Characterization of Maximal Respiratory Pressures in Healthy Children

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Key Words

Lung function · Children · Maximal respiratory pressure · Respiratory muscle strength

Abstract

Background: Measurements of maximal voluntary inspiratory ($P_{I_{max}}$) and expiratory ($P_{E_{max}}$) pressures are used in the management of respiratory muscle disease. There is little data on the appropriate reference range, success rates, or repeatability of $P_{I_{max}}$ and $P_{E_{max}}$ in children or on methodological factors affecting test outcomes. **Objectives:** To determine $P_{I_{max}}$ and $P_{E_{max}}$ in healthy children and examine which published reference equations are best suited to a contemporary population. Secondary objectives were to assess within-test repeatability and the influence of lung volumes on $P_{I_{max}}$ and $P_{E_{max}}$. **Methods:** Healthy children were prospectively recruited from the community on a volunteer basis and underwent spirometry, static lung volumes, and $P_{I_{max}}$ and $P_{E_{max}}$ testing. **Results:** Acceptable and repeatable (to within 20%) $P_{I_{max}}$ and $P_{E_{max}}$ were obtained in 156 children, with 105 (67%) children performing both $P_{I_{max}}$ and $P_{E_{max}}$ measurements to within 10% repeatability. The reference equations of Wilson et al. [Thorax 1984;39:535–538] best matched our healthy Caucasian children. There was an

inverse relationship between $P_{I_{max}}$ and the percent of total lung capacity (TLC) at which the measurement was obtained (beta coefficient -0.96 ; 95% CI -1.52 to -0.39 ; $p = 0.001$), whereas at lung volumes of $>80\%$ TLC $P_{E_{max}}$ was independent of lung volume ($p = 0.26$). **Conclusion:** We demonstrated that the Wilson et al. [Thorax 1984;39:535–538] reference ranges are most suited for contemporary Caucasian Australasian children. However, robust multiethnic reference equations for maximal respiratory pressures are required. This study suggests that 10% within-test repeatability criteria are feasible in clinical practice, and that the use of lung volume measurements will improve the quality of maximal respiratory pressure measurements.

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Introduction

Respiratory muscle dysfunction occurs in myopathies, multiple sclerosis, and motor neuron disorders and can lead to respiratory failure. Measurement of respiratory muscle function is an important tool in the diagnosis of respiratory muscle disease/dysfunction. Methods of respiratory muscle strength assessment that do not require voluntary effort (such as phrenic nerve stimulation) are

considered the gold standard approach [1]. However, these techniques can be uncomfortable for patients and in some cases technically difficult and thus have limited application in routine clinical assessments of respiratory muscle function in pediatric respiratory medicine [1]. Volitional and noninvasive methods are most suited for use in children and include sniff nasal inspiratory pressure (SNIP) or maximal voluntary inspiratory (PI_{max}) and expiratory (PE_{max}) pressures measured at the mouth. Currently PI_{max} and PE_{max} is the most widely accepted non-invasive technique used to assess respiratory muscle strength [2].

There have been a number of studies to establish reference values for PI_{max} and PE_{max} in children of different age groups, with varying degrees of success [3–9]. However, little attention has been paid to the overall success rates or repeatability of obtaining PI_{max} and PE_{max} data in children or how these may affect test outcomes. Similarly, while there is ample evidence that PI_{max} and PE_{max} are lung volume dependent [1], current guidelines do not mandate the measurement of lung volumes when assessing maximal respiratory pressures, and hence the impact of variations of inspired or expired volumes on the subsequent PI_{max} and PE_{max} outcomes in the clinical setting are not well described.

The primary aim of this study was to quantify respiratory muscle strength using PI_{max} and PE_{max} in healthy children aged 5–18 years and establish which, if any, reference equations published in the literature are suitable for application to a pediatric Australian population. We also attempted to determine the age-related feasibility of obtaining acceptable data, define within-test repeatability, and investigate the influence of lung volumes on PI_{max} and PE_{max} .

Methods

We recruited healthy children from the community on a volunteer basis. Children were excluded if they had any underlying respiratory, cardiac, or skeletal condition. The Princess Margaret Hospital ethics committee approved the study protocol and parents and children (where appropriate) gave written consent prior to commencing the study.

