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ORIGINAL RESEARCH

Comparison of STAR and GOLD in Assessing Disease Severity Among High-Risk and COPD Patients: Evidence from Enjoying Breathing Program in China

Ke Huang[1,*], Xingyao Tang[1,2,*], Xu Chu[1,*], Hongtao Niu[1], Wei Li[1], Zhoude Zheng[1,3], Yaodie Peng[1,3], Jieping Lei[4], Yong Li[1], Baicun Li[1], Ting Yang[1], Chen Wang[1,5]

[1]Department of Pulmonary and Critical Care Medicine, China-Japan Friendship Hospital, Beijing, China; National Center for Respiratory Medicine, Beijing, China; State Key Laboratory of Respiratory Health and Multimorbidity, Beijing, People's Republic of China; [2]Capital Medical University China-Japan Friendship School of Clinical Medicine, Beijing, People's Republic of China; [3]Peking University China-Japan Friendship School of Clinical Medicine, Beijing, People's Republic of China; [4]Data and Project Management Unit, Institute of Clinical Medical Sciences, China-Japan Friendship Hospital, Beijing, People's Republic of China; [5]School of Population Medicine and Public Health, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People's Republic of China

*These authors contributed equally to this work

Correspondence: Baicun Li; Ting Yang, Email dryangting@qq.com

Background: The STAR staging standard has been demonstrated to have good performance in distinguishing mortality among patients at different stages. However, the effectiveness of STAR and GOLD staging in distinguishing disease severity in high-risk and COPD patients remained unclear.

Methods: Based on Enjoying Breathing Program data through June 2023, a total of 7.924 high-risk and COPD patients were included. STAR and GOLD severity stages were based on FEV1/FVC (0.6–0.7, 0.5–0.6, 0.4–0.5, and <0.4 for stage 1 to 4 in STAR) and the proportion of predicted FEV1 value (≥80%, 50%-80%, 30%-50%, and <30% for stage 1 to 4 in GOLD), respectively. The cox regression model was used to assess the risk of medical visit due to severe respiratory symptoms according to STAR and GOLD.

Results: The current study included 1603 high-risk individuals and 6321 COPD patients. The proportions of STAR 1–4 in COPD patients were 37.1%, 33.2%, 20.5%, and 9.2%, respectively. In COPD patients only, GOLD stage distinguished disease severity well, but there was no difference in the risk of exacerbation between the different STAR stage groups. In addition, in COPD patients, by considering of GOLD and STAR together, GOLD 3 and 4 can provide more information about the exacerbation based on each STAR level, and STAR 1 and 2 can provide more information about the exacerbation in GOLD 2–4. COPD patients with GOLD 4 and STAR 2 (HR=4.08, 95% CI: 2.75–6.04) had the highest risk of exacerbation, followed by COPD patients with GOLD 4 and STAR 1 (HR=3.94, 95% CI: 2.49–6.23).

Conclusion: In COPD patients, GOLD performs better than STAR in predicting exacerbation risk. In addition, the combination of GOLD and STAR can provide more information, especially for COPD patients with GOLD 4 and STAR 1–2, which should be paid more attention in treatment and disease management.

Keywords: COPD, STAR, GOLD, disease severity

Introduction

Chronic obstructive pulmonary disease (COPD), characterized by irreversible airway obstruction, is the third leading cause of death worldwide.[1] Pulmonary function test is key to diagnosing COPD and assessing the severity of airway obstruction. In addition, it forms the basis for treatment selection and patient management.[2]

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Currently, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) scoring standard is widely used to assess the severity of airflow obstruction based on the predicted percent of forced expiratory volume in the first second (ppFEV1).[3] In previous studies, higher GOLD stage was associated with worse clinical outcomes and higher mortality.[4–6]

Bhatt et al found that the GOLD has no value in assessing disease severity and proposed a new method for staging COPD severity called STaging of Airflow Obstruction by Ratio (STAR) based on the ratio of forced expiratory volume in the first second to forced vital capacity (FEV_1/FVC), and found that the prognostic value and symptoms of STAR are better than GOLD.[7] In addition, they stated that STAR performs well in distinguishing patients with mild COPD from normal populations. In fact, STAR is a more convenient method of classifying disease severity based on the FEV1/FVC ratio without involving the predictive value equation that takes into account gender, age, height, and ethnicity.

Previous studies found that STAR performed better than GOLD in distinguishing mortality.[8] Additionally, one study found that STAR had better performance than GOLD in detecting hyperinflation, but GOLD performed better than STAR in identifying the minimal clinically important difference in 6-minute walking distance and modified Medical Research Council score (mMRC).[9] However, these studies only focused on the general population,[10] or on ever smokers.[7,11] Can STAR still perform well in distinguishing disease severity in COPD patients only? Only one Japanese study found that GOLD performed better than STAR in predicting prognosis and health status. However, the sample size was small and no distinction was made between 3 and 4 stage in either STAR or GOLD.[10]

The Enjoying Breathing Program in China is an ongoing COPD management survey involving both high-risk populations and COPD patients, which also containing smokers and non-smokers with a large sample size.[12] Based on the Enjoying Breathing Program, we aimed to test the value of STAR and GOLD in assessing disease severity in high-risk and COPD patients.

