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Reproducibility of lung volume measurements

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ABSTRACT: Test reproducibility is an important consideration when interpreting results and should be set as a goal during data collection. Reproducibility criteria may need to be different for different subject groups and are instrument and procedure-dependent. Ideally, the within-subject variability for each lung volume and measurement technique used should be established for each laboratory. These values also need to be established for each different subject group (age and disease). At a minimum, test reproducibility should be monitored and controlled and each laboratory should define their between-day reproducibility of measurements on at least one "reference" subject from ongoing periodic (*e.g.*, weekly or monthly) measurements as part of their laboratory's quality control programme. For plethysmographic measurements functional residual capacity (FRC_{pleth}) multiple determinations and a corresponding test reproducibility criteria is probably justified.

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Role of reproducibility measures

For a number of reasons, it is important to know and understand test variability or reproducibility. All pulmonary function tests are subject to: 1) technical variation related to instrument procedure, calibration, observer, subject, and their interaction; 2) biological variation; and 3) variation caused by dysfunction or disease [1]. A knowledge and understanding of test variability can enhance the interpretation of the results through the separation of variability of interest (signal) from other sources of variation (noise) both within a subject and within a population [2]. By quantifying the variability or reproducibility of a measurement for both normal subjects and patients with disease, the interpretation of the results is enhanced.

Test reproducibility can be a useful indicator of the quality of a laboratory's measurements and procedures, and changes in procedures have been shown to result in significant reductions in test variability [3]. Similarly, a trend towards an increasing variability may indicate an equipment malfunction or procedural problems. Because the sensitivity of a test can be improved with reductions in test variability, attempts should be made to monitor and control test variability.

Test reproducibility can also be useful in assessing the adequacy of a test in a particular subject. If multiple determinations of a test are made, test reproducibility provides an indication of the level of confidence in an individual's results. However, test reproducibility should not be used to exclude subjects from a study or to avoid interpreting the results. Rather, test reproducibility should be considered when the test results are interpreted.

Method of expressing variability

The within-subject biological variability for lung volumes, as with spirometry, may not be the same for all subjects, particularly for subjects with airways obstruction where functional residual capacity (FRC) and residual volume (RV) are increased. However, at least using a body plethysmograph in the measuring of FRC (FRC_{pleth}), there does not appear to be a significant increase in variability of FRC_{pleth} measurements with obstructive lung disease [4, 5]. This lack of increased variability may in part be explained by the common practice of expressing the variability as a percentage. For FVC and forced expiratory volume in one second (FEV_1), it has been shown that reproducibility should be expressed in absolute terms [6] rather than as a percentage. In addition, the trend towards lower percentage variabilities with increased volumes (total lung capacity (TLC)>FRC>RV) may be partially explained by the method of expressing these variabilities as percentages rather than in absolute terms. While most studies have reported the coefficient of variation (CV), expressed as a percentage, it may be more appropriate to express test variability in absolute terms. Additional data for each lung volume parameter are needed to resolve these issues.

Any definition of reproducibility must be considered in the context in which the reproducibility values are used and the methods by which the test is administered. For example, if only two measurements of a helium dilution determined TLC (TLC_{HE}) are made, then test reproducibility may simply be the difference between these two values. However, if five repeat measurements of FRC_{pleth} are made using a plethysmograph, then a CV might be calculated:

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(SD/mean)×100; or when only two values x_1 and x_2 are available.

$$v = |x_1 - x_2| / \bar{x}\sqrt{2}$$

Test reproducibility needs to be established for each laboratory, technique (plethysmograph, helium dilution, *etc.*), and subject group (by time period, age, disease, and perhaps height). Even when using the same technique, small differences in procedure [4, 5], equipment [3], and environmental conditions (laboratory *versus* field) [7] can affect test variability. Standardization of these factors should help reduce test variability. Variabilities may also be influenced by other factors such as diurnal variation or whether previous tests have been conducted on a subject [8, 9].

Possible values for CV

Table 1 shows a list of observed CV values from several studies of lung volumes in neonates and infants. Table 2 shows similar values for children (adapted from QUANJER *et al.* [30]) and table 3 shows values for adults. Caution is required when interpreting or comparing the results of the studies listed in these tables since each used a differing numbers of tests repeated over differing time intervals. In addition, some studies included patients with incomplete descriptions of their respiratory health status. However, these data can be useful in understanding the general variability of these tests. As shown in table 3, the TLC reproducibility is usually less than that for RV when expressed as a percentage. The reproducibility using a plethysmograph does not appear to be greatly different from the helium dilution determined values. Also, the reproducibility does
not appear to be greatly increased in patients with obstructive lung disease and there does not appear to be any great gender-related difference in test reproducibility. Therefore, it appears that procedural and inter-laboratory test reproducibility differences may be as important as any differences that may exist between patient populations.