Children underwent a testing session using a Sensormedics Spectra 6200 Body box (Care Fusion, Yorba Linda, Calif., USA) that included (in the order listed) spirometry, lung volumes by plethysmography, gas transfer, and PI_{max} and PE_{max} , and children were given opportunities to rest as required. Some lung function data (spirometry, lung volumes, and gas transfer) from these children have been reported previously [10–12]. Static lung volumes [total lung capacity (TLC), residual volume (RV), and functional residual capacity (FRC)] were obtained by body plethysmography

according to international guidelines [13–15]. Briefly, after a period of stable tidal breathing, the occlusion shutter was closed at FRC until five satisfactory panting maneuvers were obtained. The subject was then instructed to inspire maximally to TLC followed by a slow expiratory vital capacity maneuver to RV.

PI_{max} and PE_{max} data were obtained from a maximal effort against a closed shutter at RV or TLC, respectively, and performed according to current recommendations [1]. Briefly, children supported their cheeks to minimize leaks and pressure loss during expiratory efforts and were encouraged to maintain maximal respiratory pressures for ~2 s, and the pressure able to be sustained (rather than the instantaneous peak pressure) was identified for each effort. Interactive incentive software for maximal respiratory pressure testing was not used; however, following each effort children were provided feedback on that individual effort and encouraged to exceed previous attempts in an age-appropriate manner. A minimum of five measurements were performed and a test session considered acceptable and repeatable if at least three efforts were considered acceptable and the best and next best test were within 20% of the best test. Data are reported as the highest recorded PI_{max} and PE_{max} . PI_{max} volume was derived as the volume of air expired from FRC prior to the pressure maneuver (described above) subtracted from the measured FRC and expressed as a percentage of the TLC. Similarly, the PE_{max} volume was derived as the volume of air inhaled from FRC prior to the pressure maneuver added to the measured FRC and reported as a percentage of the TLC.

Data Analysis and Statistics

Feasibility was defined as the proportion of children able to produce an acceptable and repeatable test session. To assess within-session repeatability we stratified the percentage difference between the best test and the next best test as: <5%, 5–10%, and 10–20%. The influence of PI_{max} and PE_{max} volumes [as a relative (%) proportion of TLC] on maximal respiratory strength was determined using multiple linear regression modeling after taking into account significant demographic factors (as defined below).

Relationships between PI_{max} and PE_{max} and demographic data (height, weight, age, and sex) were examined to characterize healthy maximal respiratory muscle strength in children. In order to validate pediatric reference ranges, we examined reference data published in the past 50 years. Studies using similar methods and subjects and reporting continuous relationships between PI_{max} and PE_{max} and demographic information were identified. The current data was compared to the published data for appropriateness of use in contemporary Australian children.

Maximal pressures are expressed in centimeters of water and height is expressed in centimeters. The impact of PI_{max} and PE_{max} volumes on the measured maximal respiratory pressures was assessed using stepwise linear regression analysis after accounting for relevant demographics (age, height, and sex). The agreement between the data presented in this study and existing maximal respiratory pressure reference equations was evaluated by calculating the predicted values for each individual and comparing the differences between the predicted and measured values. Good agreement would be signified by a mean difference of 0 cm H₂O and was assessed using a one-sample t test against a value of zero. The impact of age, height, and sex on the absolute and relative (expressed as the percentage of the measured maximal respiratory pressure) differences between predicted and measured max-

imal respiratory pressures were assessed using multiple stepwise regression. Statistical significance was accepted at the $p < 0.05$ level. Data and statistical analysis was performed using SPSS version 16.0 (SPSS Inc., IBM, Somers, N.Y., USA).

Results

We recruited 168 healthy children (100 females; 60%) aged 5–18 years between April 2005 and November 2007. Demographic, $PI_{\max}$, $PE_{\max}$, and static lung volume data are shown in table 1. Acceptable and repeatable $PI_{\max}$ data were obtained in 156 healthy children, with an additional 4 children not able to achieve repeatable $PE_{\max}$ measurements equating to a feasibility rate of 93 and 90% of attempted measurements for $PI_{\max}$ and $PE_{\max}$, respectively. Of the 156 children, the majority ($n = 105$; 67%) were able to produce acceptable and repeatable tests for both $PI_{\max}$ and $PE_{\max}$ tests within a 10% difference between the best and next best tests, with the remaining children performing measurements with the 20% repeatability criteria advocated within testing guidelines [1]. The number and proportion of children achieving the various levels of repeatability are shown in table 2.

