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ORIGINAL ARTICLE

Lung Function In Young Adults –Which References Should Be Taken?

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Abstract: *Introduction:* Anthropometrical data of the Caucasian population have significantly changed within the last five decades. Therefore the question arises whether the commonly used reference recommendations for lung function of the European Community for Coal and Steel (ECCS) can still be accepted currently. Based on the obvious fact that there is an age independent plateau phase of lung function parameters in young adults from 18 to 25 years of age, the ECCS recommends the entry of 25 years for calculation of reference values in this age range. *Methods:* Lung function was examined by pneumotachography, recording static lung volumes and flow-volume-correlations (MasterScreen Pneumo, CareFusion, Höchberg) of 165 female and 152 male asymptomatic non smoking medical students, aged 18 to 26 years, according to the ATS/ERS criteria. Results were compared to the reference recommendations of ECCS, SAPALDIA, LuftiBus, and Bochum. *Results:* In the investigation of young adults of this narrow age range, no significant correlation between height and BMI with age was found in males and females, but a slight tendency of BMI increasing with age. Lung function parameters (IVC, FVC, FEV_1, FEV_1%FVC, PEF, $MEF_{75,50,25}$) significantly (□<0,01) correlated with height. Mean values of all investigated parameters were 5.5% higher in males and 0.6% higher in females compared to predicted values by ECCS, SAPALDIA, or LuftiBus. Data obtained from males showed the closest correlation with Bochum lung function values (98.0 ± 7.2%pred.) *Summary:* Lung function parameters of young adult males were nearly 5% higher compared to the reference values of the ECCS and showed a plateau phase. The alternatively considered reference values of the SAPALDIA-, or LuftiBus-Study do not incorporate all necessary parameters and/or the age range. A multi centre study for contemporary reference values is recommended.
Key Words: Lung function testing – reference values – young adults– spirometry – forced expiration

Introduction

Anthropometrical data of young adults significantly have changed within the last five decades, with increasing body height and body mass index. Therefore the question arises whether the commonly used reference values of ventilatory lung function testing of the European Community for Coal and Steel (ECCS) [1;2], are still valid today. ECCS values were erected by consensus in the sixties and seventies by local reference values from subjects with a limited range of age and body height. In diagnostics measured parameter values of young adults are classified by relating them to references which are calculated for an age of 25 years in subjects of 18 to 25 years of age, based on the assumption of a plateau phase of lung function in young adults [3]. Birth cohort effects and improved technology should be considered. Therefore decisions concerning impaired lung function on the basis of ECCS-values are questionable in these subjects. In the last decades several new reference studies were published, finding higher values for lung function parameters [4-9], but could not commonly replace the former recommendations [10-14]. Compared to the recently published recommendations, ECCS-values are lower, and the lower limit values or the 5th percentile may not represent a useful cut off point between "normal" and "diseased"subjects. Concerning reference values, the issue of alterations in lung function during the transition from childhood to adolescence and adulthood is an unsolved problem and needs to be studied further., The question if there is a plateau phase in lung function parameters is discussed controversial in the literature [15],[3;16-18]. Difficulties arise from the fact that in adolescence the main parameter height is changing (age or weight are potentially secondary parameters), later on height is nearly fixed and only age is changing. And there are reasons to assume different variability in Lung function parameters due to height in adolescence or later on, and in age with growing height and BMI. ECCS acts on the assumption of a plateau phase between 18 and 25 years of age. Moreover, the current reference formulas available from the literature prefer exponential functions having their maximum in early adulthood. Moreover they are incomplete concerning the spirometric parameters of interest (Hankinson [4], only FVC, FEV_1, FEV_6, PEF, $FEF_{25\text{-}75}$) the range of age (Brändli, [5] 20-60 years, FEV_1, FVC, FEV_1%FVC, PEF, $MEF_{75,50,25}$, $MEF_{25\text{-}75}$), or contain, as e. g. the Luftibus-Study, a selection bias, since only subjects were investigated who paid for a lung function test because of their personal request (Kuster [7] FEV_1, FVC, FEV_1%FVC, PEF, $MEF_{75,50,25}$). A complete set of parameters is available only from the 'historic' ECCS recommendations [1;2]. The European Task Force on standardisation of lung function testing has recently published a series of comprehensive recommendations for lung function testing and interpretation [19-21]. However, he problems in evaluating the lower limit of normal (LLN), the limited age range and the concept in handling the transition from adolescence to adults were not addressed. Current investigations try to describe lung function parameters from preschool children to senescence in one continuous formula taking into account a peak value in early adolescents [22]. On a group of healthy young adults, 18 to 26 years of age, we checked if the ECCS reference recommendations still can be accepted in daily routine measurements. Furthermore we compared our results to the references of the SAPALDIA and LuftiBus studies [5;7], and the set of "Bochum" reference values for healthy non-smoking males [23].

