

## APPENDIX

**Table 1S. Main results of some studies that compared the impacts of different COPD airflow limitation (AFL) staging classifications in predicting survival, mortality and other clinical outcomes.**

Reference	Miller, Pedersen, & Dirksen (2007)	Miller and Pedersen (2010)	Pedone et al. (2013)	Turkeshi et al. (2015)	Hegendorfer et al. (2017)	Huang et al. (2018)
<b>Yr of publication</b>	.2007	.2010	.2012	.2015	.2016	.2018
<b>Aims</b>	.To test whether raw FEV <sub>1</sub> or FEV <sub>1</sub> /Height <sup>2</sup> was better than FEV <sub>1%pred</sub> for predicting survival	.To explore the relationship between different expressions of FEV <sub>1</sub> and all-cause mortality	.To compare the prognostic implications of 3 different expressions of FEV <sub>1</sub> in an unselected elderly population	.To investigate the short term prognostic value of FEV <sub>1</sub> /Height <sup>3</sup> for all-cause mortality	.To assess and compare the predictive value of 5 expressions of FEV <sub>1</sub> for all-cause mortality, unplanned hospitalization, decline in physical/mental status	.To evaluate the staging COPD performance of 7 expressions of FEV <sub>1</sub> in predicting the risks of some clinical outcomes
<b>Study design</b>	.Retrospective .Longitudinal follow-up	.Retrospective .Longitudinal follow-up	.Retrospective .Longitudinal follow-up	.Retrospective observational .Longitudinal follow-up: 3 Yrs/until death	. Retrospective observational .Longitudinal follow-up: 3 Yrs/until death	Retrospective .Longitudinal follow-up (≥1 Yr/until death)
<b>N° of COPD (M/F)</b>	.1095 (451/644)	.1095 (451/644)	.318 (250/68)	.54 (???)	.54 (???)	.296 (279/17)
<b>Control-groups</b>	.NA	.25872	.475 non-COPD [Post-BD FEV <sub>1</sub> /FVC > LLN] (207/268)	.447	.447	.NA
<b>Age (Yrs)</b>	.61.8±9.9 <sup>a</sup>	.> 20 .COPD: 61.8±9.9 <sup>a</sup>	.COPD: > 65 .COPD: 72.9±5.52 <sup>a</sup> .non-COPD: 73.2±6.29 <sup>a</sup>	.≥ 80 .84.8±3.7 <sup>a</sup>	.≥ 80 .84.8±3.7 <sup>a</sup>	.40-95 <sup>b</sup> .71±14 <sup>a</sup>
<b>BD test practice</b>	.300 µg of salbutamol and 0.06 mg of ipratropium bromide .2 weeks of ICS	.COPD group: 300 µg of salbutamol and 0.06 mg of ipratropium bromide .COPD group: 2 weeks of ICS	.Yes (fenoterol)	No	.No	.Yes (if available, n=240)
<b>COPD definition</b>	.Pre-BD FEV <sub>1</sub> /FVC < 89% <sub>pred</sub>	.Pre-BD FEV <sub>1</sub> /FVC < 89% <sub>pred</sub>	.Post-BD FEV <sub>1</sub> /FVC < LLN	.NR	.NR	.FEV <sub>1</sub> /FVC < LLN
<b>Used FEV<sub>1</sub></b>	.NR	.NR	.Post-BD	.Pre-BD	.Pre-BD	.Post-BD, if available
<b>FEV<sub>1</sub> expressions [applied cut off points]</b>	.FEV <sub>1</sub> raw .FEV <sub>1%pred</sub> .FEV <sub>1z-score</sub> .FEV <sub>1</sub> /Height <sup>2</sup>	.FEV <sub>1</sub> raw .FEV <sub>1%pred</sub> .FEV <sub>1z-score</sub> .FEV <sub>1</sub> /Height <sup>2</sup> .FEV <sub>1</sub> /Height <sup>3</sup> .FEV <sub>1</sub> Quotient	.FEV <sub>1%pred</sub> .FEV <sub>1</sub> /Height <sup>3</sup> .FEV <sub>1</sub> Quotient	.FEV <sub>1</sub> /Height <sup>3</sup>	.FEV <sub>1%pred</sub> .FEV <sub>1</sub> /Height <sup>2</sup> .FEV <sub>1</sub> /Height <sup>3</sup> .FEV <sub>1</sub> Quotient	.FEV <sub>1%pred</sub> .FEV <sub>1%pred</sub> [quartiles] .FEV <sub>1z-score</sub> [quartiles] .FEV <sub>1</sub> /Height <sup>2</sup> [quartiles; cut off] .FEV <sub>1</sub> /Height <sup>3</sup> [quartiles] .FEV <sub>1</sub> Quotient [quartiles]