Methods

The Enjoying Breathing Program

The Enjoying Breathing program is an ongoing COPD screening and management program in China (ClinicalTrails ID: NCT04318912). The specific program design was previously published as a study protocol.[12] This study was conducted in accordance with the Declaration of Helsinki and ethical approval was granted by the China-Japan Friendship Hospital (approval number 2019–41-k29). Each participant signed an informed consent form before participation.

As part of the Enjoying Breathing Program, we used the COPD screening questionnaire (COPS-SQ) to do the initial screening, including age, smoking status, body mass index (BMI), cough, breath shortness, biofuel use and family history.[13] Participants with scores greater than 16 were identified as being at high risk of COPD and were recommended to undergo pulmonary function tests. Individuals with an FEV_1/FVC ratio less than 0.7 were recommended to perform a bronchodilation test. Finally, subjects with a postbronchodilator $FEV_1/FVC < 0.7$ were diagnosed with COPD. Some normal spirometry high-risk individuals and COPD patients were included in the management and followed up under this program. Until June 2023, a total of 7.924 high-risk and COPD patients were followed up at least once from baseline. In the current analysis, we included all participants who had qualified pulmonary function test, complete information, and at least one follow-up visits more than one year after baseline. If a subject was followed up more than two times, we chose the last time as the follow-up data.

Data Collection

Questionnaires were used to collect basic information including gender, age, resident, education level, occupational status, income, family members, smoking status, passive smoking, respiratory symptoms, body mass index (BMI), disease awareness, comorbidity, biomass exposure, occupational dust exposure, chemical dust exposure and family history of chronic respiratory disease. The COPD Assessment Test (CAT) and mMRC Dyspnea Scale were used to measure COPD symptoms. Both CAT and mMRC were assessed at baseline and follow-up. The information "Consult a doctor due to severe respiratory symptoms" was collected one year before the start of the study and three months before the follow-up examination.

All high-risk populations performed spirometry at baseline according to American Thoracic Society guidelines.[14] Trained paramedical staff administered portable pulmonary function devices to perform pulmonary function tests. An expert performed quality control based on the American Thoracic Society and European Respiratory Society criteria.[15] Both the proportion of predicted FEV1 (ppFEV1) and the proportion of predicted FVC (ppFVC) were calculated.

High-risk subjects with normal spirometry (FEV1/FVC≥0.7) were also followed up in the program and we defined them as stage 0 in both STAR (STAR 0) and GOLD (GOLD 0). COPD patients with FEV1/FVC<0.7 were classified into GOLD 1, GOLD 2, GOLD 3 and GOLD 4 according to ppFEV1, with values of ≥80%, 50%-80%, 30%-50% and <30%, respectively. For STAR stage, COPD patients were classified into STAR 1, STAR 2, STAR 3 and STAR 4 according to FEV1/FVC, with values of ≥0.60 to <0.70, ≥0.50 to <0.60, ≥0.40 to < 0.50, and <0.40, respectively.

Statistical Analysis

Depending on smoking status, participants were divided into non-smokers (never smoked) and smokers (former and current smokers). Descriptive statistics results were calculated as mean ± standard deviation (SD) for continuous variables and frequencies for categorical variables. Differences in descriptive variables between two groups were analyzed using Student's *t* test, Mann–Whitney test or one-way analysis of variance for continuous variables and $\chi 2$ test for categorical variables according to normal distribution and homogeneity of variance.

The Cox regression model was used to compare the risk of seeking medical attention for severe respiratory symptoms in both GOLD and STAR stages. Hazard ratio (HR) and 95% confidence interval (CI) were used to perform the results. The linear regression model was used to compare the CAT score and mMRC scale in different GOLD and STAR stages. The adjusted model includes the age, gender and height. To assess the effectiveness of the staging standards, we performed the analysis in all high-risk participants (with stage 0) and only in COPD patients (without stage 0). A further sensitivity analysis was performed in smokers and non-smokers.

A two-sided p value < 0.05 was considered statistically significant. All analyzes were performed using R version 4.3.1.