Paired $PI_{\max}$ and $PE_{\max}$ and static lung volume data were obtained in 116 children (74%). Eighty-nine percent of children performed $PE_{\max}$ maneuvers at a volume within 10% of TLC. After accounting for height [beta coefficient (95% CI): 0.39 (0.11–0.67); $p < 0.01$] and sex [18.72 (7.10–30.34); $p < 0.005$] the $PE_{\max}$ volume as a percent proportion of TLC did not significantly influence $PE_{\max}$ results ($p = 0.26$). Only 20% of children achieved $PI_{\max}$ volumes to within 10% of the RV/TLC ratio determined from the measurement of plethysmographic lung volumes. $PI_{\max}$ data exhibited a significant inverse relationship with $PI_{\max}$ volume as a percent proportion of TLC [–0.96 (–1.52 to –0.39); $p = 0.001$] after accounting for height [0.41 (0.19–0.62); $p < 0.001$] and sex [9.11 (0.05–18.17); $p < 0.05$]. The relationships between lung volume (as a proportion of TLC) and maximal respiratory pressures are shown in figure 1.

The differences between the predicted and measured maximal respiratory pressures are shown in table 3. The impact of age, height, and sex on the differences between predicted and measured maximal respiratory pressures was assessed using multiple stepwise regression. Absolute and relative differences in maximal inspiratory pressures were significantly associated with age (absolute: $p < 0.01$, $r^2 = 0.05$; relative: $p < 0.02$, $r^2 = 0.04$) for the reference equations of Tomalak et al. [8] and height (absolute: $p < 0.001$, $r^2 = 0.20$; relative: $p < 0.001$, $r^2 = 0.12$) for those of Domenech-

Table 1. Demographics, maximal respiratory pressures, and static lung volume measurements

	n	Values
Male/female	168	68/100 (40/60)
Age, years	168	11.5 $\pm$ 3.6 (5.1–19.0)
Height, cm	168	149.2 $\pm$ 20.7 (103.0–186.0)
Weight, kg	168	44.2 $\pm$ 17.4 (17.5–92.2)
$PI_{\max}$, cm H ₂ O	156	77.3 $\pm$ 26.2 (20.0–142.0)
$PE_{\max}$, cm H ₂ O	152	85.3 $\pm$ 32.9 (23.0–221.0)
TLC, l	124	4.20 $\pm$ 1.16 (2.0–7.2)
RV, l	124	0.77 $\pm$ 0.35 (0.18–1.93)
FRC, l	128	1.97 $\pm$ 0.68 (0.81–4.28)

Continuous data are shown as means $\pm$ SD (range), with categorical data expressed as numbers (%).

Table 2. Repeatability of maximal respiratory pressures in healthy children

	<5%	5–10%	10–20%	>20%
$PI_{\max}$	89 (57)	37 (24)	30 (19)	0
$PE_{\max}$	88 (56)	38 (24)	26 (17)	4 (3)

Data are expressed as numbers (%) of children who obtained a reproducible and acceptable test within the indicated percentage difference between the best and next best tests. Data in which the best and next best test repeatability was >20% were not considered to be acceptable and repeatable. An additional 12 children could not perform acceptable or repeatable $PI_{\max}$ or $PE_{\max}$ measurements.

Clar et al. [9], while there no associations between age, height, and sex and differences in maximal inspiratory pressures for the reference equations of Wilson et al. [6]. Similarly differences in maximal expiratory pressures were significantly associated with age for absolute differences ($p < 0.001$, $r^2 = 0.30$) and height for relative differences ($p < 0.001$, $r^2 = 0.18$) for the reference equations of Domenech-Clar et al. [9]. Absolute and relative $PE_{\max}$ differences for the reference equations of Wilson et al. [6] demonstrated significant but weak associations with age (absolute: $p < 0.005$, $r^2 = 0.06$; relative: $p < 0.01$, $r^2 = 0.05$), while there were no associations between age, height, or sex for differences in $PE_{\max}$ for the reference equations of Tomalak et al. [8]. The relationship between the absolute mean differences in maximal respiratory pressures between previous studies and this study are plotted against height in figure 2.

Fig. 1. $PE_{\max}$ (a) and $PI_{\max}$ (b) plotted against the respective lung volumes as a proportion of TLC. $PE_{\max}$ was not significantly associated with lung volume as a percent proportion of TLC ($p = 0.26$) after accounting for height ($p < 0.01$) and sex ($p < 0.005$),

with the majority of tests being measured at $>85\%$ of TLC. In contrast $PI_{\max}$ decreased significantly as lung volume as a percent proportion of TLC increased ($p = 0.001$) after accounting for height ($p < 0.001$) and sex ($p < 0.05$). See Results for full details.

