Validity of the COPD-6® Device for COPD Screening in the Primary Care Setting of China

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Research

Abstract

Background: The use of simple and affordable screening tools for chronic obstructive pulmonary disease (COPD) is limited. We aimed to assess the validity of a handheld expiratory flow meter (COPD-6®, Vitalograph Ltd., Ireland) for COPD screening in Chinese primary care settings.

Methods: In our cross-sectional study, subjects were randomly selected in eight primary care settings. Testing with the Vitalograph-COPD-6® and conventional spirometry were sequentially performed on subjects. The correlation between COPD-6® and conventional spirometry was determined. Validity was analyzed by the area under the receiver operator characteristic curve (AUC) of the forced expiratory volume in one second (FEV_1) / forced expiratory volume in six seconds (FEV_6) that used to detect airway obstruction. The sensitivity, specificity, predictive values, and likelihood ratio were calculated according to different FEV_1/FEV_6 cut-off points.

Results: 229 subjects (15.4%) were diagnosed with airflow limitation by standard spirometry. FEV_1, FEV_6, and FEV_1/FEV_6 measured by COPD-6® were correlated with FEV_1, FVC, and FEV_1/FVC measured by spirometry (r=0.889, 0.835and 0.647, p<0.001), respectively. AUC of the FEV_1/FEV_6 to determine airflow obstruction was 0.857 (95%CI: 0.826 to 0.888). No significant difference of AUC was observed between the symptomatic group and the asymptomatic population (AUC=0.869 vs. 0.843, P=0.425). A similar phenomenon was found in the AUC of smokers and never-smokers (AUC=0.862 vs.0.840; P=0.515). The value of AUC was largest (i.e., 0.80) when the cut-off point for FEV_1/FEV_6 was 0.77.

Conclusions: The handheld COPD-6® could be used as a pre-screening device on early diagnosis of COPD in Chinese primary care settings.

Introduction

Characterized by persistent airflow limitation, chronic obstructive pulmonary disease (COPD) was a high-prevalence disease with heavy mortality and morbidity burden[1, 2]. It's reported that COPD caused 2.6% of global disability-adjusted life years (DALYs) and 3.2 million death worldwide in 2015[3]. Airflow limitation is defined as a post-bronchodilator forced expiratory volume in 1 second (FEV_1) / forced vital capacity (FVC) < 0.7 and regarded as the essential test for the diagnosis of COPD[4]. In COPD patients, persistent airflow limitation might lead to the substantially impaired quality of life and higher risk of premature death[5].

For the long-term of the asymptomatic phase, countless COPD patients remained undiagnosed until the onset of severe symptom[6, 7]. Early symptoms of COPD are subtle and unrecognized for numbers of patients. The reduction of lung function was usually dramatic and irreversible when COPD was diagnosed for the first time. What is more, the reduction of lung function could lead to poor health-related quality of life[7–9]. Although undiagnosed COPD patients usually have fewer exacerbations than severe COPD patients, they also require amount of medical care services for exacerbation events that should

have been avoided[10]. Therefore, misdiagnosis of COPD could also bring considerable health burden. In this context, early screening for COPD was regarded as a potential method to reduce the burden of morbidity and mortality of patients[7]. However, the problem of underdiagnosis on COPD is obvious (ranging from 72–93%)[7]. There were increasing interests in improving the early detection of COPD in the primary care setting during the last decade. Spirometry is a well-established tool for quantifying airflow limitation and the diagnosis of patients with COPD[5]. However, there are several seasons for conventional spirometry in primary care practice. First, the expensive cost of the machine has limited technology extension. Second, shortness of professional training led to the unreliable quality of test and interpretation in primary care settings[11–14]. The U.S. Preventive Services Task Force and the American College of Physicians recommend that spirometry should not be used to screen for airflow limitation in individuals without respiratory symptoms. The use of conventional spirometry in primary care setting may result in a waste of medical resources and an overestimation of COPD burden[15, 16].

The use of simple and affordable screening tools is limited. Forced expiratory volume in 6 seconds (FEV_6), a more easily achieved and reproducible measurement, has been regarded as an alternative to FVC[17]. Primary studies had found that FEV_1/FEV_6 could be used as a substitute for the FEV_1/FVC in the diagnostic screening for COPD[18]. There is a strong correlation between FEV_1/FVC and FEV_1/FEV_6[19–22]. Consequently, inexpensive, user-friendly, and hand-held devices for measuring FEV_1 and FEV_6 have been produced to detect COPD in primary care[23–29].

Vitalograph COPD-6® (model number 4000, Vitalograph Ltd., Ireland) is one kind of emerging devices. Primary care physicians can obtain FEV_1, FEV_1% predicted, FEV_6, FEV_6%predicted, FEV_1/FEV_6, and lung age through COPD-6® test. It can also provide the diagnosis of airflow limitation and severity classification according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline[5]. However, no study has examined the validity of COPD-6® in low or middle-income countries, including China. Furthermore, the best cut-off value using to define airflow limitation remains uncertain in China. Therefore, we designed this study to assess the validity of COPD-6® device for COPD screening in primary care settings in China.

Methods

Setting

With the socioeconomic differences between rural and urban regions, two urban streets and two rural communities were randomly selected from an urban region (Guangzhou, Guangdong Province) and a rural region (Lianping, Guangdong Province), respectively. Two primary care settings were selected from each of the street/community mentioned above. Finally, eight primary care settings were involved in our study.

Study Population

The sample size of each age group was calculated according to the percentage of the population aged ≥ 40 years reported in the latest census. In selected primary care settings, 200 residents from four different age groups (40−49, 50−59, 60−69, and ≥ 70) was required. People engaged in these projects should had given informed consent before conventional spirometry and COPD-6® testing.

There were several exclusion criteria for spirometry and COPD-6® testing to avoid : (1) medical history of thoracic, abdominal or eye surgery in previous three months; (2) medical history of acute heart events (e.g., angina, acute myocardial infarction, and malignant arrhythmia) in previous three months; (3) hospitalizations for heart diseases in previous one month; (4) patients with active pulmonary tuberculosis disease or taking anti-tuberculosis drugs; (5) patients with a history of retinal detachment; (6) patients with new tumor diagnosed or undergoing a tumor treatment; (7) patients with cognitive impairment or mental disorder; (8) high paraplegia or thoracic deformity; (9) women during pregnancy or lactation.