Table 1S. Continued.						
Reference	Miller, Pedersen, & Dirksen (2007)	Miller and Pedersen (2010)	Pedone et al. (2013)	Turkeshi et al. (2015)	Hegendorfer et al. (2017)	Huang et al. (2018)
<b>Number of stages</b>	.5 (FEV <sub>1%</sub> pred - GOLD 2005 (NIHNHLBI, 2005)) .4 (FEV <sub>1</sub> /Height <sup>2</sup> : 0.5; 0.4; 0.3)	.10 (1 to 10 deciles)	.5 (worst, 2 <sup>nd</sup> , 3 <sup>rd</sup> , 4 <sup>th</sup> , best quintiles)	.2 (≤ the lowest quartile and the rest)	.4 (1 <sup>st</sup> , 2 <sup>nd</sup> , 3 <sup>rd</sup> and 4 <sup>th</sup> quartiles)	.4 (1;2;3;4)
<b>Outcomes</b>	.AFL severity .Survival	.All-cause mortality	.Prognostic implications (NR) .Mortality risk at 5, 10 and 15 Yrs	.All-cause mortality at 3 Yrs .Unplanned hospitalization .Decline in physical status .Decline in mental status	.All-cause mortality at 5 Yrs .Unplanned hospitalization .Decline in physical status .Decline in mental status	.SAE .All-cause mortality
<b>Mains results</b>	<b>COPD AFL severity</b> .FEV <sub>1%</sub> pred [GOLD] Light*: 40.05% <sup>c</sup> Severe*: 59.94% <sup>c</sup> .FEV <sub>1</sub> /Height <sup>2</sup> : Light*: 54.14% <sup>c</sup> Severe*:45.86% <sup>c</sup> <b>COPD survival</b> .FEV <sub>1%</sub> pred: not as good as either raw FEV <sub>1</sub> or FEV <sub>1</sub> /Height <sup>2</sup> at predicting survival. .FEV <sub>1</sub> /Height <sup>2</sup> : stratify COPD subjects into survival groups better than GOLD criteria without recourse to other data such as arterial gases. .FEV <sub>1</sub> /Height <sup>2</sup> : better than both raw FEV <sub>1</sub> and FEV <sub>1%</sub> pred for expressing degree of lung function impairment	<b>AUC for predicting survival</b> .FEV <sub>1</sub> Quotient: 0.631 [0.624-0.637] <sup>d</sup> (p: NR) .FEV <sub>1</sub> /Height <sup>3</sup> :0.626 [0.619-0.633] <sup>d</sup> .FEV <sub>1</sub> /Height <sup>2</sup> :0.621 [0.614-0.628] <sup>d</sup> .raw FEV <sub>1</sub> :0.606 [0.599-0.612] <sup>d</sup> .FEV <sub>1%</sub> pred: 0.586 [0.579-0.592] <sup>d</sup> .FEV <sub>1z</sub> -score: 0.571 <sup>e</sup> <b>Cox regression analysis</b> .The best model for predicting survival was with FEV <sub>1</sub> Quotient followed by FEV <sub>1</sub> /Height <sup>3</sup> and FEV <sub>1</sub> /Height <sup>2</sup> then FEV <sub>1%</sub> pred (p<0.05) <b>Data from a single sex</b> .FEV <sub>1</sub> Quotient: no advantage over raw FEV <sub>1</sub>	<b>COPD group</b> .FEV <sub>1%</sub> pred compared to FEV <sub>1</sub> /Height <sup>3</sup> and FEV <sub>1</sub> Quotient: weaker association with mortality. . FEV <sub>1</sub> Quotient: stronger association with mortality. . FEV <sub>1</sub> Quotient: better performance compared to FEV <sub>1</sub> /Height <sup>3</sup> in predicting mortality.	.FEV <sub>1</sub> /Height <sup>3</sup> : associated with all-cause mortality and hospitalizations as well as decline in physical and mental functioning .FEV <sub>1</sub> /Height <sup>3</sup> : takes into account body size variability and does not require reference equation.	<b>Predicting all cause mortality and hospitalization</b> .FEV <sub>1</sub> /Height <sup>3</sup> : highest relative IDI <b>Physical and mental decline</b> .Only FEV <sub>1</sub> /Height <sup>3</sup> was independently associated with physical decline (adjusted OR= 1.93) .FEV <sub>1</sub> Quotient: highest adjusted OR (2.80) and highest relative IDI (0.348) for mental decline .FEV <sub>1</sub> Quotient: best performance in predicting mental decline compared with FEV <sub>1%</sub> pred, followed closely by FEV <sub>1</sub> /Height <sup>3</sup> and FEV <sub>1</sub> /Height <sup>2</sup>	<b>SAE</b> .Staging based on FEV <sub>1</sub> Quotient and FEV <sub>1</sub> /Height <sup>2</sup> [quartiles]: discriminated the risk of SAE .Staging based on FEV <sub>1%</sub> pred [GOLD] and FEV <sub>1z</sub> -score [quartiles]: stratified unsatisfactorily the risks of SAE <b>All-cause mortality</b> .FEV <sub>1%</sub> pred [quartiles], FEV <sub>1</sub> Quotient [quartiles] and FEV <sub>1</sub> /Height <sup>2</sup> [cut off]: stratified the mortality risk