Results

Characteristics of Enrolled Participants

A total of 1603 normal spirometry high-risk individuals and 6321 COPD patients were included in the current study. Of these COPD patients, 2345 were classified as STAR 1, 2100 as STAR 2, 1297 as STAR 3 and 579 as STAR 4, while in the GOLD standard, 516 were classified as GOLD 1, 2176 as GOLD 2, 2369 as GOLD 3 and 1260 as GOLD 4. (SFigure 1)

STable 1 shows the characteristics of enrolled participants, including 3711 non-smokers and 4213 smokers. A total of 91.0% of participants had respiratory symptoms and the mean CAT score was 15.34, the mean mMRC was 1.58. Statistical results showed that 40.4% of all high-risk populations visited a doctor for severe respiratory symptoms one year before the start of the study. The median follow-up period of the current study was 406 days. At follow-up, the mean CAT score was 14.81 and the mean mMRC was 1.43. 18.1% of participants consulted a doctor 3 months before follow-up due to severe respiratory symptoms. Among enrolled high-risk and COPD patients, smokers were more likely to be males, and more likely to live in rural areas, but had similar symptoms to non-smokers. STables 2 and 3 provided the baseline and follow-up information according to the different STAR stage and GOLD stage, respectively. Table 1 shows the information only in COPD patients, including smokers and non-smokers. Similar results were found as in the overall high-risk population.

Figure 1A shows the proportion of STAR and GOLD levels. The proportion of STAR 1 was 37.1%, which was higher than the proportion of GOLD 1. Figure 1B and C showed the proportion of STAR stage in each GOLD stage, and GOLD stage in each STAR stage, respectively. In GOLD 2, the highest proportion of STAR stage was STAR 1 (54.2%), while in STAR 1, the highest proportion of GOLD was GOLD 2 (50.3%). SFigure 2 performed the scatterplot. The correlation analysis showed a positive relationship between STAR 1 and GOLD 2, and STAR 2 and GOLD 3, respectively. (SFigure 3) There is a big difference between the two staging methods.

Table 1 Characteristics of COPD Patients

	Total	Non-Smokers	Smokers
N	6321	2773	3548
Sex (female, %)	1861 (29.4)	1712 (61.7)	149 (4.2)
Age (mean (SD))	67.59 (9.78)	67.52 (10.19)	67.65 (9.46)
Age range (%)			
<40 years old	40 (0.6)	23 (0.8)	17 (0.5)
40–49 years old	232 (3.7)	113 (4.1)	119 (3.4)
50–59 years old	930 (14.7)	439 (15.8)	491 (13.8)
60–69 years old	2370 (37.5)	969 (34.9)	1401 (39.5)
≥70 years old	2749 (43.5)	1229 (44.3)	1520 (42.8)
Resident (%)			
Rural	4348 (69.3)	1958 (71.2)	2390 (67.8)
Urban	1930 (30.7)	793 (28.8)	1137 (32.2)
Education (%)			
Primary school or less	3973 (63.3)	1888 (68.6)	2085 (59.1)
Middle or high school	2091 (33.3)	780 (28.4)	1311 (37.2)
College or above	213 (3.4)	83 (3.0)	130 (3.7)
Profession (%)			
At work	2979 (47.5)	1323 (48.1)	1656 (47.0)
Retired	3298 (52.5)	1427 (51.9)	1871 (53.0)
Income (%)			
<=10000 yuan/month	1073 (47.3)	493 (54.5)	580 (42.5)
>10000 yuan/month	1196 (52.7)	412 (45.5)	784 (57.5)
Family members number (%)			
1	173 (2.8)	80 (3.0)	93 (2.7)
2	2421 (39.4)	1052 (39.0)	1369 (39.8)
3–5	2963 (48.2)	1322 (49.0)	1641 (47.7)
>5	585 (9.5)	246 (9.1)	339 (9.8)
Know COPD (%)			
Do not know	3533 (59.8)	1471 (57.6)	2062 (61.5)
Little known	1730 (29.3)	813 (31.8)	917 (27.4)
Known	490 (8.3)	208 (8.1)	282 (8.4)
Well known	95 (1.6)	34 (1.3)	61 (1.8)
Very well known	57 (1.0)	28 (1.1)	29 (0.9)

(*Continued*)

Table 1 (Continued).