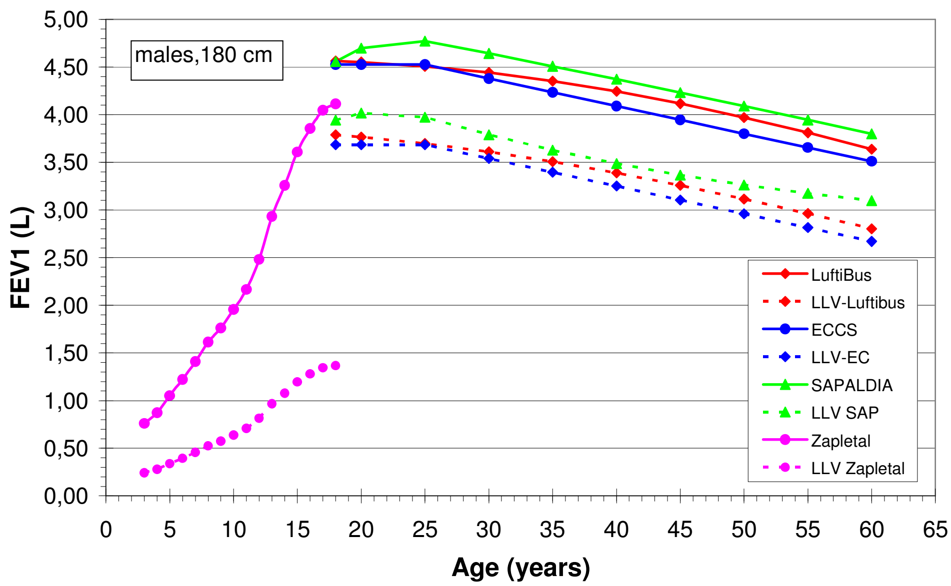
Materials and Methods

Lung function was examined using pneumotachography for recording static lung volumes and parameters from the forced flow-volume-loops in 317 asymptomatic non smoking Caucasian male and female medical students, aged 18 to 26 years.

Subjects were without diseases of the lung, heart or other organs with influence on lung function. They were recruited among non-smoking students performing a course in physiology in their preclinical medical classes. Anthropometrical data are presented in Table 1.

References for lung function in children and adults: The commonly accepted reference values for children were published in 1987 by Zapletal and co-workers [24] for 3 to 16 years old boys and girls. In Europe reference values of the ECCS were published in 1983, and in 1993 in revised version [1;2]. In the 90ties the SAPALDIA study was published by Brändly and co-workers [5;25] and recently in 2008 the Luftibus study by Kuster et al. [7]. Reference value for FEV_1 for males of 180 cm body height and children and adolescents between 3 and 18 years of age with a final height of 180 cm along with the corresponding lower limit of normal (LLN) and the differences between predicted values and LLN are graphically presented in figure 1. The differences between Zapletal reference values of an 18 years old adolescent of 180 cm height and other reference definitions for adults of 180 cm height is ranging from 100 to 400 ml (Fig. 1).

Fig. 1: Correlation of reference values for FEV_1 with age from Zapletal for boys and adolescents and from ECCS, SAPALDIA and LuftiBus study for males of 180 cm height.



Anthropometrical data: The body height of males (182 ± 6.9 cm), recruited in the cross sectional study did not correlate with age, height = 0.0062*age + 181.7 cm (r^2 = 0.0062). As observed in males, body height (169 ± 6.8 cm) did not correlate with age in females, height = 0.0725*age + 167.4 cm (r^2 = 0.0004) either.

