 yrs (males *versus* females).

No systematic effect of sex on exercise V_T/IC was found

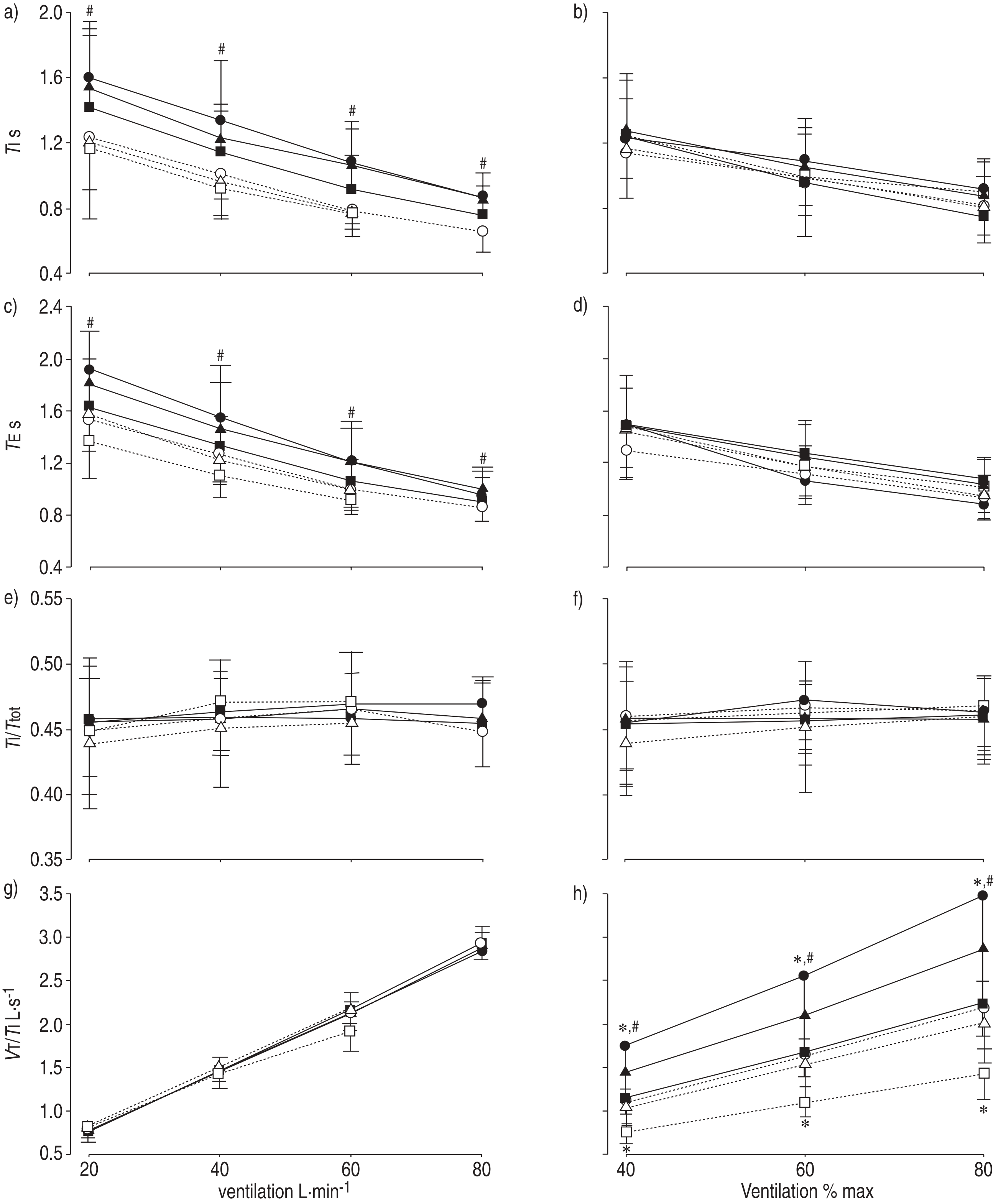

Fig. 2. – Time-related components of the breathing cycle during incremental exercise expressed as a function of absolute (a, c, e and g) and relative (b, d, f and h) ventilatory response in males (——) and females (·········) aged 20–39 (●, ○), 40–59 (▲, △) and 60–80 yrs (■, □). Vertical bars represent SD. Note that, in the female group, only the youngest subjects reached ventilation at 80 L·min^{-1}. T_I: inspiratory time; T_E: expiratory time; T_tot: total respiratory time; V_T: tidal volume; % max: percentage of maximal attained. *: $p<0.05$ *versus* other age groups within sex; #: $p<0.05$ *versus* females of same age.