	Total	Non-Smokers	Smokers
Smoking status (%)			
Never	2773 (43.9)	2773 (100.0)	0 (0.0)
Former	1646 (26.0)	0 (0.0)	1646 (46.4)
Current	1902 (30.1)	0 (0.0)	1902 (53.6)
Second-hand smoking exposure (%)	1724 (66.0)	1693 (66.0)	31 (66.0)
BMI (kg/m^2, %)			
<18.5	738 (11.7)	287 (10.3)	451 (12.7)
18.5–23.9	3556 (56.3)	1474 (53.2)	2082 (58.7)
24–27.9	1629 (25.8)	775 (27.9)	854 (24.1)
≥28	398 (6.3)	237 (8.5)	161 (4.5)
Family history of chronic respiratory disease (%)	1507 (23.8)	706 (25.5)	801 (22.6)
CAT total score (mean (SD))	15.68 (7.34)	15.42 (7.47)	15.89 (7.23)
CAT score (%)			
0–9	1286 (20.3)	604 (21.8)	682 (19.2)
10–19	3173 (50.2)	1374 (49.5)	1799 (50.7)
20–29	1643 (26.0)	704 (25.4)	939 (26.5)
30–40	219 (3.5)	91 (3.3)	128 (3.6)
mMRC (mean (SD))	1.64 (0.91)	1.62 (0.94)	1.66 (0.88)
mMRC (%)			
Grade 0	529 (8.4)	256 (9.2)	273 (7.7)
Grade 1	2446 (38.7)	1117 (40.3)	1329 (37.5)
Grade 2	2194 (34.7)	878 (31.7)	1316 (37.1)
Grade 3	1053 (16.7)	467 (16.8)	586 (16.5)
Grade 4	99 (1.6)	55 (2.0)	44 (1.2)
Seeking medical attention for severe respiratory symptoms (%)	2672 (42.3)	1207 (43.5)	1465 (41.3)
Number of seeking medical attention for severe respiratory symptoms (mean (SD))	0.72 (1.10)	0.74 (1.11)	0.71 (1.10)
Comorbidity (%)	4336 (68.6)	2074 (74.8)	2262 (63.8)
Exposure to occupational dust (%)	346 (5.5)	121 (4.4)	225 (6.3)
Exposure to chemical dust (%)	52 (0.8)	16 (0.6)	36 (1.0)
Use biofuels (%)	3309 (52.3)	1585 (57.2)	1724 (48.6)
Symptom (%)	5855 (92.6)	2586 (93.3)	3269 (92.1)
Cough	4571 (72.3)	2105 (75.9)	2466 (69.5)

(*Continued*)

Table 1 (Continued).

	Total	Non-Smokers	Smokers
Cough before 14 years old (%)			
Rarely	3914 (74.1)	1509 (66.9)	2405 (79.5)
Sometimes	905 (17.1)	459 (20.3)	446 (14.7)
Always	464 (8.8)	288 (12.8)	176 (5.8)
Phlegm	4077 (64.5)	1836 (66.2)	2241 (63.2)
Dyspnea	3822 (60.5)	1571 (56.7)	2251 (63.4)
Breathlessness (%)			
No shortness of breath	1163 (18.4)	511 (18.4)	652 (18.4)
Feel shortness of breath when walking quickly on flat ground or climbing hills	3646 (57.7)	1626 (58.6)	2020 (56.9)
Feel shortness of breath when walking normally on flat ground	1512 (23.9)	636 (22.9)	876 (24.7)
Chest tightness	25 (0.4)	15 (0.5)	10 (0.3)
Adherence to medication (%)	5399 (85.4)	2288 (82.5)	3111 (87.7)
Home oxygen (%)	472 (7.5)	198 (7.1)	274 (7.7)
Follow up days (median (IQR))	401.00 [340.00, 536.00]	420.00 [356.00, 563.00]	389.50 [327.75, 495.00]
Follow up CAT total score (mean (SD))	15.06 (7.62)	14.53 (7.34)	15.47 (7.81)
Follow up CAT score (%)			
0–9	1506 (23.8)	691 (24.9)	815 (23.0)
10–19	3281 (51.9)	1456 (52.5)	1825 (51.4)
20–29	1137 (18.0)	502 (18.1)	635 (17.9)
30–40	397 (6.3)	124 (4.5)	273 (7.7)
Follow up mMRC (mean (SD))	1.49 (0.83)	1.48 (0.86)	1.49 (0.81)
Follow up mMRC (%)			
Grade 0	553 (8.7)	276 (10.0)	277 (7.8)
Grade 1	2961 (46.8)	1274 (45.9)	1687 (47.5)
Grade 2	2032 (32.1)	863 (31.1)	1169 (32.9)
Grade 3	733 (11.6)	338 (12.2)	395 (11.1)
Grade 4	42 (0.7)	22 (0.8)	20 (0.6)
Follow up acute exacerbation (%)	1232 (19.5)	516 (18.6)	716 (20.2)
Follow up acute exacerbation number (mean (SD))	0.30 (0.75)	0.29 (0.74)	0.31 (0.75)
FVC (L, mean [SD])	2.32 (0.95)	2.23 (0.93)	2.39 (0.96)
ppFVC (mean [SD])	0.71 (0.27)	0.74 (0.29)	0.68 (0.25)
FEV1 (L, mean [SD])	1.28 (0.60)	1.24 (0.56)	1.31 (0.62)
ppFEV1 (mean [SD])	0.49 (0.21)	0.52 (0.22)	0.46 (0.20)
FEV1/FVC (mean [SD])	0.55 (0.10)	0.56 (0.10)	0.54 (0.10)

(*Continued*)

Table 1 (Continued).