Fig. 2. Absolute difference in predicted and measured $PE_{\max}$ (a) and $PI_{\max}$ (b) against height. Differences derived from Tomalak et al. [8] are shown in open triangles, those from Domenech-Clar et al. [9] are in open circles, and those from Wilson et al. [6] are in closed squares. The prediction equations of Wilson et al. [6]

best matched the population of contemporary Caucasian healthy children in this study, with a mean (SD) difference between the measured and predicted $PE_{\max}$ and $PI_{\max}$ of -4.26 (30.53) and -3.66 (30.57), respectively. See Results and table 3 for more details.

Discussion

Here we present data on 168 healthy children in whom $PI_{\max}$, $PE_{\max}$, and static lung volume testing was attempted. When we compared our data with previous similar studies, we found that the prediction equations of Wilson

et al. [6] best matched our contemporary healthy Caucasian children. We report that maximal respiratory pressure testing is feasible with a high degree of within-test repeatability in healthy children. In our study, we found that maximal pressures were higher in males and increased with height as reported previously [3, 5, 16]. We

Table 3. Differences between the predicted and measured maximal respiratory pressures

Source	p value	Mean difference (SD)	Minimum difference	Maximum difference
Tomalak et al. [8]				
PI _{max}	0.17	2.89 (25.96)	-53.94	75.09
PE _{max}	<0.001	11.30 (29.95)	-45.98	120.45
Domenech et al. [9]				
PI _{max}	<0.001	-12.11 (27.76)	-73.42	67.04
PE _{max}	<0.001	-28.77 (36.75)	-122.40	56.18
Wilson et al. [6]				
PI _{max}	<0.001	6.09 (24.89)	-56.53	76.20
PE _{max}	0.14	-3.66 (30.57)	-66.36	98.00

Differences (in cm H₂O) calculated as predicted minus measured maximal respiratory pressures (i.e. a positive value indicates that the measured values were lower than that predicted). The mean differences were compared to zero using a one-sample t test (p value shown) where a mean difference of zero indicates a good fit to the predicted maximal respiratory pressures.

demonstrated an inverse relationship between PI_{max} and the lung volume at which the measurement was obtained whereas, at lung volumes >80% of TLC, PE_{max} was independent of lung volume.

Black and Hyatt [16] were the first to publish reference range values for maximal respiratory pressures in adults. Since then, there have been a number of studies in children that demonstrated that maximal static pressure testing can be performed with varying degrees of success [3–9, 17, 18]. However, there are relatively few studies that have described reference ranges in healthy children [3–9]. Limitations in some of these studies include a narrow age range [4, 19] or insufficient information from which to derive predicted values [5, 16, 17, 19, 20]. Additionally only some studies have reported population variances (i.e. the standard error of the estimates of the regression equations) with which the lower limit of normal or z- or standard deviation scores can be derived [3, 6, 9]. In order to compare previously published reference ranges in children with our population, we identified those studies which included a wide age range in a sufficient number of children to reasonably derive continuous regression equations and which also used similar techniques and criteria for acceptability as reported here [6, 8, 9].

We found that the study of Wilson et al. [6] best matched our population of contemporary Caucasian healthy children. That paper was published in 1984 and more recent studies attempting to validate reference

ranges in children did not match our population as closely. However, using outdated equations to calculate reference ranges may lead to misinterpretation and incorrect assumptions on the child's respiratory function. To nullify the significant differences in reference ranges across many studies, it has been suggested that collating lung function data from a number of centers is a more robust approach to interpreting lung function results [21–24]. This approach has been applied to spirometry [12, 24, 25], interrupter resistance [26], and gas transfer [11], and the application of this approach to measurements of maximal respiratory pressures in children requires investigation.

According to international testing guidelines for respiratory muscle testing, the maximum value of at least three acceptable maneuvers that vary by less than 20% should be an acceptable and reproducible result and these were the a priori limits used in this study during testing [1]. More recently it has been suggested that a minimum of five maneuvers be performed to minimize learning effect and that that within-test repeatability should be within 5–10% [2]. Similarly, Faroux et al. [27] suggested that <20% was an achievable within-test repeatability level. The majority of studies of maximal respiratory pressures in children have not reported within-test repeatability, therefore limiting the available information to inform the revision of testing guidelines. In this study the majority of children (67%) were able to achieve repeatable maximal inspiratory and expiratory respiratory pressure to within 10%. In this study we considered between-test repeatability <20% acceptable and it is possible that the proportion of children able to achieve repeatability to within 10% may be higher. It is feasible that children with neuromuscular disease may not be able to achieve this level of within-test repeatability due to progressive muscle weakness associated with repeated efforts [27, 28]. The results of the current study support that a difference of <10% between the best and next best PI_{max} and PE_{max} is achievable in the majority of healthy children and that future testing guidelines take these into account.