(tables 2 and 3; fig. 1a), *i.e.* absolute *V*T was lower in females than in males ($p<0.05$). Conversely, older and leaner subjects used greater proportions of their resting IC during exercise; the prediction equations for this ratio, as a function of age and weight, are presented in table 3.

As a consequence of the lower *V*T at isoventilation, females and older subjects exhibited a more tachypnoeic breathing pattern at all exercise intensities, *i.e.* higher *f*R and *f*R/*V*T (fig. 1c and e; table 2). Interestingly, no independent effect of "age" was found when "height" was considered in a multiple regression analysis; stature and sex, therefore, were sufficient to predict *f*R and *f*R/*V*T in both sexes (table 3).

Timing of breathing at absolute isoventilation

As already mentioned, females and older subjects exhibited higher *f*R than males and younger individuals; lower *T*tot in these groups were associated with proportional declines in *T*I and *T*E (fig. 2a and c; table 2). Therefore, *T*I/*T*tot did not differ between sexes or among age groups (fig. 2e; table 2). On multiple regression analysis, however, age had only a marginally significant effect on *T*I and *T*E ($p=0.10$), *i.e.* sex was the only predictor of the respiratory times (table 3). Considering that *V*′E=*V*T/*T*I×*T*I/*T*tot [34], *V*T/*T*I remained constant across age strata and ventilatory intensities (fig. 2g; table 2).

Pattern and timing of breathing at relative isoventilation

The pattern and timing of breathing during rapidly incremental exercise can be influenced by the estimated LT and the RCP [1, 35]. In order to make the sex and age groups more comparable, the data were also analysed at relative isoventilation, *i.e.* 40, 60 and 80% of maximal *V*′E (*V*′E,max) (fig. 1b, d and f and 2b, d, f and h). For the great majority of the subjects (48 males and 50 females), these points corresponded to sub-LT, LT/RCP, and supra-RCP intensities.

In keeping with the large differences in *V*′E,max (table 1), absolute *V*′E were lower in females and older subjects at each of the relative submaximal intensities ($p<0.01$). Results from this complementary analysis were consistent with those mentioned above: older and female subjects presented a more tachypnoeic breathing pattern (fig. 1f), with proportional reductions in *T*I and *T*E (fig. 2b, d and f). As a consequence, the reduced *V*′E in these subjects was largely a result of lower *V*T/*T*I ($p<0.01$) (fig. 1h).

Table 2. – Pattern and timing of breathing at different levels of ventilatory stress according to sex and age