	Total	Non-Smokers	Smokers
Star (%)			
Star 1	2345 (37.1)	1118 (40.3)	1227 (34.6)
Star 2	2100 (33.2)	910 (32.8)	1190 (33.5)
Star 3	1297 (20.5)	519 (18.7)	778 (21.9)
Star 4	579 (9.2)	226 (8.2)	353 (9.9)
Gold (%)			
Gold 1	516 (8.2)	273 (9.8)	243 (6.8)
Gold 2	2176 (34.4)	1114 (40.2)	1062 (29.9)
Gold 3	2369 (37.5)	986 (35.6)	1383 (39.0)
Gold 4	1260 (19.9)	400 (14.4)	860 (24.2)

Abbreviations: COPD, chronic obstructive pulmonary disease; SD, standard deviation; BMI, body mass index; CAT, COPD assessment test; mMRC, Modified Medical Research Council Dyspnea Scale; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; FEV1/FVC, ratio of FEV1/FVC; ppFEV1, percentage of predicted FEV1 value; ppFVC, percentage of predicted FVC value; GOLD, Chronic Obstructive Lung Disease; STAR, Staging of Airflow obstruction by Ratio.

Results of Comparing the Risk of See a Doctor Due to the Severe Respiratory Symptoms in Different Staging Groups

We initially carried out the analysis only in COPD patients and set STAR 1 or GOLD 1 as the reference group. Seeking medical attention for severe respiratory symptoms led to exacerbation in COPD patients. GOLD stage differentiated disease severity well in COPD patients, with GOLD 2 showing an HR of 1.84 (95% CI: 1.38 to 2.45) in predicting exacerbation risk, GOLD 3 showing an HR of 2.42 (95% CI: 1.83 to 3.22), and GOLD 4 shows an HR of 2.94 (95% CI: 2.19 to 3.94). However, there was no difference in the risk of seeking medical attention for severe respiratory symptoms between the different STAR stage groups. The analysis of smokers also showed similar results. In non-smokers, STAR 3 was better than STAR 1 in predicting exacerbation risk, with an HR of 1.29 (95% CI: 1.02 to 1.62). GOLD staging showed good predictive quality in all stages after adjusting for covariables. (Table 2)

In all high-risk populations, STAR staging performed well compared to stage 0 (normal spirometry high-risk subjects) in predicting the risk of seeking medical attention for severe respiratory symptoms. The HR of STAR 1 was 1.69 with a 95% CI of 1.43 to 2.00 after adjusting for age, sex and height, while the HR of GOLD 1 was 0.83 (95% CI: 0.61 to 1.12). The STAR allowed good discrimination of patients with mild COPD with a higher predicted value in STAR 1 and STAR 2 (STAR 2: HR=1.85, 95% CI: 1.56 to 2.19 and GOLD 2: HR=1.50, 95% CI: 1.26). up to 1.78). In contrast, GOLD was good at detecting severe patients and had a higher HR value than STAR (GOLD 3: HR=1.98, 95% CI: 1.69 to

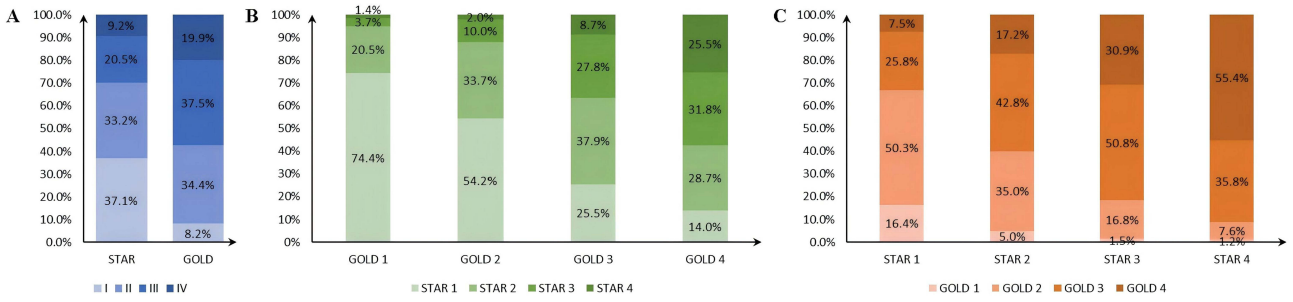

Figure 1 Proportion of STAR and GOLD staging in COPD patients.