We report associations between PI_{max} but not PE_{max} and the relative proportion of TLC at which the measurements were obtained after accounting for demographic effects (height and age). It is likely that this difference in relationships is primarily due to the wide spread of lung volumes (at which PI_{max} measurements were made). It has been shown that maximal respiratory pressures in children, as in adults, change with lung volumes [3]. It is likely that children are better able to achieve the maximal

inhalation to TLC required for $PE_{\max}$ testing than a maximal expiration to RV for the assessment of $PI_{\max}$. This has been demonstrated in other studies in which most children achieved reproducible spirometry with regard to FEV_1 in comparison to FVC, especially in younger children [15, 29–31]. In this study there was no association between $PE_{\max}$ and the proportion of TLC at which the measurement was obtained after accounting for demographic effects (height and age). The likely reason for this is that 88% of children were able to perform $PE_{\max}$ measurement at lung volumes $>90\%$ of TLC. These data suggest that the accepting $PE_{\max}$ measurements at volumes $>90\%$ of TLC may assist in improving the quality of maximal respiratory pressure measurements and therefore maximize the clinical utility of this technique. Conversely lung volumes for maximal inspiratory pressures ranged from 12 to 45 % of TLC and demonstrated an inverse relationship between $PI_{\max}$ and $PI_{\max}$ volume. In this study only 19.8% of children achieved $PI_{\max}$ volumes to within 10% of the RV/TLC ratio determined from the measurement of plethysmographic lung volumes. This result is likely to be influenced by the difficulty that young children have in achieving exhalations to RV. It is not clear at what lung volume $PI_{\max}$ measurements should be considered unacceptable in the context of being at or near the RV. However, our results suggest that the measurement of the static lung volumes and in particular RV when assessing $PI_{\max}$ may assist in improving the overall quality of testing outcomes.

There are some limitations in this study. Firstly, testing the feasibility of the maximal respiratory pressures does not always match the maximal effort as it has been demonstrated that adults performing deliberate submaximal efforts may give reproducible measurements [28]. Also, another limitation to testing feasibility is the learning effect in subjects performing maximal respiratory pressures which has been demonstrated in a number of studies to date [32–35]. To counteract this learning effect it has been suggested that warm-up maneuvers should be used to reduce the number of measurements taken to obtain in-test repeatability [36, 37]. Alternative respiratory muscle tests such as SNIP measurements are generally easier for children to perform and do not have such a learning effect [1]. One study reported that using a combination of the two methods increased diagnostic precision in adults [38] and this should be confirmed by further studies in children. We have reported the influence of lung volumes on $PE_{\max}$ and $PI_{\max}$ by comparing the volume at which maximal respiratory pressures were obtained with TLC and RV obtained during static lung vol-

ume measurement (as described in Methods). This approach assumes that FRC does not appreciably vary between static lung volume and maximal respiratory pressure measurements. A stable FRC over time would be confirmed by repeatable maximal inspiratory capacities with a fixed TLC. In those individuals with paired static lung volume and maximal respiratory pressure measurements, the mean (SD) inspiratory capacity obtained during lung volume measurements was 2.22 liters (0.59) and was statistically higher than the inspired volume recorded prior to $PE_{\max}$ measurements [2.10 liters (0.60)], with a mean difference of 120 ml (paired t test $p < 0.001$). We would contend that a mean difference of <150 ml between test sessions is within the acceptable between-test repeatability and not physiologically relevant. These results suggest that FRC was stable over time and confirm that the estimates of lung volumes at which $PE_{\max}$ and $PI_{\max}$ were obtained (as a proportion of TLC) are accurate.

In summary, we have demonstrated the paucity of reference ranges for maximal respiratory pressures in children. The fact that the reference equations of Wilson et al. [6] from 1984 were the most suitable for use in contemporary Caucasian Australasian children highlights the urgent need for further research developing robust reference equations for maximal respiratory pressures in children. The majority of children are able to perform acceptable measurements of maximal respiratory pressures to within 10% repeatability, suggesting that this repeatability criterion could be adopted in clinical practice. Children were able to perform maximal expiratory pressures at or near TLC while measurements of maximal inspiratory pressures showed a high degree of variability that could be attributed to the wider range of volumes. The introduction of static lung volume measurements prior to maximal respiratory pressures and the targeting of $PI_{\max}$ maneuvers to be obtained at or near the RV are likely to improve the quality of maximal respiratory pressure measurements in children.

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