<b>Reference</b>	<b>Miller, Pedersen, &amp; Dirksen (2007)</b>	<b>Miller and Pedersen (2010)</b>	<b>Pedone et al. (2013)</b>	<b>Turkeshi et al. (2015)</b>	<b>Hegendorfer et al. (2017)</b>	<b>Huang et al. (2018)</b>
<b>Conclusions</b>	.FEV <sub>1</sub> /Height <sup>2</sup> : better related to survival in COPD than FEV <sub>1</sub> % <sub>pred</sub> <sup>d</sup> . .FEV <sub>1</sub> /Height <sup>2</sup> : best method for expressing degree of FEV <sub>1</sub> impairment	.FEV <sub>1</sub> % <sub>pred</sub> : not ideal for expressing lung function impairment .FEV <sub>1</sub> Quotient: best method, with FEV <sub>1</sub> /Height <sup>3</sup> being the next alternative	.FEV <sub>1</sub> Quotient and FEV <sub>1</sub> /Height <sup>3</sup> : appealing way of standardizing the FEV <sub>1</sub> .FEV <sub>1</sub> % <sub>pred</sub> : not the best prognostic indicator in elderly people with COPD	.Low FEV <sub>1</sub> /Height <sup>3</sup> : associated with all-cause mortality and higher risk of hospitalizations as well as decline in physical and mental functioning .FEV <sub>1</sub> /Height <sup>3</sup> : more suitable for use in elderly	.FEV <sub>1</sub> /Height <sup>3</sup> and FEV <sub>1</sub> Quotient: better at predicting all-cause mortality, hospitalization and physical and mental decline	.Staging severity based on FEV <sub>1</sub> % <sub>pred</sub> [GOLD]: predicted inadequately the risks of adverse outcomes .Staging severity based on FEV <sub>1</sub> Quotient [quartiles]: predicted the risks of SAE and mortality and well stratified the differences in survival
<p><b>AUC</b>: area under the curve. <b>BD</b>: bronchodilator. <b>COPD</b>: chronic obstructive pulmonary disease. <b>F</b>: female. <b>FEV<sub>1</sub></b>: forced expiratory volume in one second. <b>Quotient</b>: lowest sex-specific first percentile (0.5 L for males). <b>FVC</b>: forced vital capacity. <b>GOLD</b>: global initiative for chronic obstructive lung disease. <b>ICS</b>: inhaled corticosteroids. <b>IDI</b>: integrative discrimination index. <b>LLN</b>: lower limit of normal. <b>M</b>: male. <b>N°</b>: number. <b>NA</b>: non-applied. <b>NR</b>: not-reported. <b>OR</b>: odds-ratio. <b>p</b>: probability. <b>SAE</b>: severe acute exacerbation. <b>SD</b>: standard deviation. <b>Yr</b>: year. %<sub>pred</sub>: % of the predicted value.</p> <p>Data were:</p> <p><sup>a</sup>Mean±SD  <sup>b</sup>Minimum-maximum  <sup>c</sup>Percentage  <sup>d</sup>Mean (Confidence interval)  <sup>e</sup>Mean</p> <p>Notes: <b>**"light"</b> : FEV<sub>1</sub>%<sub>pred</sub> at stage 0, 1 and 2 of GOLD 2005 (<b>NIHNHLBI, 2005</b>) or FEV<sub>1</sub>/Height<sup>2</sup> &gt; 0.4 L/m<sup>2</sup>  <b>**"severe"</b>: FEV<sub>1</sub>%<sub>pred</sub> at stage 3 and 4 of GOLD 2005 (<b>NIHNHLBI, 2005</b>) or FEV<sub>1</sub>/Height<sup>2</sup> ≤ 0.4 L/m<sup>2</sup></p>						

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