In males and females as well, BMI showed a tendency to increase with age, BMI = 0.307*age + 16.8 (r^2 = 0.036) and BMI = 0.452*height + 11.5 (r^2 = 0.097) respectively.

Table I: Anthropometrical Data of male and female students

	Females (n = 165)				Males (n = 140)			
	Age (years)	Height (cm)	Weight (kg)	BMI	Age (years)	Height (cm)	Weight (kg)	BMI
MW	21.7	169	61.8	21.7	22.9	182	78.8	23.8
STD	± 1.9	± 6,8	± 8.9	± 2.8	± 2.0	± 6.9	± 11.1	± 2.1
MAX	26	187	107	37.0	26	203	110	32.1
MIN	18	152	48	16.2	20	164	55	20.0
MED	21	168	60	21.3	22.5	182	76	22.5

Lung function measurements: After a detailed explanation of the lung function test including the measuring procedure, a minimum of three lung function measurements were recorded [26]. The investigations included static and dynamic lung volumes and maximal expiratory flows, using MasterScreen Pneumo systems (CareFusion, Höchberg). All tests were performed according to the recommendations of the ATS/ERS Task Force on lung function testing [27] and compared to the reference formulas of the ECCS [2]. Following the manufacturer's guidelines, the systems were flow-volume-calibrated daily. After three satisfying recordings of static lung volumes, minimal three forced flow volume manoeuvres were performed, starting from residual volume (RV) with a deep and forced inspiration, followed by a forced and maximal expiration. Only those measurements were accepted where the expiratory time (T_E) exceeded four seconds, the variation of end-expiratory flow was below 25 mL/s and no cough disturbed the expiratory phase.

Data analysis: The results are presented as mean values and standard deviations ($x \pm s_x$), along with the median. Using Fisher's paired t-test, mean values were proofed to be significantly different from reference values of ECCS, SAPALDIA- or LuftiBus-values [28]. Differences with P-values < 0.05 were regarded as threshold for significance. Linear regression analysis was performed for age, body height and BMI. Exponential or logarithmic functions did not show a closer correlation to age. Therefore the results from the simple linear regression analysis are presented. The mean values in %predicted according to the ECCS, SAPALDIA, LuftiBus and Bochum reference formulas of spirometric parameters were compared.

Results

1. *Lung function parameters compared to ECCS, LuftiBus, SAPALDIA, and Bochum reference values in males:* Values of lung function parameters in the group of younger males were higher than predicted. Mostly mean lung function parameters were 104 ± 7.4% of the reference values predicted by ECCS, and 106.2 ± 8.6% for LuftiBus and 106.1 ± 8.2% for SAPALDIA references. Lung function parameters of male students closely correlate to Bochum reference values (Table II). The mean value obtained from all parameters investigated was 98.0 ± 7.8% pred. The lowest values were obtained according to Bochum values for PEF (93.6 ± 15.7% pred), and the highest for MEF_{25} (103.5 30.1% pred).

Table II: Lung function parameters in %pred of ECCS, LuftiBus, SAPALDIA, and Bochum in young adult males (n = 140)

Parameter	ECCS	LuftiBus	SAPALDIA	Bochum
VC_{IN} (%pred)	101.5 ± 11.1 n.s.	-	-	97.7 ± 11.0 n.s.
FVC (%pred)	105.8 ± 11.4 ***	106.5 ± 11.4 ***	99.5 ± 10.7 n.s.	97.6 ± 10.3 n.s.
FEV_1 (%pred)	107.4 ± 13.5 ***	106.9 ± 13.4 ***	101.9 ± 12.8 **	99.5 ± 10.7 n.s.
$FEV_1\%VC_{IN}$	101.4 ± 7.4 n.s.	100.4 ± 7.2 ***	101.4 ± 7,23 *	97.6 ± 3.3 *
PEF (%pred)	104.8 ± 17.3 **	94.4 ± 15.6 ***	110.6 ± 18.1 ***	93.6 ± 15.6 ***
MEF_{75} (%pred)	105.0 ± 22.6 **	106.7 ± 22.9 ***	107.3 ± 22.8 ***	97.5 ± 15.3 n.s.
MEF_{50} (%pred)	106.7 ± 24.9 **	114.2 ± 26,6 ***.	112.6 ± 26.2 ***	99.1 ± 23.1 n.s.
MEF_{25} (%pred)	101.6 ± 30.1 n.s.	114.6 ± 33.4 ***	109.1 ± 31.8 ***	103.1 ± 30.1 n.s.
Mean ± std	104.3 ± 7.4	106.2 ± 8.6	106.1 ± 8.2	98.0 ± 7.2
n.s. non significant, * p<0.05, ** p<0.01, *** p<0.001				