Data Collection

Procedures

Unique ID number was assigned to each participant. A standardized questionnaire, COPD-6® testing, and conventional spirometry were conducted for each participant sequentially.

COPD-6® testing

COPD-6® testing was executed by well-trained primary care physicians. At least three maneuvers were performed for each participant without the use of bronchodilator. Results should have met criteria for acceptability (forced expiration for at least 6 s) and reproducibility (at least three acceptable flow-volume curves and the second-highest FEV_6 and FEV_1 were within 0.2L or 10% of highest value). We selected the best value for the report.

Spirometry

Spirometry testing was performed independently by trained operators according to American Thoracic Society/European Respiratory Society guidelines[30]. Operators were blinded to the COPD-6® results. All study sites used the same model spirometer (JAEGER-Master Screen Pneumo®, Carefusion™, GER). Spirometers were calibrated before each day's testing. Lung function parameters were measured before and 15 ~ 25 minutes after inhaling a dose of 400 µg salbutamol through a 500 ml spacer. We determined a quality grade (A ~ F) based on acceptable maneuvers and repeatability of the FEV_1 and FVC[31]. Spirometry results with grades A, B, or C were considered acceptable for analysis.

Definitions and diagnostic criteria of COPD

Conventional spirometry results were classified as COPD if the post-bronchodilation FEV_1/FVC ratio was < 0.7. COPD was classified as stage I ($FEV_1 > 80\%$ of predicted value), stage II ($50\% \leq FEV_1 < 80\%$ of predicted value), stage III ($30\% \leq FEV_1 < 50\%$ of predicted value), and stage IV ($FEV_1 < 30\%$ of predicted value).

Analysis

Standard validation measures, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratio (for a positive test, LR+) were calculated at different cut-off points of FEV_1/FEV_6. ROC curve will be used to facilitate the cut-off point. The correlations of FEV_1, FEV_6, FEV_1/FEV_6 measured by the COPD-6® (pre-bronchodilator), with FEV_1, FVC, FEV_1/FVC measured by spirometry (post-bronchodilator), were examined by Pearson's correlation analysis and Bland–Altman plots[28]. The 95% confidence interval was presented for all variables.

Our study protocol was approved by the Medical Ethics Committee of the Guangzhou Institute of Respiratory Diseases. Analysis was performed in SPSS (version 24).

Results

1,650 subjects were initially recruited (978 from urban region, 672 from the rural county). We excluded 120 subjects because of missing data, and 43 subjects whose quality results of spirometry were under grade C. Information about symptoms was available from 1486 subjects. There were 845 (56.9%) never-smokers and 641 (43.1%) smokers in our study. The prevalence of COPD was different among diverse smoking status and respiratory symptoms population (Table 1). 1258 (84.7%) subjects with FEV_1/FVC ≥ 70%, 229 (15.4%) were diagnosed COPD (FEV_1/FVC < 70%). 105 COPD patients (45.9%) were GOLD stage I, 91(39.7%) were GOLD stage II, 28(12.2%) were GOLD stage III, and 5(6.3%) were GOLD stage IV.

Table 1
Characteristics of all participants

	Non-COPD (N = 1258)	COPD (N = 229)
Area		
Urban	945	121
Rural	542	108
Sex		
men	877	188
women	610	41
Age (years)		
40 ~ 49	222	7
50 ~ 59	641	73
60 ~ 69	464	92
≥70	160	57
BMI (kg/m^2)		
<18.5	116	32
18.5 ~ 23.9	782	129
24.0 ~ 27.9	460	57
≥28.0	129	11
Smoking status		
Never-smoker	845	70
Smoker	641	159
Respiratory symptoms		
With respiratory symptom	362	111
Without respiratory symptom	1124	117
Lung function		
FEV1/FVC > 0.7	1258	-
GOLD stage I	-	105
GOLD stage II	-	91

	Non-COPD (N = 1258)	COPD (N = 229)
GOLD stage III	-	28
GOLD stage IV	-	5

Figure 1 (A) shows the strong correlation between FEV_1 measured by two machines in total population ($r_1 = 0.889$, P < 0.001), non-COPD group ($r_2 = 0.869$, P < 0.001) and COPD group ($r_3 = 0.907$, P < 0.001). Significant difference was observed between non-COPD group and COPD group (z = 2.509, P = 0.012). Figure 1 (B) shows strong relationships between FEV_1 measured by spirometry and COPD-6® in groups of GOLD stage I (r_I=0.810, P < 0.001), stage II (r_{II}=0.802, P < 0.001) and stage III (r_{III}=0.637, P < 0.001) but nonsignificant correlation was found in GOLD stage IV group (r_{IV}=0.844, P = 0.072). No statistical significance was found among GOLD stage I, stage II and stage III (r_I vs. r_{II}: z = 0.141, P = 0.887; r_I vs. r_{III}: z = 1.675, P = 0.094; r_{II} vs. r_{III}: z = 1.558, P = 0.119). Bland-Altman graph of FEV_1 measured by spirometry and COPD-6® is shown in Fig. 1 (C). The limit of Agreement (LoA) was 0.445 ~ 0.816 L, and 4.5% (67/1487) points were out of the 95% LoA.

Figure 2 (A) shows strong correlations between FVC measured by spirometry with FEV_6 measured by COPD-6® in total population ($r_1 = 0.835$, P < 0.001), non-COPD group ($r_2 = 0.865$, P < 0.001) and COPD group ($r_3 = 0.807$, P < 0.001). Statistical difference was detected between non-COPD group and COPD group (z = 2.668, P = 0.008). Figure 2 (B) shows strong relationships between FVC measured by spirometry and FEV_6 measured by COPD-6® in groups of GOLD stage I (r_I=0.737, P < 0.001), stage II (r_{II}=0.724, P < 0.001), stage III (r_{III}=0.574, P = 0.0014), but no significant correlation was found in GOLD stage IV group (r_{IV}=0.615, P = 0.269). No significant difference was found among groups (r_I vs. r_{II}: z = 0.187, P = 0.851; r_I vs. r_{III}: z = 1.301, P = 0.193; r_{II} vs. r_{III}: z = 1.161, P = 0.246). Figure 2(C) shows the Bland–Altman graph of FVC by spirometry and FEV_6 by COPD-6®. LoA was 0.514 ~ 1.297L, and 5.2% (77/1487) points were out of the 95%LoA.