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Table 2 Comparison of See a Doctor Due to Severe Respiratory Symptoms in 3 Months Before Follow-Up by Severity Stage in COPD Patients Using HR and 95% CI

stage	Star		Gold	
	Unadjusted	Adjusted	Unadjusted	Adjusted
All population				
I	Ref	Ref	Ref	Ref
II	1.12 (0.98, 1.29)	1.10 (0.96, 1.26)	1.69 (1.27, 2.26)	1.84 (1.38, 2.45)
III	1.10 (0.95, 1.28)	1.04 (0.90, 1.22)	2.36 (1.78, 3.12)	2.42 (1.83, 3.22)
IV	1.15 (0.94, 1.41)	1.13 (0.92, 1.38)	2.65 (1.99, 3.54)	2.94 (2.19, 3.94)
Smokers				
I	Ref	Ref	Ref	Ref
II	1.06 (0.89, 1.27)	1.06 (0.88, 1.26)	1.93 (1.28, 2.90)	2.12 (1.41, 3.21)
III	0.95 (0.77, 1.16)	0.93 (0.76, 1.14)	2.36 (1.58, 3.53)	2.40 (1.61, 3.60)
IV	1.02 (0.78, 1.34)	1.06 (0.81, 1.38)	2.58 (1.71, 3.89)	2.91 (1.92, 4.41)
Non-smokers				
I	Ref	Ref	Ref	Ref
II	1.17 (0.94, 1.44)	1.14 (0.92, 1.41)	1.49 (0.99, 2.22)	1.61 (1.07, 2.40)
III	1.28 (1.02, 1.61)	1.29 (1.02, 1.62)	2.30 (1.55, 3.41)	2.48 (1.67, 3.69)
IV	1.27 (0.92, 1.75)	1.26 (0.91, 1.74)	2.63 (1.74, 3.98)	3.03 (2.00, 4.60)

Note: Adjusted model: model adjusted for age, sex, and height.
Abbreviations: GOLD, Chronic Obstructive Lung Disease; STAR, Staging of Airflow obstruction by Ratio; ref, reference; HR, hazard ratio; CI, confidence interval.

2.34, and STAR 3: HR= 1.77, 95% CI: 1.48 to 2.12; GOLD 4: HR=2.39, 95% CI: 2.00 to 2.86 and STAR 4: HR=1.90, 95% CI: 1.52 to 2.39). Sensitivity analysis in smokers and non-smokers showed similar results. (STable 4)

In addition, we considered the STAR and GOLD staging combined. For all high-risk populations, GOLD 3 and 4 can provide more information about the risk of seeking medical attention for severe respiratory symptoms, with a higher HR than using the STAR alone. For GOLD 2–4, STAR 1 can help identify the population at higher risk of seeking medical attention due to severe respiratory symptoms. However, for GOLD 1, the STAR grading cannot provide any further information. (Table 3) Analysis in COPD patients showed similar results, and not only STAR 1 but also STAR 2 provide

Table 3 Comparison of See a Doctor Due to Severe Respiratory Symptoms in 3 Months Before Follow-Up by Severity Stage Combining STAR and GOLD in All High Risk Population Using HR and 95% CI

	STAR 1	STAR 2	STAR 3	STAR 4
GOLD 1	0.78 (0.55, 1.12)	1.19 (0.72, 1.98)	0.35 (0.09, 1.44)	0.60 (0.08, 4.25)
GOLD 2	1.61 (1.33, 1.96)	1.48 (1.18, 1.85)	1.15 (0.77, 1.73)	0.61 (0.20, 1.91)
GOLD 3	2.28 (1.83, 2.84)	1.89 (1.55, 2.30)	1.94 (1.57, 2.40)	1.79 (1.24, 2.58)
GOLD 4	3.03 (2.14, 4.27)	3.13 (2.44, 4.01)	1.95 (1.54, 2.48)	2.23 (1.72, 2.89)

Notes: Reference group: STAR/GOLD 0. Adjusted for age, sex, and height.
Abbreviations: COPD, chronic obstructive pulmonary disease; GOLD, Chronic Obstructive Lung Disease; STAR, Staging of Airflow obstruction by Ratio; HR, hazard ratio; CI, confidence interval.

further information on exacerbation risk based on GOLD 2–4. COPD patients with GOLD 4 and STAR 2 (HR=4.08, 95% CI: 2.75–6.04) had the highest risk of exacerbation, followed by COPD patients with GOLD 4 and STAR 1 (HR=3.94, 95% CI: 2.49–6.23). (STable 5)

Results of Comparing Symptoms at Follow-Up in Different Staging Groups

Although the high-risk subjects had normal spirometry, they were initially selected based on apparent symptoms and exposure risk factors using COPD-SQ.[13] The mean CAT score was 13.80 and the mean mMRC was 1.19 in high-risk subjects with normal spirometry, also called STAR 0 or GOLD 0. In each STAR stage group, the mean values of the CAT score increased with increasing stage classification (STAR 1: 13.67, STAR 2: 15.33, STAR 3: 16.02 and STAR 4: 17.55), the mean values of mMRC (STAR 1: 1.31, STAR 2: 1.47, STAR 3: 1.65, and STAR 4: 1.88). (STable 6) Each GOLD group showed similar results in mean CAT score (GOLD 1: 11.63, GOLD 2: 13.09, GOLD 3: 15.90 and GOLD 4: 18.28) and mMRC (GOLD 1: 1.09, GOLD 2: 1.28, GOLD 3: 1.59 and GOLD 4: 1.80). (STable 7)