2. *Lung function parameters compared to ECCS, LufitiBus and SAPALDIA reference values in females:* The values of spirometric lung function parameters in the group of younger females were up to 9.9% higher compared to the ECCS reference values. On average mean lung function parameters were 101.5 ± 3.64% of the reference values predicted by ECCS, and 101.7 ± 6.1% for LuftiBus and 98.5 ± 4.5% for SAPALDIA references.

Table III: Lung function parameters in %pred of ECCS, LuftiBus and SAPALDIA in young adult females (n = 165)

Parameter	ECCS	LuftiBus	SAPALDIA
VC_{IN} (%pred)	104.8 ± 12.2 ***	-	-
FVC (%pred)	109.9 ± 13.3 ***	105.7 ± 12.8 ***	99.1 ± 12.1 n.s.
FEV_1 (%pred)	103.6 ± 12.5 ***	105.1 ± 12.7 ***	99.8 ± 12.0 n.s.
$FEV_1\%VC_{IN}$	101.7 ± 7.8 **	98.5 ± 7.72 ***	99.3 ± 7.77 n.s.
PEF (%pred)	97.8 ± 15.1 n.s.	89.9 ± 13.9 ***	108.0 ± 16.7 ***
MEF_{75} (%pred)	99.3 ± 18.0 n.s.	97.8 ± 17.8 n.s.	101.4 ± 18.5 n.s.
MEF_{50} (%pred)	96.9 ± 19.6 *	107.9 ± 21.8 ***	104.1 ± 21.1 *
MEF_{25} (%pred)	98.0 ± 25.4 n.s.	107.2 ± 27.5 ***	77.1 ± 19.7 n.s.
Mean ± std	101.5 ± 3.4	101.7 ± 6.1	98.4 ± 4.5
n.s. non significant, * p<0.05, ** p<0.01, *** p<0.001			

3. *Correlation of lung function parameters to age:* No noticeable correlation between age and investigated respiratory parameters (VC, FVC, FEV_1, FEV_1%FVC, PEF, $MEF_{75,50,25}$) was found in the small age range of 18 to 26 years (Table IV and Fig. 2 and 3).

Table IV: Correlation of Lung function parameters to age in young adults aged 18 to 26 Years

Parameter	Males	Females
VC_{IN} (%pred)	y = -0,0021x + 5,987, $r^2 < 0{,}001$ n.s.	y = -0,0089x + 4,329, $r^2 < 0.001$ n.s.
FVC (%pred)	y = 0.0069x + 5,663, $r^2 < 0.001$ n.s.	y = -0.0055x + 4.276, $r^2 < 0.001$ n.s.
FEV_1 (%pred)	y = 0.0008x + 4,936, $r^2 < 0.001$ n.s.	y = -0.0237x + 4.086, $r^2 = 0.008$ n.s.
FEV_1 %VC_{IN}	y = -0.2426x + 112.9, $r^2 = 0.001$ n.s.	y = -0.699x + 118.8, $r^2 = 0.011$ n.s.
PEF (%pred)	y = 0,1591x + 7,102, $r^2 = 0.028$ n.s.	y = -0.0566x + 8.491, $r^2 = 0.008$ n.s.
MEF_{75} (%pred)	y = 0.2173x + 4.281, $r^2 = 0.050$ n.s.	y = - 0.0755x + 7.999, $r^2 = 0.014$ n.s.
MEF_{50} (%pred)	y = -0.0033x + 6.230, $r^2 < 0.001$ n.s.	y = -0.0388x + 5.370, $r^2 = 0.006$ n.s.
MEF_{25} (%pred)	y = 0.0035x + 3.619, $r^2 = 0.007$ n.s.	y = -0.0656x + 3.634, $r^2 = 0.042$ n.s.
n.s. p>0.05, * p<0.05, ** p<0.01, *** p<0.001		

Fig. 2: Correlation of body height and age for non-smoking male (♦) and female (o) medical students, aged 18 to 26 years.