Figure 3 (A) shows the relationship between FEV_1/FVC measured by spirometry and FEV_1/FEV_6 measured by COPD-6® in total group ($r_1 = 0.647$, P < 0.001), non-COPD group ($r_2 = 0.343$, P < 0.001) and COPD group ($r_3 = 0.686$, P < 0.001). Figure 3 (B) presented the relationship between FEV_1/FVC measured by spirometry and FEV_6/FVC measured by COPD-6® in groups of GOLD stage I (r_I=0.197, P < 0.044), stage II (r_{II}=0.641, P < 0.001), stage III (r_{III}=0.715, P < 0.001) and stage IV (r_{IV}=0.784, P = 0.117). Figure 3 (C) is the Bland–Altman graph of FVC by spirometry and FEV_6 by COPD-6® and the 95%LoA is -20.944 to 12.822.

Table 2 presented the AUC, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and positive likelihood ratio (LR+) at different cut-off points of FEV_1/FEV_6 ratios. The AUC was largest (i.e., 0.80) when the cut-off point is 0.77.

Table 2
The measures on sensitivity and specificity at different cut-off points of
FEV_1/FEV_6.

Cut-off point	AUC[a]	SE%[b]	SP%[c]	PPV%[d]	NPV%[e]	LR +[f]
< 0.65	0.62	25.82	98.93	80.80	88.02	23.15
< 0.70	0.70	41.95	97.92	78.75	90.34	20.28
< 0.75	0.77	60.22	92.96	60.83	92.37	8.52
< 0.77	0.80	69.94	89.98	55.78	94.29	6.92
< 0.80	0.79	77.78	80.13	41.63	95.24	3.91

[a] AUC = area under the receiver operator characteristic curve

[b] SE = sensitivity

[c] SP = specificity

[d] PPV = positive predictive value

[e] NPV = negative predictive value

[f] LR + = positive likelihood ratio

ROC curve was used to determine the best corresponding cut-off for FEV_1/FEV_6 (Fig. 4A). When the FEV_1/FEV_6 cut-off value of was 0.77, the area under the receiver operator characteristic curve (AUC) was 0.86 (95% CI: 0.83–0.89) and the sensitivity (71.2%) and specificity (89.8%) was greatest. Table 2 shows AUC, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and positive likelihood ratio (LR+) at different cut-off points of FEV_1/FEV_6 ratios.

Figure 4 (B) shows ROC curves of FEV_1/FEV_6 measured by COPD-6® to identify airflow obstruction in the symptoms group and asymptomatic patients. AUC were 0.87 (95%CI: 0.82–0.916) and 0.84 (95%CI: 0.802–0.884), no significant difference (z = 0.789, P = 0.425) was observed between two groups. The AUC of FEV_1/FEV_6 that used to identify airflow obstruction in the smoker group (including current smokers and ex-smokers) and the never-smokers were 0.86 (95%CI: 0.82 to 0.90) and 0.84 (95%CI: 0.79 to 0.89), respectively. No significant difference was observed (z = 0.651, P = 0.515) (Fig. 4C).

Discussion

This is the first study to confirm the validity of a handheld expiratory device (COPD-6®) for COPD screening for primary care settings in China. We also came out with result that the appropriate cut-off

value for FEV_1/FEV_6 to determine airflow limitation was 0.77 in Chinese primary care settings, including both rural and urban area.

It has already been demonstrated that FEV_6 is a reliable alternative for FVC to detect airway obstruction and restriction[20]. There are two types of handheld tools for measuring FEV_6 and FEV_1/FEV_6: the Piko-6 (Ferraris Co., UK) and the COPD-6® (Vitalograph Ltd., Ireland). Previous studies have demonstrated that these devices could be useful in detecting pulmonary obstructive pathologies[23–28, 32]. However, the best cut off point to use for defining airflow obstruction remained uncertain. Vandevoorde et al. [33]and Melbye et al.[34] reported that $FEV_1/FEV_6 < 70–73\%$ can be used as a valid alternative to $FEV_1/FVC < 70\%$ for the detection of obstruction using conventional spirometers. Rosa et al. reported that the best cut-off point for the FEV_1/FEV_6 ratio was 0.75 in subjects aged 40 years or over[35]. However, these studies were performed with conventional spirometers. Since we used the COPD-6®, a handheld spirometer, we cannot blindly adapt these values to our study directly.

In our study, we use $FEV_1/FVC < 70\%$ as the "gold standard" to detect airflow obstruction. The AUC for FEV_1/FEV_6 to identify airflow limitation was 0.857. The best cut-off point for FEV_1/FEV_6 was 77.15% with a sensitivity of 71.2% and specificity of 89.8%. Besides, almost all of the discordant cases were close to the cut-off value. Our results in line with previous study which determined 73% as the cut-off value with greatest sensitivity and specificity[27]. The latest study from United Kingdom also support our result with closely cutoff (e.g., 78%)[36].

There are several seasons lead to the heterogeneity of studies: methodological measures, different prevalence of airway limitation and the cut off points used to define airflow obstruction. Previous results of multiple meta-regression presented that the prevalence of airway limitation may have an effect on diagnostic-odds ratio[21]. According to previous study, sensitivity and specificity was dependent on the prevalence of moderate-to-severe airway obstruction. Low prevalence of severe airway obstruction may reduce the sensitivity of FEV_6, and Low prevalence of mild airway obstruction reduced the specificity of FEV_6 [37]. In our study, subjects were randomly selected and representative of the real world. Subjects included smokers and non-smokers, rural and urban residents, previous diagnosed and never diagnosed COPD patients. In this study, the prevalence of obstruction was 15.3% (229/1487). The best cut-off point for FEV_1/FEV_6 was 77.15% with a sensitivity of 71.2% and specificity of 89.8%. In previous study, (population aged 45–85 years and with smoking history of > 15 pack-years), sensitivity and specificity were 79.2% and 80.3% when cut-off value was set as 73%[27]. Despite the inconstant result of cut-off point of FEV_1/FEV_6, our findings show that COPD-6® device was effective in detecting previously undiagnosed COPD and ought to be used as a tool for COPD screening in Chinese primary care settings. We came out with a result that about one of two patients whose $FEV_1/FEV_6 < 0.77$ will exhibit airflow limitation with spirometry.

Furthermore, similar AUC values were obtained in the symptomatic population (AUC = 0.87) and asymptomatic population (AUC = 0.84). No significant difference was observed between smoking group

(including smokers and ex-smokers) (AUC = 0.86) and non-smokers (AUC = 0.84). The results remind us that the COPD-6® device was effective in detecting airflow limitation for population with diverse characteristics, especially in non-smokers and asymptomatic patients.