	Males			Females		
	20–39 yrs	40–59 yrs	60–80 yrs	20–39 yrs	40–59 yrs	60–80 yrs
*V*T/IC						
20 L·min^{-1}	0.35±0.10	0.35±0.06	0.38±0.10	0.27±0.09	0.42±0.08	0.45±0.10
40 L·min^{-1}	0.56±0.10	0.54±0.09	0.61±0.11	0.57±0.11	0.57±0.10	0.65±0.10
60 L·min^{-1}	0.68±0.11	0.69±0.09	0.72±0.11	0.66±0.11	0.70±0.10	0.73±0.11
80 L·min^{-1}	0.71±0.11	0.76±0.10	0.75±0.10	0.67±0.09		
*f*R breaths·min^{-1}						
20 L·min^{-1}	19±5	19±4	21±4	24±4$^{\#}$	23±5$^{\#}$	25±5$^{\#}$
40 L·min^{-1}	22±5	24±5	26±5	28±4$^{\#}$	31±5$^{\#}$	33±4$^{\#}$
60 L·min^{-1}	28±4	28±4	31±4	37±5$^{\#}$	37±4$^{\#}$	40±3$^{\#}$
80 L·min^{-1}	34±5	34±5	38±5	44±5$^{\#}$		
*f*R/*V*T breaths·min^{-1}·L^{-1}						
20 L·min^{-1}	18.9±6.1	18.5±6.6	21.6±6.7*	26.6±6.9$^{\#}$	27.3±7.3$^{\#}$	30.3±6.1$^{*,\#}$
40 L·min^{-1}	12.6±5.1	14.3±6.6	16.3±6.2*	20.3±5.8$^{\#}$	22.8±7.3$^{\#}$	26.7±5.8$^{*,\#}$
60 L·min^{-1}	13.1±5.7	13.4±5.8	16.6±6.1*	21.9±6.0$^{\#}$	24.2±6.6$^{\#}$	28.1±4.8$^{*,\#}$
80 L·min^{-1}	14.3±4.3	14.3±4.3	18.3±8.6*	24.9±5.9$^{\#}$		
*T*I s						
20 L·min^{-1}	1.6±0.4	1.5±0.4	1.4±0.3	1.2±0.3$^{\#}$	1.2±0.3$^{\#}$	1.1±0.3$^{\#}$
40 L·min^{-1}	1.3±0.4	1.2±0.2	1.1±0.2	1.0±0.1$^{\#}$	1.0±0.2$^{\#}$	0.9±0.2$^{\#}$
60 L·min^{-1}	1.1±0.3	1.1±0.2	0.9±0.2	0.8±0.1$^{\#}$	0.8±0.1$^{\#}$	0.7±0.1$^{\#}$
80 L·min^{-1}	0.9±0.1	0.9±0.2	0.8±0.2	0.7±0.1$^{\#}$		
*T*E s						
20 L·min^{-1}	1.9±0.4	1.8±0.4	1.6±0.4	1.5±0.3$^{\#}$	1.5±0.3$^{\#}$	1.3±0.3$^{\#}$
40 L·min^{-1}	1.6±0.4	1.5±0.4	1.3±0.2	1.2±0.2$^{\#}$	1.1±0.2$^{\#}$	1.0±0.2$^{\#}$
60 L·min^{-1}	1.2±0.3	1.2±0.3	1.0±0.1	0.9±0.1$^{\#}$	0.9±0.1$^{\#}$	0.8±0.1$^{\#}$
80 L·min^{-1}	1.0±0.2	1.0±0.2	0.9±0.1	0.8±0.1$^{\#}$		
*T*I/*T*tot						
20 L·min^{-1}	0.45±0.03	0.46±0.03	0.46±0.04	0.45±0.04	0.45±0.04	0.46±0.04
40 L·min^{-1}	0.46±0.04	0.46±0.03	0.46±0.03	0.45±0.04	0.45±0.04	0.47±0.03
60 L·min^{-1}	0.47±0.04	0.47±0.03	0.46±0.03	0.47±0.04	0.46±0.03	0.47±0.03
80 L·min^{-1}	0.47±0.02	0.46±0.03	0.45±0.03	0.45±0.03		
*V*T/*T*I mL·s^{-1}						
20 L·min^{-1}	765±74	773±102	758±79	783±98	801±100	826±182
40 L·min^{-1}	1454±167	1477±128	1471±125	1450±113	1511±161	1427±169
60 L·min^{-1}	2151±213	2120±131	2168±190	2127±202	2155±151	2027±236
80 L·min^{-1}	2830±225	2882±244	2936±188	2933±188		

Data are presented as mean±SD (n=20 for each group). VT: tidal volume; IC: inspiratory capacity; *f*R: respiratory frequency; *T*I: inspiratory time; *T*E: expiratory time; *T*tot: total respiratory time. Note that insufficient numbers of 40–59- and 60–80-yr-old females reached ventilation at 80 L·min^{-1}. *: $p<0.05$ *versus* other age groups within sex; $^{\#}$: $p<0.05$ *versus* males of same age.