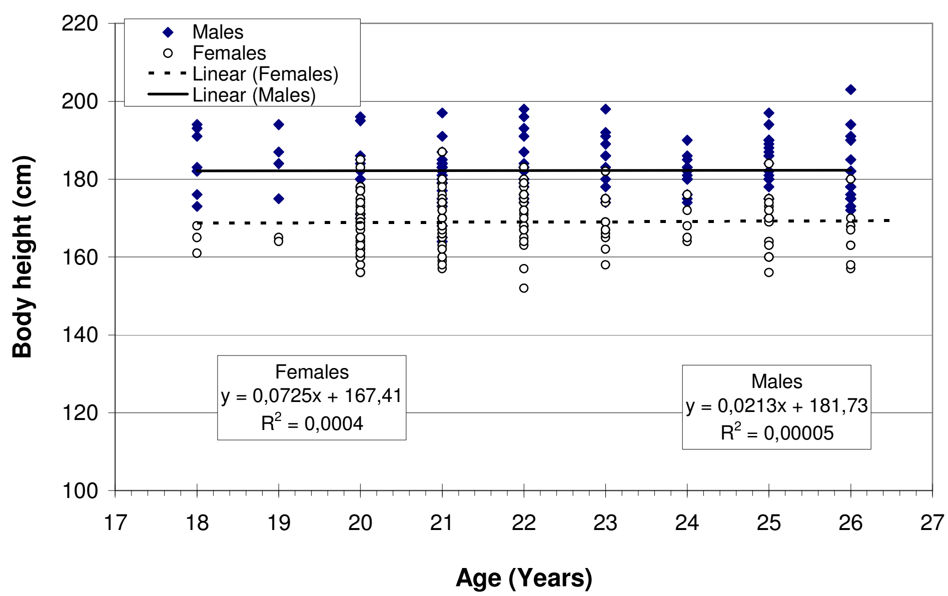
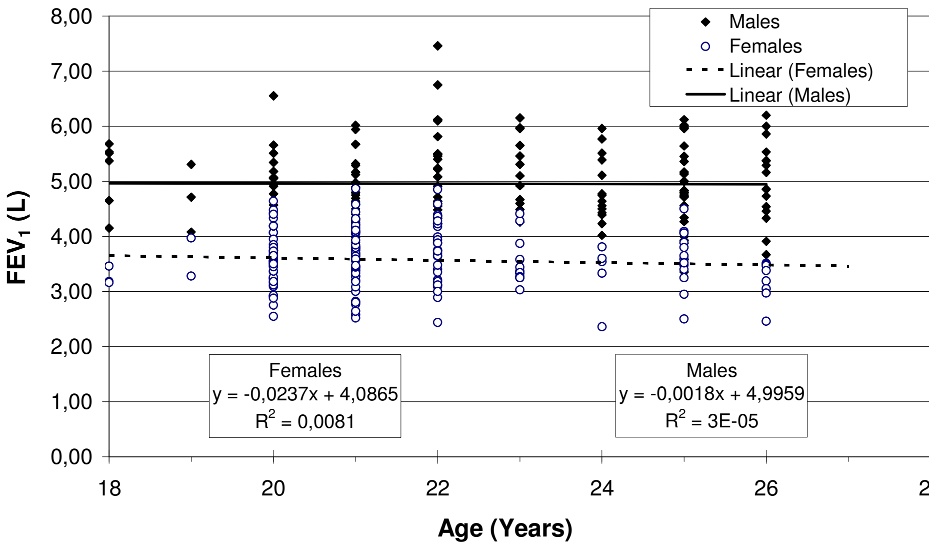


Fig. 3: Correlation of FEV_1 and age for non-smoking male (♦) and female (o) medical students, aged 18 to 26 years.