To our best knowledge, handheld spirometric measurements (i.e., COPD-6®) are not identical to conventional spirometry. The most limitation of this approach was handheld spirometric measurements may not be appropriate to be used for determining the grade of airflow limitation. We assessed the correlation of several measures by COPD-6® and spirometry in different stages of COPD. No significant correlations were observed between FVC measured by spirometry and FEV_6 measured by COPD-6® in GOLD stage IV. FEV_1/FVC measured by spirometry was also not correlated with FEV_1/FEV_6 measured by COPD-6® in GOLD stage IV.

These phenomena indicated the fact that COPD-6® may not be appropriate to be used for determining the grade of airflow limitation.

There are several potential reasons for differences and inconsistency mentioned above: (1) FEV_1/FVC and FVC are more dependent on the FET(Forced expiratory time) than FEV_1/FEV_6 and FEV_6[38]; (2) Instead of measuring the whole FVC, COPD-6® testing stops measuring after 6 s and results in the risk of overstating FEV_1/FEV_6 ratio; (3) COPD-6® does not provide graph analysis of the volume/time or flow/volume curves that are essential (especially the later ones) in quality control; (4)In this study, COPD-6® were performed before the use of bronchodilation, and the conventional spirometry were adapted after the process of post-bronchodilation; (5) In our study, only five patients were GOLD stage IV, which might cause statistical bias.

However, limitations mentioned above is irrelevant for the COPD screening in primary care settings. Utilization of handheld expiratory flow meter (COPD-6®) was aimed to reduce misdiagnosis rate and avoid the waste of medical resources at the same time. Our study, including the handheld expiratory flow meter and its cutoff value, can be widely recommended for the practice of COPD screening in Chinese communities.

Conclusions

The handheld Vitalograph COPD-6® meter could be used as a pre-screening device in early diagnosis of COPD in Chinese primary care settings. Furthermore, it should be noted that the cut-off value for FEV_1/FEV_6 to determine airflow limitation was 0.77.

List Of Abbreviations

COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in one second; FEV_6, forced expiratory volume in six seconds; FVC, forced vital capacity; AUC, area under the receiver operator characteristic curve; GOLD, global initiative for chronic obstructive lung disease; LoA, limit of Agreement.

Declarations

Ethics approval and Consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data which were generated or analysed are included in this published article and also its supplementary information files.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Pixin Ran, Shuyun Chen, Yumin Zhou, Xiaochen Li and Zihui Wang designed the study. Shuyun Chen and Xiaochen Li participated in data organization. Shuyun Chen and Zihui Wang participated in data analysis. Shuyun Chen, Yumin Zhou, and Zihui Wang contributed to interpretation of the findings. Shuyun Chen and Zihui Wang drafted the manuscript. Yumin Zhou and Zihui Wang contributed to article modification. Other authors participated in data collection. All authors have contributed to the last version of the manuscript. The authors read and approved the final manuscript.

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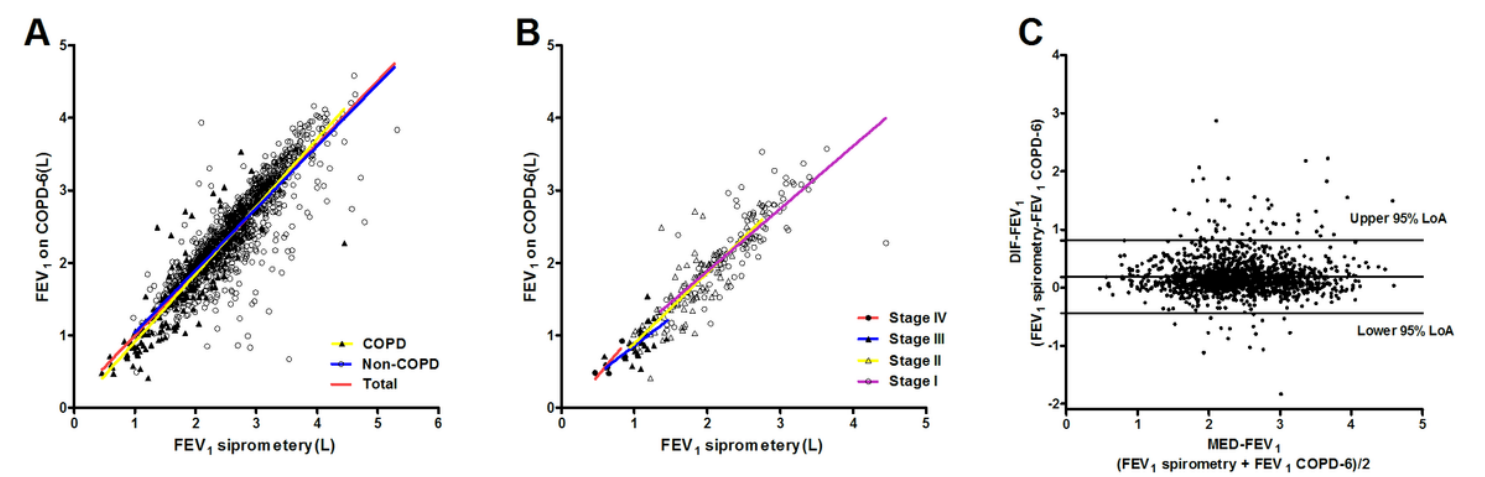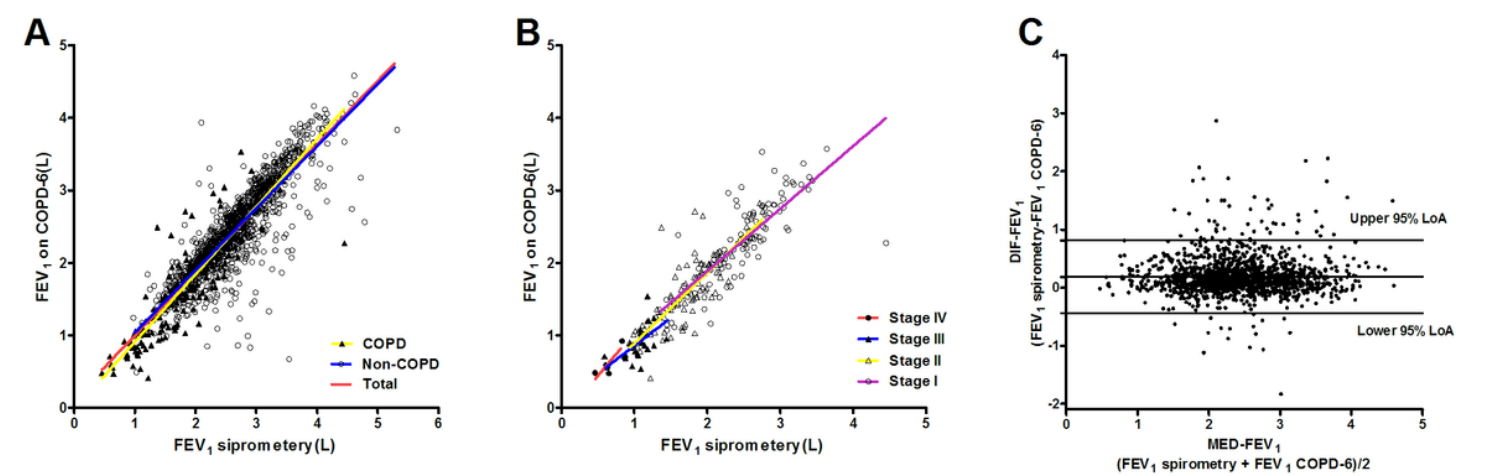
Figures

