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Poor standardisation of plethysmographic specific airways resistance measurement despite widespread use

To the Editor:

Plethysmographic specific airways resistance (sR_{aw}) has remained the most recognised measure of airway resistance for almost 60 years [1]. Studies in both adults and children (including preschoolers) suggest clinical utility across important obstructive lung diseases [2–5]. Measurement protocols based on rapid panting or tidal breathing exist, and are incorporated into many current commercial plethysmographs. Tidal breathing measurement offers feasibility across a wide age range, and a relatively stable index with

which to distinguish effects of disease from those of growth and development [6]. Both adult and paediatric reference data exists [7, 8]; however, the wide variation in methodology existing between centres has recently been highlighted [8], and sR_{aw} remains one of the few lung function measurements without formal standardisation guidelines [9]. Despite the wide availability of plethysmographic equipment in lung function laboratories, its use is frequently confined to lung volume measurements. Although simultaneous measures of airway resistance can easily be recorded at no extra cost, the clinical applications of sR_{aw} remain unclear. As part of ongoing sR_{aw} standardisation work, we sought to describe current international use of sR_{aw} across paediatric and adult respiratory laboratories.

Online surveys were distributed through members of four different societies: the European Respiratory Society, American Thoracic Society, Thoracic Society of Australia and New Zealand and the UK Association of Respiratory Technology and Physiology. Centres currently performing sR_{aw} testing were asked to complete the surveys and indicate whether measurements were performed for clinical and/or research purposes, the type of device used, age range tested and how many tests were performed each year. The questionnaire was intentionally brief to aid response rate. Respondents were asked to complete a second online questionnaire regarding specific methodology used (including respiratory rate targeted during measurements), clinical/research situations of use, perceived clinical utility within their laboratory and sR_{aw} outcomes reported. sR_{aw} outcomes of interest were total resistance (sR_{tot} ; calculated as the difference between points of maximum plethysmographic box pressure), effective resistance (sR_{eff} ; calculated from multiple points throughout the breathing cycle using an integration method), peak resistance (calculated between points of peak inspiratory and expiratory flow) and resistance over a fixed flow range (e.g. -0.5 to $+0.5$ L·s⁻¹) [8].

Overall, 47 centres indicated current use of sR_{aw} , across 16 countries and four continents; the highest number of centres being in Europe (34 centres) and Australasia (10 centres). The greatest reported usage was within the Netherlands and UK (seven centres each), and Australia (six centres). Adults, school-aged, and pre-school children (aged <6 years) were assessed in 81%, 72% and 49% of centres, respectively. The majority of centres where adult testing was performed reported >100 adult tests per year, with 37% of centres reporting >1000 adult tests per year. The volume of tests performed in children was lower, with the majority of school age paediatric centres (55%) performing 100–1000 tests per year whilst 74% of pre-school testing centres performed 10–100 tests per year.

A wide variety of commercial equipment existed across centres (eight different devices). Although most data had been collected using either Jaeger (27 centres) or SensorMedics (10 centres) equipment, both of which are now incorporated within CareFusion, several different software versions were being used within such devices. The remaining manufacturers were Medgraphics and Zan (three centres each), Medisoft (two centres), Morgan, Medical Equipment Europe and nSpire (one centre each).

Among the respondents completing the initial questionnaire, 87% indicated that sR_{aw} results were used clinically, while 57% used sR_{aw} in respiratory research and 36% were actively collecting healthy control data. This high reported clinical sR_{aw} use prompted distribution of the second more detailed questionnaire, which was completed by 77% of those initial respondents.

Significant variation of testing protocol was observed in the replies. The median (range) number of trials per session was 3 (1–5), with each trial comprising 5 (1–10) individual breaths. 14 centres reported a maximum

FIGURE 1 Summary of a) reported specific airways resistance (sR_{aw}) outcomes (across 47 centres) and b) the targeted respiratory rates reported by the 22 centres (out of 36; 55%) indicating this was part of local sR_{aw} testing protocol. sR_{tot} : total resistance; sR_{eff} : effective resistance. b) Centres are categorised according to whether both paediatric and adult (grey), paediatric only (white), or adult only subjects are measured (black); centres indicating a specific target rate (breaths per minute; bpm) are shown as circular symbols and those indicating a respiratory rate range are shown as bars.

number of attempted trials which ranged between 5 and 10 trials. Use of a specific target for breathing frequency during sR_{aw} measurements occurred at 72% of centres, but this target showed marked variation (figure 1). Only two centres varied the targeted rate according to the subject's age. The remaining 28% of centres specified either no target for respiratory rate (19% of centres) or a "normal tidal breathing rate".

Reported parameters were poorly described by manufacturers, with almost half the centres (44%) unable to give a full description of the primary outcome reported, simply indicating that the manufacturer reported a "generic sR_{aw} ". At the remaining centres, the primary outcome reported was sR_{tot} (22%), sR_{eff} (19%), or sR_{aw} over a fixed flow range (14%). Five centres (14%) indicated use of more than one outcome, depending on the clinical situation. Among the 72% of centres where relevant information concerning equipment software was retrievable, results were summarised as median values in 35% and mean in the remaining 65%. One centre reported results from only one acceptable trial. Despite recent recommendations [8], manual adjustment of automatically generated tangents of pressure–flow loops was still occurring at 42% of centres. Abnormal results were defined based on reference equations at over half the centres (58%), but the majority (12/21) could not identify which equation was used in the equipment. The other nine centres used several different equations, including those of KIRKBY *et al.* [8] (2010), BRISCOE and DUBOIS [10] (1958), and in-house reference equations based on self-collected data. A fixed "upper limit of normal", set as default by the manufacturer without specification of reference material, was used by the remaining 42% of centres.