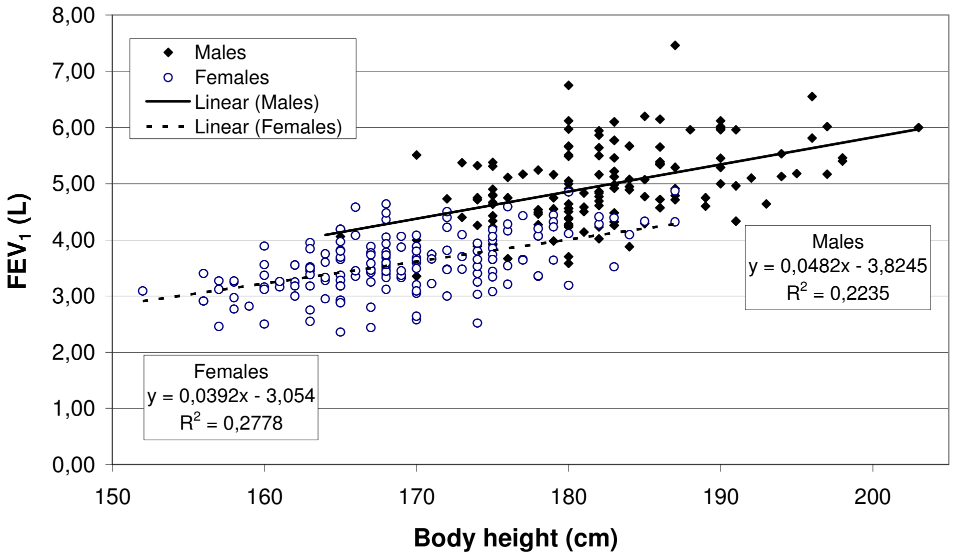


4. *Correlation of lung function parameters to body height:* Lung function parameter values increased with body height (Table V, Fig. 4). The most important parameters VC_{IN}, FVC, and FEV_1 were significantly correlated.

Table V: Correlation of Lung function parameters and body height in young adults aged 18 to 26 Years

Parameter	Males	Females
VC_{IN} (%pred)	y = 0.0729x – 7.428, r^2 = 0.382 **	y = 0,0519x – 4,633, r^2 = 0.356 **
FVC (%pred)	y = 0.0712x – 7.136, r^2 =0.379 ***	y = 0.0557x -5.250, r^2 = 0.369 **
FEV_1 (%pred)	y = 0.0482x – 3.835, r^2 =0.224 ***	y = 0.0392x – 3.054, r^2 = 0.2778 **
FEV_1 %VC_{IN}	y = 0.0554x +97.3, r^2 >0.001 n.s.	y = -0.0550x + 112.9, r^2 < 0.001 n.s.
PEF (%pred)	y = 0.0466x – 0.614, r^2 =0.074 n.s.	y = 0.0718x -2,321, r^2 = 0.072 n.s.
MEF_{75} (%pred)	y = 0.018x + 3.316, r^2 =0.011 n.s.	y = 0.0678x – 3.092, r^2 = 0.062 n.s.
MEF_{50} (%pred)	y = 0,0208x + 1.014, r^2 =0.024 n.s.	y = 0.0227x + 2.019, r^2 = 0.012 n.s.
MEF_{25} (%pred)	y =0.0198x – 1.1242, r^2 =0.053 n.s.	y = 0.014x + 0,192, r^2 = 0.014 n.s.
n.s. p>0.05, * p<0.05, ** p<0.01, *** p<0.001		

Fig. 4: Correlation of FEV_1 and body height for non-smoking male (♦) and female (o) medical students with body heights ranging from 154 to 204 cm.