Figure 1

Correlation of FEV1 measured by spirometry with FEV1 measured by COPD-6 (A) Relationship between FEV1 measured by spirometry and FEV1 measured by COPD-6® in total group (r1=0.889, P<0.001), non-COPD group (r2=0.869, P<0.001) and COPD group (r3=0.907, P<0.001). (B) Relationship between FEV1 measured by spirometry and COPD-6® in the groups of GOLD stage I (rl=0.810, P<0.001), stage II

(rII=0.802, P<0.001), stage III (rIII=0.637, P<0.001) and stage IV (rIV=0.844,P<0.001). (C) Bland−Altman graph of FEV1 measured by spirometry and COPD-6®. 4.5% (67/1487) plots were out of the 95%LoA(-0.445~0.816L).
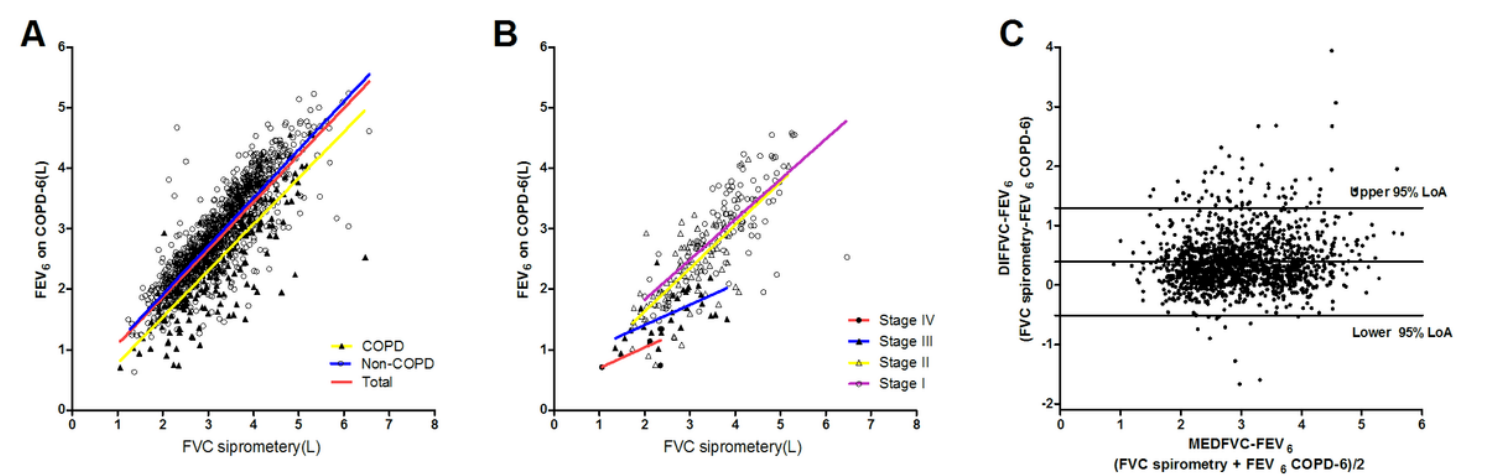

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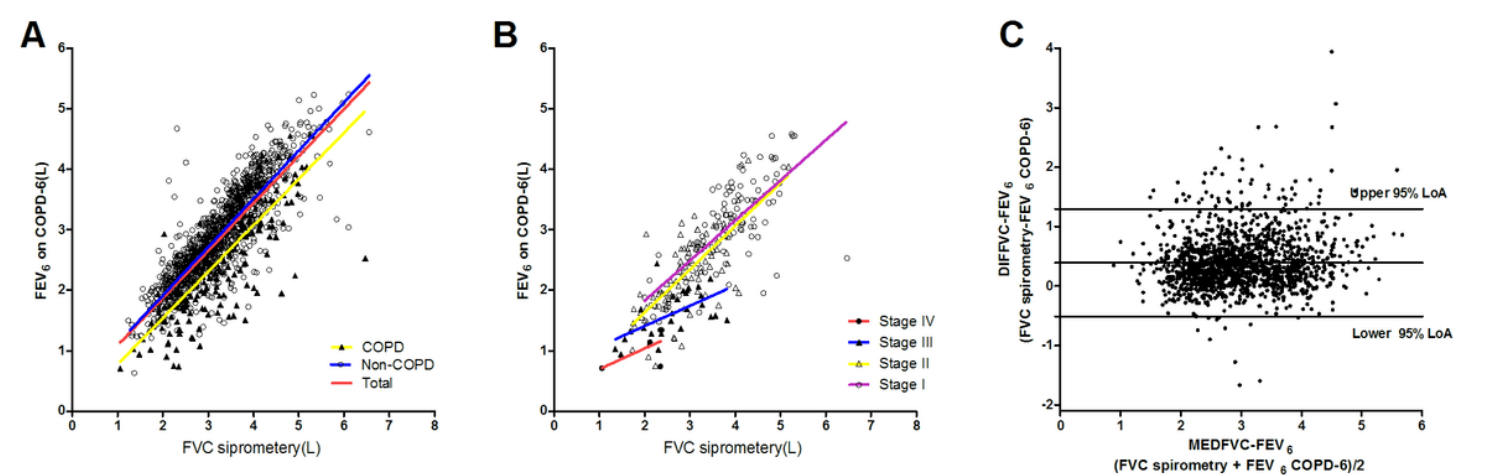