Table 1. – Coefficient of variation (CV) for functional residual capacity (FRC) from several studies in infants and neonates

Coefficient of variation			Comments	[Ref.]
FRC_{HE}	FRC_{N_2}	FRC_{box}		
-	-	2.5	33 healthy infants 2–15 months	[10]
4.0	-	-	70 infants & children without respiratory disease 0.5–36 months	[11]
Ý12	-	-	44 healthy infants <2 months	[12]
Ý5			40 infants 2–14 months (25–75% quartile CV = 2–18%)	
6	6.6	-	22 infants 0–31 months; 8 healthy; 14 resp. disease. Similar variability in groups	[13]
-	-	10.0	40 wheezy infants 1–13 months	[14]
-	-	5.6[WT]	10 wheezy infants 2–8 months	[15]
		11.4[BT]		
-	-	10.8	15 neonates <1 week	[16]
-	-	3.7	10 healthy infants 0–12 months	[17]
-	3.6	3.9	11 healthy infants 2–13 months	[18]

Values are presented as percentages. FRC_{HE}: FRC measured using helium dilution; FRC_{N_2}: FRC measured using multiple breath nitrogen tests; FRC_{box}: FRC measured using a body plethysmograph or body box; resp.: respiratory; [WT]: within test; [BT]: between test.

Table 2. – Coefficients of variation for several lung volume parameters in children

Coefficients of variation			RV	[Ref.]
TLC	FRC_{HE}	FRC_{box}		
-	7.0	5.5	-	[19]
-	-	-	8.1	[20]
-	6.6	-	-	[21]
-	4.1	-	8.5	[22]
-	4.0	-	-	[23]
-	4.1[M], 5.9[F]	-	-	[24]
-	5.9±4.6	-	-	[25]
-	-	-	13.8[M]	[26]
-	3.3	-	-	[27]
-	<3.5	-	8.5[F]	[28]
			8.5[F]	
3–9	-	-	-	[29]

Values are presented as percentages. TLC: total lung capacity; FRC_{HE}: FRC values measured using helium dilution; FRC_{box}: using a body plethysmograph or body box; RV: residual volume; [M]: males; [F]: females. For further definition refer to table 1. Data adapted from QUANJER *et al.* [30].

Table 3. – Coefficients of variation for several lung volume parameters in adults

Coefficient of variation						[Ref.]
TLC_{pleth}	TLC_{HE}	FRC_{pleth}	FRC_{HE}	RV_{pleth}	RV_{HE}	
		5.38[Pr]				[2, 3]
		6.70[F]				
4.25		6.83		9.5		[4]
				8.9		
4.0		4.5		11.0		[5]
	2.4[L]		4.9[L]		7.3[L]	[7]
	3.7[F]		10.4[F]		14.0[F]	
		6.6[1]				[8]
		3.5[2]				
		3.8[T]				[9]
		6.1[UT]				
			8.1[N]			[31]
			8.8[P]			|d|
		5.0	7.6			[32]
3.0				12.4		[33]
					7.3[B]	[34]
					2.4[R]	
	2.6				6.0	[35]
4.0		6.7		11.8		[36]
2.2	1.5[sb]	3.9				*
2.2	2.5[sb]	4.7				

Values are presented as percentages. TLC_{pleth}: TLC measured by plethysmography; TLC_{HE}: TLC measured using helium dilution; FRC_{pleth}: FRC measured using plethysmography; RV_{pleth}: residual volume measured using plethysmography; RV_{HE}: residual volume measured using helium dilution. [Pr]: pressure plethysmograph; [F]: flow plethysmograph; [L]: laboratory study; [1]: 1st week of test; [2]: 2nd week of test; [T]: trained subjects; [UT]: untrained subjects; [N]: healthy subjects; [P]: patients; $|d|$: absolute value of the difference between two test values x_1-x_2; [B]: biological variability; [R]: random errors; sb: single-breath technique; *: personal communication. For further definitions refer to tables 1 and 2.

There have been several attempts at establishing limits for lung volume reproducibility. The European Respiratory Society statement [37] concluded that the CV for FRC reproducibility using the single breath nitrogen technique is 8%. For FRC_{pleth}, they concluded that a lower variability was appropriate or 5% for both healthy individuals and patients with airways obstruction. The Intermountain Thoracic Society concluded that with three tests, the CV for plethysmographic measurement of total lung capacity (TLC_{pleth}) should be within 5%. For helium dilution tests (two tests), a 5% reproducibility criterion was recommended when using an automated method and 8% with a manual method. The American College of Chest Physicians in 1986 recommended that 3 tests of FRC_{pleth} be reproduced to within 10%. One textbook [38] recommends that for multiple breath nitrogen tests the FRC in normal subjects should agree within 200–400 mL in adults and 100–200 mL in children whether the tests are done within hours or days.

Compared to adults, there are increased difficulties when assessing test reproducibility in infants and children. For example, infants and children grow rapidly and therefore their lung volumes are constantly changing. Infants do not sleep long and cannot easily be restudied on separate occasions and children have a limited span of co-operation.

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