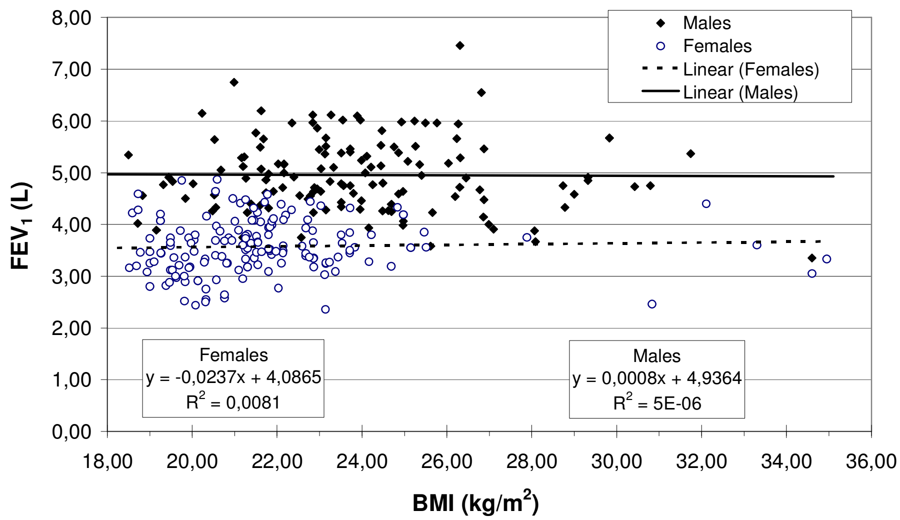


5. *Correlation of lung function parameters to body mass index:* BMI slightly increased with age in males (y = 0.3065x + 16.76, r^2 = 0.036) and females (y = 0.4519x + 11.75, r^2 = 0.097). There was no correlation of lung function parameters and BMI in the range between 18 and 35 kg/m^2 (Table. VI, Fig. 5).

Table VI: Correlation of Lung function parameters and body mass index in young adults aged 18 to 26 Years

Parameter	Males	Females
VC_{IN} (%pred)	y = 0.0034x +5.768, $r^2 < 0.001$	y = 0.0192x +3.720, $r^2 = 0.008$
FVC (%pred)	y = 0.0090x + 5.607, $r^2 = 0.001$	y = 0.0153x + 3.827, $r^2 = 0.004$
FEV_1 (%pred)	y = 0.0008x +4.936, $r^2 <0.001$	y = -0.0237x +4.087, $r^2 = 0.008$
FEV_1 %VC_{IN}	y = 0.0889x + 105.3, $r^2 < 0.001$	y = 0.5700x + 91.29, $r^2 = 0.015$
PEF (%pred)	y = 0.0159x + 10.37, $r^2 < 0.001$	y = 0.0298x + 6.623, $r^2 = 0.005$
MEF_{75} (%pred)	y = 0.0707x + 7.578, $r^2 = 0.012$	y = 0.0506x + 5.269, $r^2 = 0.014$
MEF_{50} (%pred)	y = 0.0218x + 5.639, $r^2 = 0.002$	y = 0.0239x + 4.012, $r^2 = 0.005$
MEF_{25} (%pred)	y = -0.0179x + 3.226, $r^2 = 0.004$	y = -0.0225x + 2.703, $r^2 = 0.011$
n.s. = non significant, * p<0.05, ** p<0.01, *** p<0.001		

Fig. 5: Correlation of FEV_1 and BMI for non-smoking male (♦) and female (o) medical students ranging from 18.5 to 35 kg/m^2.



