203. GOLD guidelines 2011: new assessment of COPD

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GOLD 2011: Combined COPD assessment of patients from the European health-related quality of life study

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The 2011 Global Initiative for chronic obstructive lung disease (GOLD) guidelines recommend a combined assessment for measuring the impact of COPD which considers current symptoms and future exacerbation risk (A: low risk, less symptoms; B: low risk, more symptoms; C: high risk, less symptoms; D: high risk, more symptoms). Two symptom cut-points are proposed: COPD Assessment Test (CAT) score ≥10 and modified Medical Research Council Dyspnoea (mMRC) score ≥2.

This analysis examined health status scores split by these cut-points, using CAT and mMRC data together with SGRQ and SF-12 Physical Function (PC) scores, in a primary care population from the Health Related Quality of Life in European COPD Study.

Data from 1817 patients (mean [SD] FEV_1 1.6 [0.6] L; age 64.9 [9.6] years; males 72%) could be used. The SGRQ and SF-12PC scores are tabulated. The mMRC classified 57.2% patients as having low symptoms versus 17.2% with the CAT. The distribution of low symptom patients into low risk and high risk categories differed. Patients categorised by mMRC as having low symptoms (Groups A & C) had much higher SGRQ scores (>3 times the minimum clinically important difference) than those categorised by CAT.

	CAT (≥ 10)			mMRC (≥ 2)		
Patient group	Patients n (%)	SGRQ mean±SD	SF-12 PC mean±SD	Patients n (%)	SGRQ mean±SD	SF-12 PC mean±SD
A	147 (8.1)	19.5±9.7	46.7±7.6	372 (20.5)	30.5±15.4	43.2±8.1
B	348 (19.2)	41.6±15.8	38.7±8.3	124 (6.8)	48.3±16.5	34.8±8.0
C	165 (9.1)	24.2±10.9	45.1±7.6	666 (36.7)	38.6±15.9	40.3±8.0
D	1150 (63.3)	51.9±17.1	35.1±8.3	653 (35.9)	58.1±16.4	32.3±7.7
Missing	7 (0.4)	-	-	2 (0.1)	-	-

The mMRC cut-point of ≥ 2 classified a high proportion of these patients as having low symptoms, despite having moderately high SGRQ scores and poor SF-12 PC scores.

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Prediction of the clinical course of COPD using the old and the new GOLD classification

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Using data from The Copenhagen General Population Study and The Copenhagen City Heart Study comprising more than 50,000 individuals, we identified 6,628 persons older than 40 years of age with spirometrically defined COPD (FEV_1/FVC ratio below 0.7 and no asthma). These individuals were subdivided according to the GOLD 2007 into stages 1, 2 3 and 4 (based on spirometry only) and according to the GOLD 2011 (using spirometry, mMRC-dyspnea scale and the number of exacerbations in the previous year) into stages A, B, C and D. They were followed for the subsequent year with regard to important COPD outcomes.

Conclusions: 1. The distribution of the individuals according to the two stratifications differs considerably

2. With regard to prediction of exacerbations, the A-D GOLD 2011 classification performes well

3. Compared with the group D, the lack of symptoms in group C is, not surprisingly, associated with lower frequency of treament with inhaled medications, but also with a sligthly higher frequency of exacerbations

4. Presence of dyspnea and a low level of FEV_1 are both predictors of high risk of hospitalisation/casualty ward visit due to COPD, whereas dyspnea seems to be a better predictor of all cause mortality than FEV_1.

Distribution of individuals with COPD according to the 2007 and 2011 GOLD stratification and the 1-year prognosis

GOLD stage	n	FEV1 % predicted at baseline	% on inhaled medication	% with exacerbation	% hospitalized due to COPD	% dead
GOLD 1	3306	95	5.5	2.6	0.2	0.7
GOLD 2	2851	68	18.4	4.2	1.3	1.0
GOLD 3	426	43	50.2	10.8	7.7	2.3
GOLD 4	45	25	73.3	22.2	24.4	2.2
GOLD A	5126	84	8.5	2.0	0.3	0.6
GOLD B	936	74	26.6	3.7	3.0	2.0
GOLD C	271	52	32.1	23.2	2.6	0.7
GOLD D	295	43	62.0	20.3	13.6	3.4

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Characteristics of GOLD 2011 grading system in the COPDGene cohort

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Background: The 2011 GOLD summary report outlines a new COPD grading system based on symptoms, exacerbation history and FEV1. Here we use the COPDGene patient cohort to better understand how well this grading system describes a large, general COPD cohort.

Methods: All COPD subjects from the 10,000 subject COPDGene cohort were grouped per the GOLD 2011 grading system: "A" MMRC ≤1, FEV1 ≥50% and ≤1 exacerbation in the prior year; "B" MMRC ≥2, FEV1≥50% and ≤ 1 exacerbation; "C" MMRC ≤1, FEV1<50% and ≥2 exacerbations; and "D" MMRC ≥2, FEV1<50% and ≥2 exacerbations. Per guidelines, subjects not meeting these criteria were classified as C or D based on MMRC and the worse of FEV1 or exacerbation history categories.