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Figure 2

Correlation of FVC measured by spirometry with FEV6 measured by COPD-6 (A)Relationship between FVC measured by spirometry and FEV6 measured by COPD-6® in total group (r1=0.835, P<0.001), non-COPD group (r2=0.865, P<0.001) and COPD group (r3=0.807, P<0.001). (B) Relationship between FVC measured by spirometry and FEV6 measured by COPD-6® in groups of GOLD stage I (rI=0.737, P<0.001), stage II (rII=0.724, P<0.001), stage III (rIII=0.574, P=0.0014) and stage IV (rIV=0.615, P=0.269). (C) Bland−Altman graph of FVC by spirometry and FEV6 by COPD-6®. 5.2% (77/1487) plots were out of the 95%LoA(0.514~1.297L).
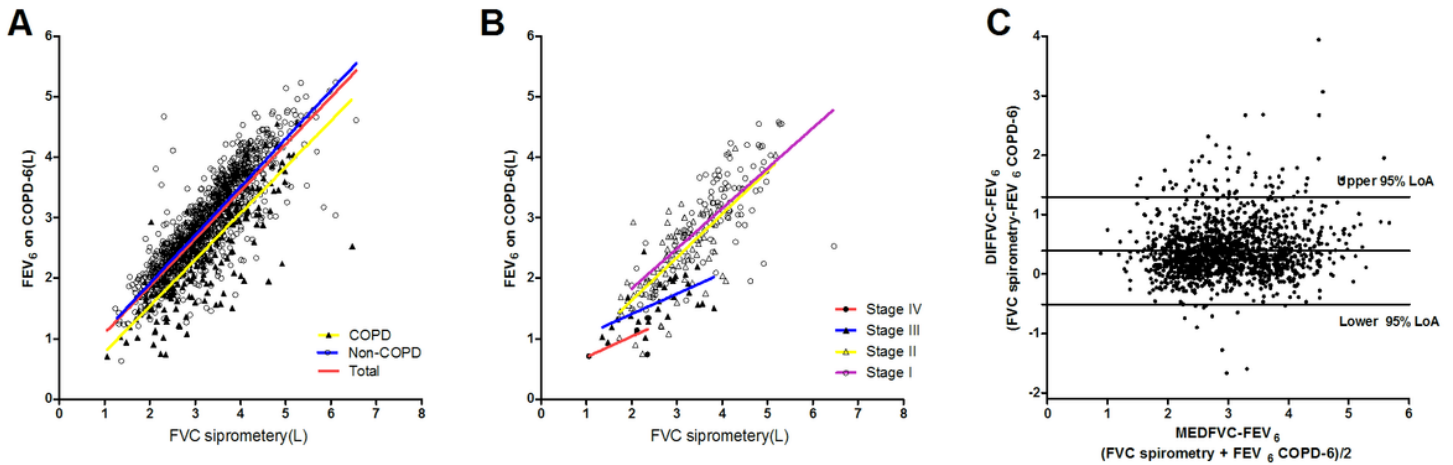

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Correlation of FVC measured by spirometry with FEV6 measured by COPD-6 (A)Relationship between FVC measured by spirometry and FEV6 measured by COPD-6® in total group (r1=0.835, P<0.001), non-COPD

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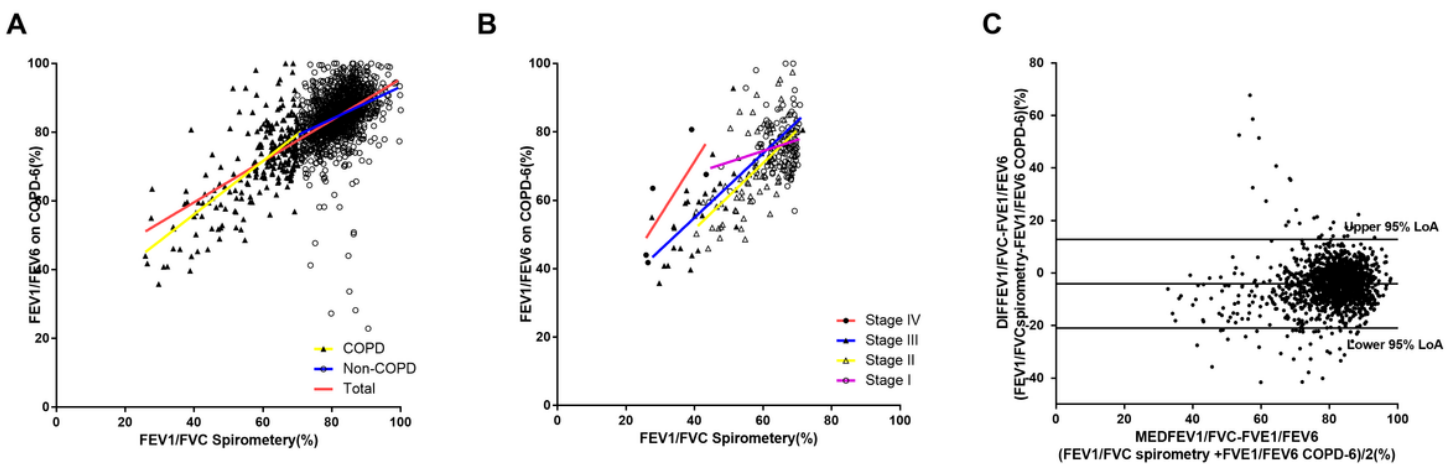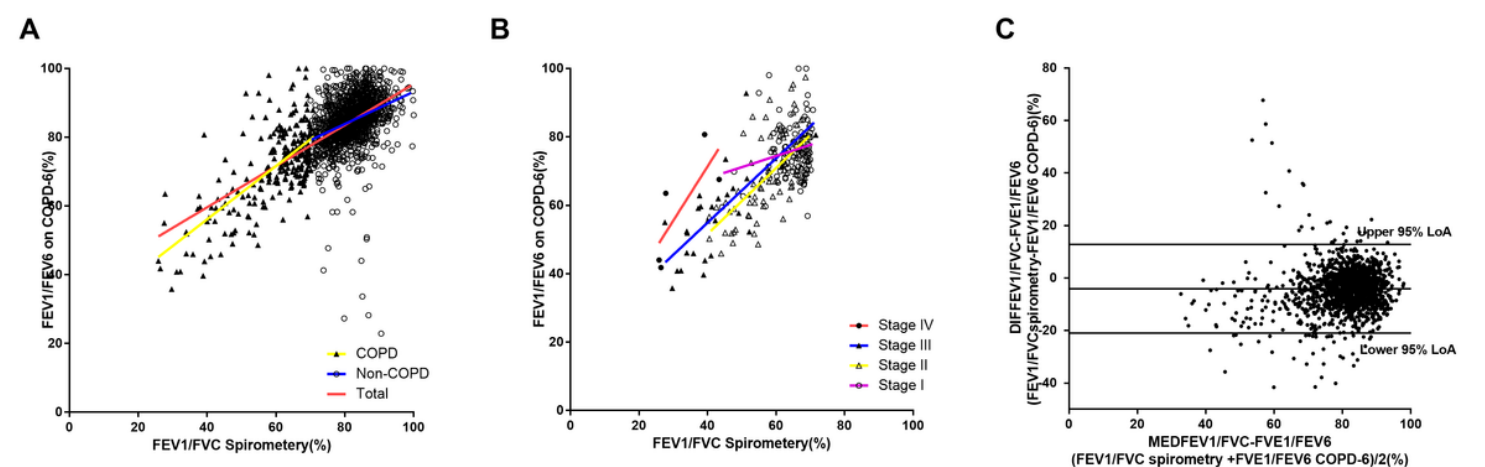