In COPD patients, the higher STAR stage had higher CAT scores at follow-up compared to STAR 1 (STAR 2: 1.42, 95% CI: 0.98 to 1.86, STAR 3: 2.06, 95% CI: 1.56 to 2.57, and STAR 4: 3.64, 95% CI: 2.96 to 4.31). The staging standard of GOLD also produced similar results, and the value of discriminating CAT scores at different stages was better than that of STAR (GOLD 2: 1.44, 95% CI: 0.75 to 2.14, GOLD 3: 4.04, 95% CI: 3.34 to 4.73, GOLD 4: 6.51, 95% CI: 5.77 to 7.26). (STable 8) When considering mMRC, GOLD staging also demonstrated better value in distinguishing disease severity than STAR staging (compared to STAR 1, STAR 2: 0.13, 95% CI: 0.08 to 0.17, STAR 3: 0.31, 95% CI: 0.26 to 0.37, STAR 4: 0.55, 95% CI: 0.48 to 0.63; compared to GOLD 1, GOLD 2: 0.19, 95% CI: 0.12 to 0.27, GOLD 3: 0.49, 95% CI: 0.41 to 0.57, GOLD 4: 0.73, 95% CI: 0.64 to 0.81). (STable 9) The sensitivity analysis in smokers and non-smokers gave the same results.

For all high-risk populations, the analysis was performed considering the normal spirometry high-risk subjects as the reference group. With STAR, more severe symptoms of COPD patients were better detected, especially when using mMRC (CAT score: STAR 1: −0.23, 95% CI: −0.70 to 0.23, STAR 2: 1.17, 95% CI: 0.69 to 1.64, STAR 3: 1.83, 95% CI: 1.29 to 2.36, STAR 4: 3.40, 95% CI: 2.71 to 4.10; mMRC: STAR 1: 0.12, 95% CI: 0.07 to 0.17, STAR 2: 0.25, 95% CI: 0.19 to 0.30, STAR 3: 0.44, 95% CI: 0.38 to 0.49, STAR: 0.67, 95% CI: 0.60 to 0.75). (STables 10 and 11)

Discussion

Our study compared the value of STAR and GOLD in distinguishing disease severity. According to the results, GOLD is better than STAR in assessing disease severity in COPD patients. In all high-risk populations, STAR is good at detecting patients with mild COPD, while GOLD is good at detecting patients with severe COPD. In COPD patients with GOLD 4, STAR 1–2 can provide further information about the exacerbation risk. Similar results were also found in non-smokers or smokers.

Some other studies also confirmed the effectiveness of GOLD staging in distinguishing disease severity, including healthcare resource utilization, medical-related costs and exacerbation events.[16,17] A comparison between GOLD classification (based on exacerbation times, CAT-Score or mMRC scale, and divided the COPD patients into GOLD A, GOLD B and GOLD E respectively) and the GOLD stage showed that the performance of the GOLD stage in distinguishing disease severity, exacerbation rate, quality of life, and symptoms was better than the GOLD classification.[18]

In previous studies, some other parameters were collected to assess disease severity in COPD. Absolute value of FEV1 and FEV1/height^2 were used to assess disease severity and performed equally well with ppFEV1 in six-minute walk distance, quality of life and mMRC.[19] Another FEV1 ratio parameter (FEV1Q, standardize FEV1 using the sex-specific lowest 1st percentile) showed better discrimination in mortality than ppFEV1 and the FEV1 Z-score.[20,21] The difference in these parameters was based on the consideration of the virous covariates for age, gender, race and height. In a sense, these are indicators of the same kind that related to FEV1. STAR is created considering the absolute value of FEV1/FVC, which is easily applicable in clinical practice. The advantage of the STAR was that it did not require a predicted value that was influenced by gender, age, race, and height.[22] The predicted value equation has changed over time and more researches have been done in white and black.

STAR is a new staging method for which insufficient evidence has been found. In the general US population, STAR 1 was more significantly different from non-obstructive stage compared to GOLD stage 1 in both symptoms and mortality.[7,8] Our results showed similar results in all high-risk populations, including those with normal pulmonary function test values and risk factors exposure in the meantime. However, few studies focused only on COPD patients. A previous study of 141 people in Japan found GOLD to be more discriminatory than STAR in all-cause mortality and COPD-specific health status.[10] The sample size was very small and GOLD 3 and 4 were counted together. We confirmed the results in a large sample and focused on the risk of exacerbation in COPD patients by using STAR and GOLD. GOLD performed better than STAR in predicting exacerbation risk in COPD patients. A possible explanation is that in COPD patients the proportion of STAR 1 was much higher than that of GOLD 1, and therefore more COPD patients at risk of exacerbations were included in STAR 1. The effectiveness of distinguishing patients with mild COPD in STAR 1 may be influenced by the identification of additional individuals, but not accurately. A study in Italy focused on patients with acute exacerbation COPD undergoing pulmonary rehabilitation.[9] They found that GOLD performed better at staging chronic respiratory failure, while STAR performed better at detecting hyperinflation. In the current analysis, we considered both high-risk and COPD patients, and added the results to the existing evidence that STAR is good at detecting patients with mild COPD, while GOLD is good at detecting patients with severe COPD.