Consistent with responses from the first questionnaire, 30 respondents (83%) to the second questionnaire indicated clinical use of sR_{aw} . All performed baseline measurements, with 61% also using sR_{aw} to assess bronchodilator response and 23% for bronchial challenge (four out of seven of whom indicated a change in standard testing protocol when sR_{aw} was used for such purposes). All 30 centres stated that they found sR_{aw} measurements clinically useful across a wide range of respiratory conditions, but primarily in the evaluation of obstructive lung disease. Utility from sR_{aw} was perceived for asthma (all 13 centres providing more detailed information), cystic fibrosis, chronic obstructive pulmonary disease, interstitial lung disease and bronchopulmonary dysplasia. Utility was perceived to be higher when other lung function techniques, such as spirometry, were not technically feasible for the patient.

These results highlight widespread paediatric and adult use of sR_{aw} in respiratory function laboratories, centred in Europe and Australasia. Popularity probably reflects relative ease of data collection and availability of suitable equipment, but also high perceived clinical utility (almost 90% of respondents). This occurred despite striking lack of agreement with respect to methodology, outcomes and reference data. Variation in several of these important methodological aspects can significantly affect recorded sR_{aw} values [8, 11] and interpretation in the clinical setting [12]. Publication of recommendations in 2010 for testing protocol using the most common device in our survey has failed to prevent marked variation in practice [8]. These findings and the high reported volume of current testing highlight the urgent need for generalisable recommendations to standardise all aspects of sR_{aw} measurement and interpretation.

The formation of a task force, endorsed by international respiratory societies, and including representation from countries with heavy current use, would be an important step towards optimising potential clinical utility of this widely used technique. Until standardisation has been achieved, these authors would advise centres to adhere to existing recommendations [8] and interpret sR_{aw} results with caution.

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sR_{aw} is widely used but results should be interpreted with caution until its recording is better standardised <http://ow.ly/QvJRJ>

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Multiple breath washouts in children can be shortened without compromising quality

To the Editor:

Lung clearance index (LCI) derived from multiple breath washout (MBW) is a sensitive, noninvasive measure of ventilation heterogeneity and is used for the assessment of cystic fibrosis (CF) [1], asthma [1] and primary ciliary dyskinesia (PCD) [2]. LCI is the number of lung turnovers (functional residual capacity (FRC)) required to washout an inhaled inert gas to 1/40 of its initial concentration: a historically set end-point of no physiological significance [3]. The number of lung turnovers needed to wash out the gas, and hence the LCI, increases with disease severity. It is non-effort-dependent and requires only passive cooperation. The test can be time-consuming, especially with severe airway obstruction as more time is required to wash out the tracer gas. This is a particular problem in young children, in whom a test lasting several minutes is intolerable. This could be shortened by stopping the test at a higher concentration of tracer gas. We propose that instead of 1/40 of the initial concentration being used as an end-point (“LCI standard” (LCI_{std})), the concentration could be raised to 1/30 (LCI_{0.75}), 1/20 (LCI_{0.5}) or 1/10 (LCI_{0.25}) of the starting concentration of tracer gas, or using a fixed time period of washout, for example 20 s, or a fixed number of breaths.

In 17 preschool children (median age 3.9 years), our pilot data showed that only 35% could perform LCI_{std}, but 65% completed LCI_{0.5} [4].

Two studies, demonstrated that LCI_{0.5} can be performed in school age children with CF with the same diagnostic performance as LCI_{std} [5, 6] and a recent study [7] showed LCI_{0.5} is sensitive to improvements with dornase alpha and hypertonic saline in CF. We aimed to investigate the utility of shortened washouts in school age children with asthma, PCD and CF, and to assess the sensitivity of change in LCI to two interventions (intravenous antibiotics in CF [8] and intramuscular triamcinolone injection in severe asthma [9]). We hypothesised that LCI measurements can be shortened without compromising the quality of the information obtained and are as responsive to therapeutic intervention as LCI_{std}.

We performed a retrospective analysis of previously collected data from MBW measurements at the Royal Brompton Hospital (London, UK) between January 2008 and May 2014. All research studies had been approved by the appropriate research ethics committees, and informed consent obtained. Data from 20 children with CF (median age 13.85 years, seven male), 19 with PCD (median age 13.89 years, six male), 21 with asthma (median age 13.29 years, 12 male) and 17 healthy controls (median age 9.76 years, nine male) were analysed initially, followed by data from 32 children with asthma who had MBW prior to and 1 month after an intramuscular injection of triamcinolone, and a cohort of 17 people with CF who had MBW at the beginning and end of a course of intravenous antibiotics. LCI_{std} data for the CF intervention cohort have been reported