Figure 3

Correlation of FEV1/FVC measured by spirometry with FEV1/FEV6 measured by COPD-6 (A)Relationship between FEV1/FVC measured by spirometry and FEV1/FEV6 measured by COPD-6® in total group (r1=0.647, P<0.001), non-COPD group (r2=0.343, P<0.001) and COPD group (r3=0.686, P<0.001). (B) Relationship between FEV1/FVC measured by spirometry and FEV6/FVC measured by COPD-6® in groups of GOLD stage I (rI=0.197, P<0.044), stage II (rII=0.641, P<0.001), stage III (rIII=0.715, P<0.001) and stage IV (rIV=0.784, P=0.117). (C) Bland−Altman graph of FVC by spirometry and FEV6 by COPD-6®.
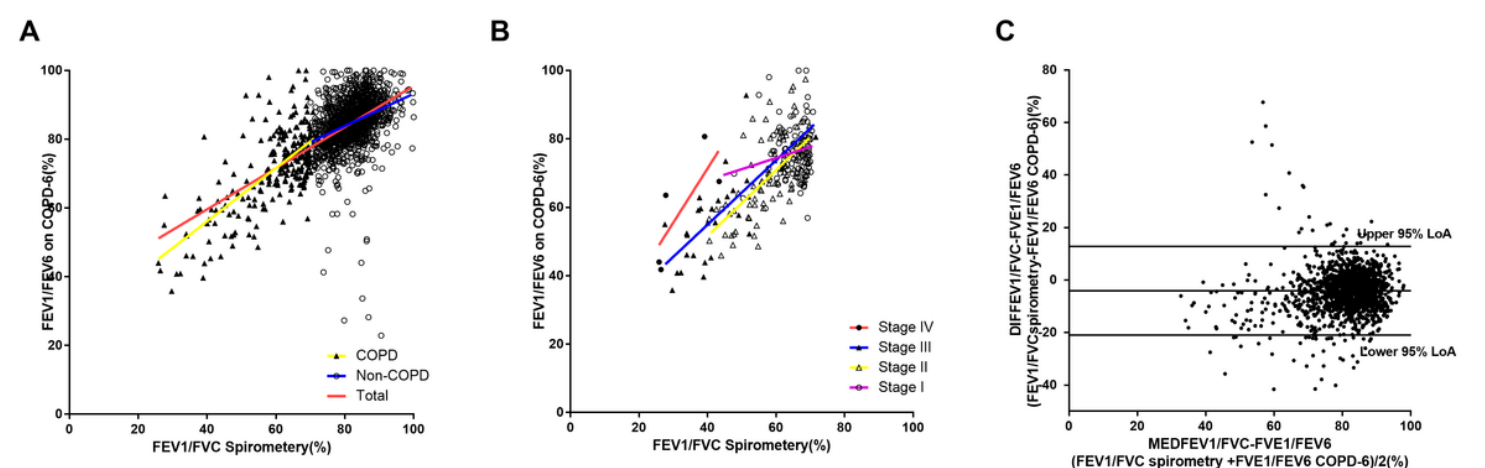

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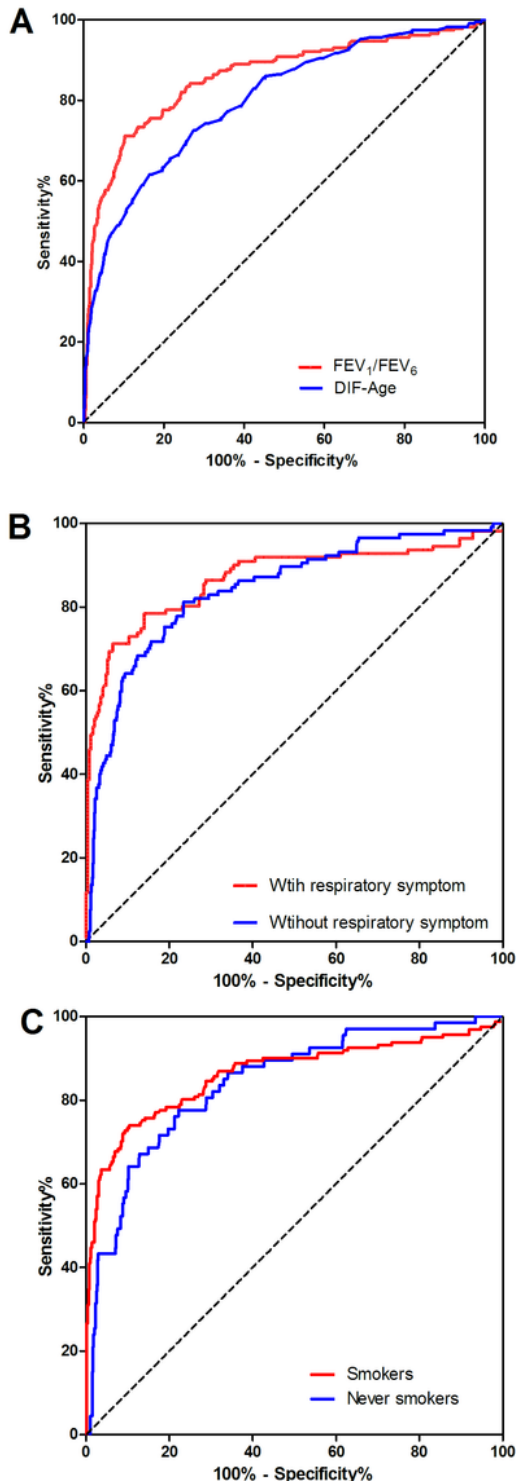