No previous studies combine consideration of GOLD and STAR. In our analysis, STAR 1 and 2 can provide more information about disease severity in GOLD 2–4, and GOLD can provide more information in each STAR stage. COPD patients in GOLD 4 and STAR 1–2 had the highest risk of exacerbation. COPD patients with high GOLD grade combined with low STAR stage were represented as patients with low FEV1 and low FVC, while COPD patients with high GOLD stage and high STAR stage were represented as patients with low FEV1 and high FVC. Therefore, it is easy to understand that in the low FEV1 and low FVC situation, the risk of exacerbation was higher than in the low FEV1 and high FVC situation.

Only in COPD patients, the values of CAT score and mMRC increased with each stage, both in STAR and GOLD. However, stages II, III, and IV identified with GOLD each had a higher value than the corresponding stages identified with STAR. Previous studies in the general population found the STAR score to be more predictive than the GOLD score. In the Enjoying Breathing Program, the COPD screening questionnaire (COPD-SQ) was used for initial screening.[13] Those with scores above 16 were classified as a high-risk group and were recommended to undergo pulmonary function test. Some high-risk populations with normal lung function were also followed in the program and we defined them as STAR 0 or GOLD 0 in the current analysis. High-risk groups with more symptoms were more willing to participate in follow up care because they have a more intuitive sense of their health status.[23] This could be an explanation for the higher CAT score and mMRC scale in subjects with normal spirometry and high-risk individuals than in stage I or II.

STAR was conducted in the Genetic Epidemiology of COPD (COPDGene) study and the combined Pittsburgh cohort study. The COPDGene study did not include Asians, and the Pittsburgh study only included four Asians. Both the COPDGene and Pittsburgh studies included participants with current or past smoking history. A general US population study that included both smokers and non-smokers, but no separate analysis was conducted for smokers and non-smokers. To confirm the effectiveness of STAR and GOLD in COPD patients, another Japanese study was conducted, but the sample size was too small to combine stage 3 and 4.[10] The current study was conducted on a large sample in China and differentiates between stages 3 and 4 in both STAR and GOLD. Sensitivity analyzes in smokers and non-smokers showed similar results. Smoking status is not a determining factor in distinguishing the disease severity, and STAR and GOLD are also effective in non-smokers.

In clinical practice, it is important to recognize the severe status only in COPD patients, which is necessary for clinical decision making and treatment. Adequate and timely treatment contributes to disease recovery and quality of life.[24–26] Importantly, according to our results, GOLD 4 COPD patients with stage STAR 1–2 are at the highest risk of exacerbation and require more care need to be treated and managed. Patients with mild COPD also need attention. Some recent studies suggest that people with mild lung impairment have a faster FEV1 decline than those with severe status, meaning there is "more to lose".[27,28] Early detection and prevention can prolong the decline in lung function, especially

in these mild COPD patients. Therefore, identifying mild and severe COPD patients is equally important, and both STAR and GOLD are important in clinical practice.

Our study has several strengths. We performed the analysis in all high-risk populations, not only in COPD patients. We also thought about smokers and non-smokers. There were also some limitations. First, the follow-up period of the current analysis was short, with a median of 406 days, and mortality information was limited for further analysis. The endpoints of the current analysis were limited to one visit. Second, we used normal spirometry high-risk people as reference, who have more obvious symptoms than normal people. The lack of asymptomatic healthy populations also limited the analysis. Third, we used only "seeking medical attention for severe respiratory symptoms", the CAT score and the mMRC scale as outcomes. However, our results were still of value when assessing disease severity using STAR or GOLD in high-risk COPD patients in China. Future general population studies with longer follow-up are needed.

Conclusion

In conclusion, in all high-risk populations, STAR is good at detecting patients with mild COPD, while GOLD is good at detecting patients with severe COPD. Additionally, GOLD performs better than STAR discriminating disease severity in COPD patients. Considering both GOLD and STAR, STAR 1–2 can provide more information, especially in GOLD 4 patients. COPD patients with GOLD 4 and STAR 1–2 should receive more attention in treatment and disease management as they are at highest risk of exacerbation.

Data Sharing Statement

The data are available from the corresponding authors upon reasonable request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare no conflicts of interest.

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