Discussion

The commonly accepted reference formulas of the ECCS [1;2] for assessment of ventilatory lung function measurements of Caucasians are limited in fulfilling the current requirements of lung function testing. As for all other reference recommendations, the handling of the transition from adolescence to adults is an unsolved problem. The formulas were compiled by the ECCS experts from different investigations and subsets of individuals in the seventies and earlier. Meanwhile anthropometrical parameters significantly altered, the population is getting older, and technology has improved. The stringent definition of the lower limits of normal by subtracting 1.64*RSD with over age constant RSD has significant drawbacks for older and smaller subjects. The most frequently used reference values in Europe (ECCS 1983) include a plateau phase [6, 15], which would be appropriate for only 63% of the subjects according to the data of Robbins [15]. Prediction equations with no plateau, as used by most pulmonary function laboratories in the USA, are only appropriate for 22% of the men aged 18–33 yrs in this study. Van Pelt and co workers, studying FEV1 in a cross-sectional and longitudinal study in young adults [17], found a plateau phase or a period of continued of lung growth when data were correlated to age. There is consent, that FEV1 in smokers declines earlier in smoking young adults, compared to non smoking controls [15;17]. We cannot conclude, that pulmonary function development in young adults reaches a plateau phase since we performed a cross sectional study. In the relevant age range of 18 to about 33 years, longitudinal studies have shown either an ongoing lung growth or a decline in lung function parameters has already started. Taking the mean values, the different slopes may compensate each other and result in a plateau. Follow up periods of 10 years, reported in the literature are quite a long time, but do not cover the period from 17 to 45 years. More research is needed to come to a final conclusion.

Multi centre study for new European lung function recommendations: The need for a complete set of reference values, replacing the ECCS recommendations due the altered structures of our population can be realized only with a great financial, material and personal engagement in a multi centre European research project. At least a number of 20,000 subjects has to be recruited from local registration offices. Only subjects with verified heath status and non-restricted cooperation in the measurement are allowed to be selected, whereas smokers and diseased subjects carefully have to be excluded from evaluation. In a comprehensive reference value project not only static and dynamic lung volumes and maximal flows should be studied, but also parameters of body plethysmography, diffusion testing and blood gas analysis should be studied with standardised and well calibrated devices. Recently, the European Respiratory Society established a task force for generation of new reference values of lung function with the aim of compiling current normals from early childhood to senescence. A set of sustained references across all ages will be derived from their investigations, solving the problems of overlaps from adolescence to adults. But for statistical reasons this procedure is highly problematic. In childhood the independent variables for lung function parameters are mainly height and weight, however, for adolescents and adults height, age and sex are determining. So there is a discontinuity in the underlying mathematical models. Stanojevic and co-workers have published something like reference values spanning from early childhood to senescence [22;29].

ECCS reference values compared to LuftiBus and SAPALDIA-predictions: ECCS predicted values for FEV_1 in comparison to the LuftiBus-Study differ in about 200 mL in young adult males. For middle aged and older subjects differences are even smaller. The reference values of the SAPALDIA-Study are about 200 mL higher for young and middle aged males and about 300 mL for subjects older than 65 years. Values of LLN are largely similar in young subjects by ECCS and LuftiBus, LLN values for middle aged subjects are about 200 mL higher in the LuftiBus study. Despite the decrease of more than 1.5 L from 25 to 80 years of age, the difference between the predicted value and the 5^{th} percentile is nearly constant over the whole range of age. In the original version of the SAPALDIA-Study the value of the lower limit of normal approximates the predicted values with increasing age.[5]. Due to a simplified mathematical model, with respect to the small number of older subjects, the authors newly computed the equations for the LLN [25]. Now the reference values and their LLN are almost parallel in the SAPALDIA-Study as we know from ECCS formulas. In the Bochum study, based on data of only 257 healthy males, the coefficients of variation of the parameters in %predicted did not remarkable differ in the younger and older group as one might expect with respect to the differences in FEV_1 of about 2.0 L between a 25 years and an 85 years old male of 180 cm body height.

Summary and Conclusion

No correlation between age and body height was found in the age range of 18 to 26 years in males and females, whereas BMI slightly increases with age. However, in the small age range of investigation, lung function parameters did not correlate with age or BMI but the expected correlation to body height could be confirmed. According to our limited data, the recommendation of a plateau phase from ECCS entering an age of 25 years for calculation of reference values in the age range between 18 and 25 years can be supported. Static and dynamic parameters of younger adults were significantly higher than predicted by ECCS, SAPALDIA and LuftiBus study reference values. Considering the increasing age and height of our population and the changes in working conditions, a comprehensive multi centre study on lung function of Caucasians should be initiated by the international respiratory societies. Between Zapletal references for adolescents and ECCS, SAPALDIA, and LuftiBus predictions a non acceptable difference of 300 to 500 millilitres was found, which is not acceptable.

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