Figure 4

Area under ROC curves for FEV1/FEV6 measured by COPD-6 (A) FEV1/FEV6 by COPD-6® and DIF-Age("lung age" by COPD-6® − actual age) to identify airflow obstruction.(B) FEV1/FEV6 by COPD-6® to identify airflow obstruction in the population with respiratory symptoms and the population without respiratory symptom. (C) FEV1/FEV6 by COPD-6® to identify airflow obstruction in the smokers (including current smokers and ex-smokers) and never-smokers. Using post-bronchodilators FEV1/FVC<70% as a "gold standard" for determination of airflow obstruction.
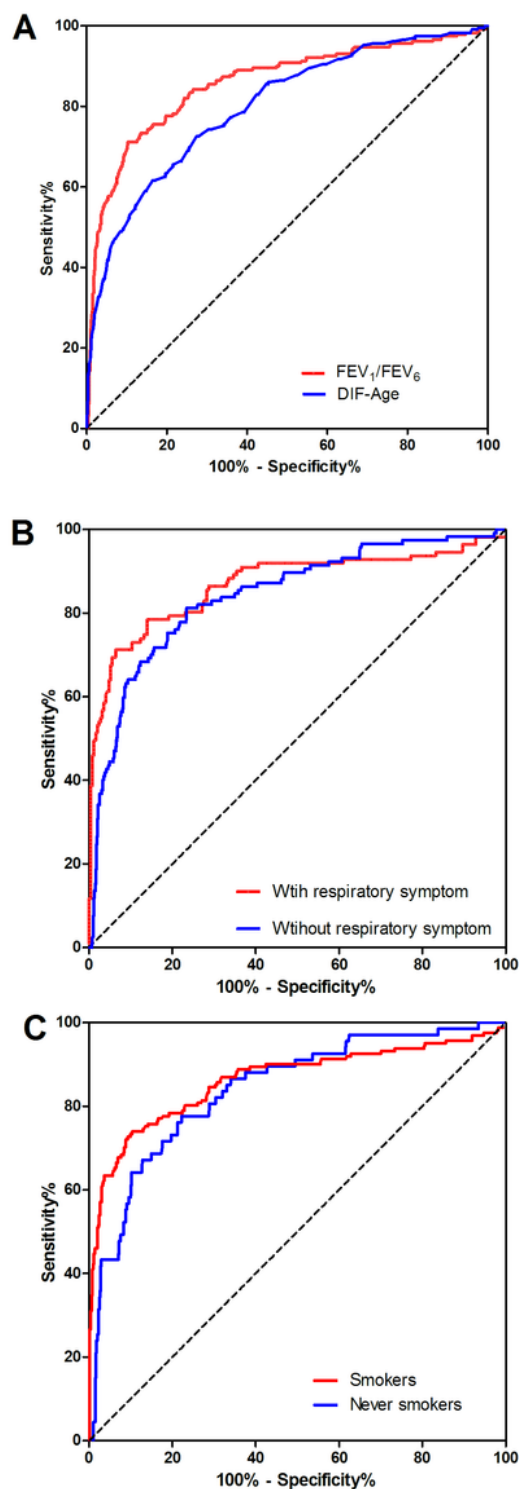

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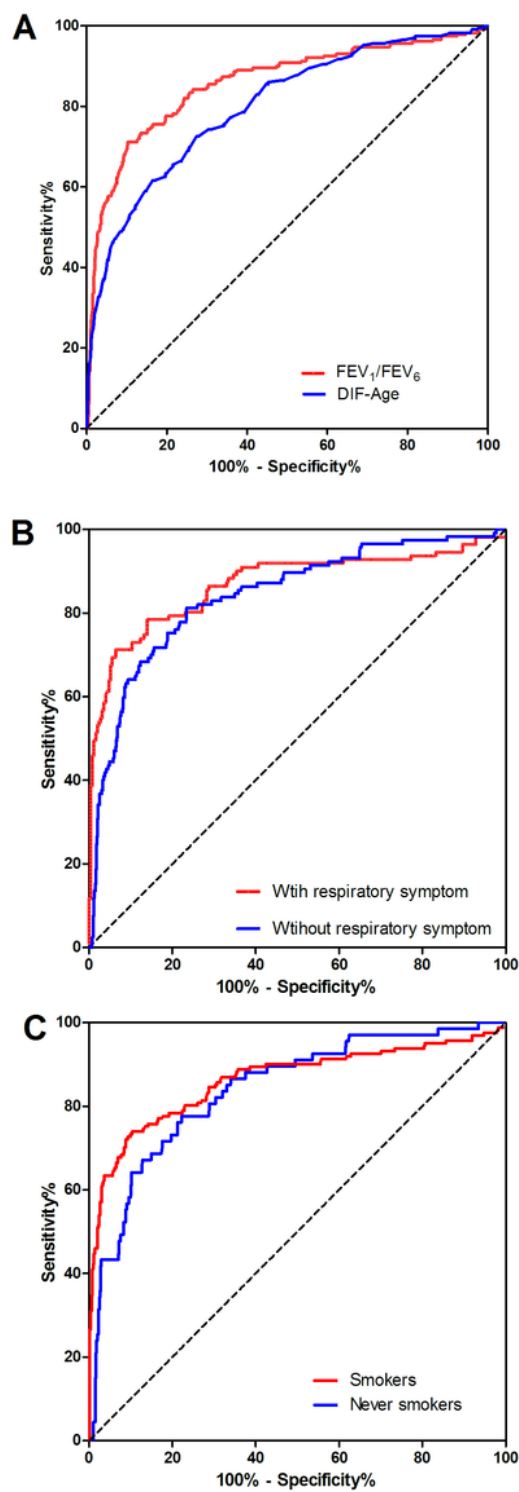

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