Table 3. – Linear prediction equations for pattern and timing of breathing at different levels of ventilatory stress according to age, anthropometric attributes and sex

	Age yrs	Weight kg	Height cm	Sex$^{\#}$	Constant	R^2	95% CI
V_T/IC							
20 L·min^{-1}	0.00107±0.001	-0.00312±0.001			0.55±0.06	0.175	0.17
40 L·min^{-1}	0.00147±0.001	-0.00382±0.001			0.78±0.07	0.177	0.21
60 L·min^{-1}	0.00124±0.001	-0.00297±0.001			0.83±0.08	0.115	0.24
f_R breaths·min^{-1}							
20 L·min^{-1}			-0.177±0.073	-2.364±1.236	52±10	0.183	8
40 L·min^{-1}			-0.233±0.069	-4.074±1.166	67±9	0.358	8
60 L·min^{-1}			-0.252±0.082	-6.071±1.332	77±12	0.420	8
f_R/V_T breaths·min^{-1}·L^{-1}							
20 L·min^{-1}			-0.362±0.140	-4.359±2.376	84.9±22.1	0.189	19.7
40 L·min^{-1}			-0.376±0.093	-4.782±1.560	82.4±14.6	0.358	12.9
60 L·min^{-1}			-0.326±0.094	-6.452±1.530	75.6±14.9	0.421	12.4
T_I s							
20 L·min^{-1}				0.33±0.08	1.19±0.06	0.117	0.42
40 L·min^{-1}				0.28±0.04	0.96±0.03	0.251	0.26
60 L·min^{-1}				0.25±0.04	0.77±0.02	0.283	0.20
T_E s							
20 L·min^{-1}				0.32±0.08	1.46±0.06	0.119	0.45
40 L·min^{-1}				0.32±0.05	1.12±0.04	0.241	0.28
60 L·min^{-1}				0.28±0.04	0.89±0.03	0.291	0.21

Data are presented as mean±SEM. CI: two-sided confidence limits; V_T: tidal volume; IC: inspiratory capacity; f_R: respiratory frequency; T_I: inspiratory time; T_E: expiratory time. $^{\#}$: males 1, females 0.

Discussion

A new frame of reference for evaluating the normality of the pattern and timing of breathing during rapidly incremental cycle ergometry is presented. These data can be used to assess the mechanical/ventilatory consequences of cardiorespiratory disorders and to interpret the efficacy of selected interventions [10–16]. The main original aspects of the present study are: 1) to the present authors' knowledge, it is the first normative study that has looked comprehensively at these responses in a large number of randomly selected males and females, with an age span of six decades; 2) the study design permits assessment of very sedentary subjects who are unfamiliar with cardiopulmonary exercise tests, and, therefore, resembling the population usually referred for clinical evaluation; and 3) this study provides not only descriptive data but also a set of linear prediction equations which consider age, sex and anthropometric attributes (tables 2 and 3, respectively). The present reference study, therefore, might provide representative values which are particularly suitable for clinical use during routine cardiopulmonary exercise testing in sedentary subjects aged up to 80 yrs.

Breathing pattern

The present results indicate that the smaller volume available for inspiration (IC) has a profound effect on breathing pattern during exercise in older and female subjects. As shown in figure 1, there were no differences in V_T/IC ratios between the sexes and only a small positive effect of age could be found, *i.e.* absolute V_T were markedly lower at the same ventilation in these groups. These results are consistent, for example, with those of McCLARAN *et al.* [9], who also found that females show similar isoventilation V_T/vital capacity to males. Interestingly, GALLAGHER *et al.* [34] demonstrated that this Hering-Breuer inspiratory volume threshold is reached as a stereotypic response to the level of ventilation attained. Although a rapid shallow breathing pattern can reduce peak inspiratory muscle effort and, therefore, the sense of respiratory effort, this pattern induces greater ventilation of the anatomical dead space, *i.e.* a lower ventilatory efficiency. Indeed, it was found, in these same subjects, that the slope of the linear V'_E/V'_{CO_2} relationship, an index of ventilatory "inefficiency", increased with age, especially in females [25].

The effects of senescence on the respiratory/mechanical adjustments that occur during dynamic exercise have been extensively described [9, 21, 23, 24, 35, 36]. A more superficial breathing pattern is particularly deleterious in older subjects, who characteristically exhibit an enlarged dead space [8]. Previous studies have also shown that end-expiratory lung volume during exercise increases with age [23, 24, 36]. Although operational lung volumes were not measured, it is conceivable that the shallower breathing pattern could constitute an adaptive response in order to avoid further decrease in inspiratory reserve volume. It should be noted, however, that the negative effect of age on some aspects of the breathing pattern response did not remain significant when height was considered in the multiple regression analysis (table 3); this finding was probably related to the high degree of multicollinearity between age and anthropometric characteristics in the present sample.

Timing of breathing

The behaviour of the timing component was remarkably reproducible across age groups; the rates of decline in T_I and T_E were not different between old and young subjects for both sexes. As expected from the lower T_{tot} (f_R=1/T_{tot}), however, absolute values of T_I and T_E tended to be lower in the older subjects and females (table 2). Similar results were described by PRIOUX *et al.* [35], who found that increased V'_E for a given power output in older subjects was due to higher V_T/T_I, with T_I/T_{tot} being constant with age. Interestingly, BURDON *et al.* [13] found that the tachypnoeic breathing pattern in patients with pulmonary fibrosis was associated with a shorter T_I and decreased T_I/T_{tot}, a strategy thought to reduce the peak force developed. The same changes could be expected in patients with advanced chronic obstructive pulmonary disease; an increase in T_E would allow more time for expiration, reducing the "autopositive end-expiratory pressure" effect. However, these changes are rarely seen in practice, probably because, as exercise progresses, the tachypnoeic pattern imposes a constraint on the maximal rate of T_I shortening. In addition, it is likely that these patients would exhibit impaired ability to further increase the velocity of shortening of the diaphragm during exercise. The same rationale could be applied for older, but healthy, subjects, such as those evaluated in the present study (fig. 2, table 2).

Clinical implications

The reference data provided in the present study might be clinically useful in various contexts: 1) evaluation of mechanisms of exercise impairment, particularly with respect to the adequacy of the mechanical/ventilatory response to metabolic demands [10, 14]; 2) interpretation of the effects of selected interventions, such as pulmonary rehabilitation [15], oxygen therapy, noninvasive ventilation and lung volume-reduction surgery [16]; and 3) identification of an erratic breathing pattern, which can be valuable in the diagnosis of psychosomatic complaints [11], insufficient cooperation and even malingering. The prediction equations given in table 3, therefore, can be easily used as a frame of reference for judging the adequacy of the pattern and timing of breathing during cardiopulmonary exercise tests; for this purpose, however, it is particularly advisable that the relatively wide 95% confidence intervals should be taken into consideration.

Study limitations

It should be recognised that a number of operational and technical aspects could, at least theoretically, influence the breathing pattern during exercise. Initially, the use of mouthpiece and nose clip are known to alter the depth and rate of breathing [37], although this effect seems to be restricted to lower levels of ventilation [38]. The present data, therefore, should be used with caution when the ventilatory variables are recorded using a mask or canopy. Different responses can also be obtained with lower- and upper-limb exercise [20] or when a cycle or treadmill is used; application of the present data should, therefore, be restricted to rapidly incremental cycle ergometry performed by sedentary subjects with little experience with cycling. Conversely, no effect of the rate of cycling was found when subjects were free to choose their own pedalling frequency [19], as was the case in the present study (see Methods section).

Previous findings that the rate of ramp incrementation has no systematic effect on the submaximal pattern or timing of breathing were also confirmed [39]. Another potential confounding factor is related to the entrainment effect, *i.e.* some subjects tend to match their breathing pattern to the cycling rate. Considering that the chosen pedalling rate was invariably >45 rpm and breathing frequency only reached this rate at near-maximum exercise (table 2), the authors are confident that this was not a relevant issue in the present study. Finally, it should be recognised that a large number of older subjects were not evaluated; DEMPSEY and coworkers [23, 24, 36], for instance, have shown that high-intensity exercise is associated with substantial constraints on ventilatory performance in these subjects, particularly in the well-trained.

In conclusion, sex, age and anthropometric attributes should be considered in assessing the normalcy of the pattern and timing of breathing at submaximal ventilatory intensities during rapidly incremental cycle ergometry. Clinical interpretation of cardiopulmonary exercise testing could be substantially enhanced by integrative analysis considering both maximal and submaximal data.

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