Results: Of 4,475 subjects, 33.8%, 20.9%, 8.3% and 41.0% were classified as GOLD A, B, C and D respectively. FEV1 was lowest (37.1%), BODE index highest (4.7), SGRQ highest (54.0) and walk distance lowest (960 ft) in grade D. Grade D subjects were most frequently on a recommended medication regimen (93.1%), followed by C (68.1%), B (61.0%) and A (24.2%). As grades C and D are defined by MMRC, ≤1 and ≥2 respectively, and either FEV1<50 or ≥2 exacerbations in the prior year, significant heterogeneity in disease severity range is seen: FEV1%, C (18-103) and D (9-103); exacerbations in prior year, C (0-6) and D (0-6); SGRQ C (0-83) and D (2-98); and emphysema C (0.1-52.3%) and D (0.02-61.2%).

Conclusions: A relatively small proportion of subjects met criteria for grade C suggesting patients with low FEV1 and frequent exacerbations but mild dyspnea are less common. While subjects within grades C and D have similar dyspnea severity, they are quite dissimilar with respect to other markers of disease severity.

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Combined COPD assessment using the new GOLD guidelines

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GOLD guidelines advocate symptomatic assessment using the CAT or mMRC,

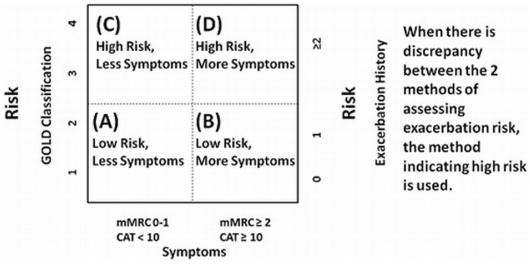

Figure 1. Association between symptoms, spirometric classification and future risk of exacerbations (adapted from GOLD guidelines).

followed by spirometry and/or exacerbation history to determine exacerbation risk (Fig 1). We examined this guidance in the London COPD cohort.
106 patients completed daily symptom diary cards for ≥1 year and the CAT at least once when stable. All exacerbations received additional systemic and/or inhaled therapy.
Mean age was 72.6 years (SD 8.3), FEV1 1.1L (0.5), and FEV1 predicted 48.5% (16.4).

Risk Stratification using CAT

Patient Category	Characteristics	Number of patients according to CAT + GOLD grade	Number of patients according to CAT + Exacerbation History	Number of patients using CAT + combined exacerbation risk
A	Low Risk, Less Symptoms	9	14	8
B	Low Risk, More Symptoms	37	57	27
C	High Risk, Less Symptoms	8	3	9
D	High Risk, More Symptoms	52	32	62

Risk Stratification using mMRC

Patient Category	Characteristics	Number of patients according to mMRC + GOLD grade	Number of patients according to mMRC + Exacerbation History	Number of patients using mMRC + combined exacerbation risk
A	Low Risk, Less Symptoms	15	19	12
B	Low Risk, More Symptoms	31	52	23
C	High Risk, Less Symptoms	8	4	11
D	High Risk, More Symptoms	52	31	60

Using CAT and GOLD grade to assess exacerbation risk yielded significantly more high risk patients (category C&D) than when exacerbation history was used (56.6% vs. 33.0%, p=0.001).
After combined assessment using both GOLD grade and exacerbation history, few patients were included in the high risk, less symptoms category C: 8.5% (9/106) using CAT and 10.4% (11/106) using mMRC.
In a specialist outpatient setting, few patients fulfil criteria for inclusion in the high risk, less symptoms category C. Furthermore, the method chosen to assess exacerbation risk had a large influence on risk stratification. Additional work is required to examine the utility of this aspect of GOLD guidance in primary care to screen for exacerbation risk.

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Combined assessment according to the new GOLD guidelines and its relation to outcome in COPD

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Background: The new GOLD guidelines recommend pharmacological and non-pharmacological management of COPD to be individualized based on the assessment of symptoms and exacerbation risk (A=low risk, less symptoms, B=low risk, more symptoms, C=high risk, less symptoms, D=high risk, more symptoms). We hypothesize that functional parameters and the risk of future events differ among patients categorized by the combined assessment according to the guidelines.
Methods: We prospectively evaluated 638 patients with stable COPD for ≥ 6 weeks, > 10 PY and GOLD II-IV seeking care in pulmonary tertiary hospitals in 8 European countries and included in the PROMISE cohort. The outcome variables were exacerbation and death from any cause. Median observation time was 24 months.
Results: There were 1152 exacerbations, 225 severe exacerbations and 63 deaths among 586 patients classified as A=50 (7.8%), B =184 (28.8%), C =27 (4.2%), and D=325 (50.9%). Health-related QoL as assessed by all domains of the SGRQ ($p<0.0001$) and most but not all domains of the SF-36, circulating proadrenomedullin ($p=0.0287$), 6 MWD ($p<0.0001$), exacerbations rate ($p< 0.0001$), severe exacerbation rate ($p<0.0001$) and mortality ($p<0.0001$) differ significantly among the 4 groups. Mortality was highest in the group D (12%) followed by groups A (10%), B (6%). Remarkably, mortality was lowest in group C (0%).
Conclusion: The combined assessment according to the new GOLD guidelines is only partially associated with quality of life and the risk of future events in COPD.

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Differences in the recommended initial therapy of COPD according to GOLD guidelines 2006 and 2011

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Background: The last GOLD Guideline revision was released in late 2011. We hypothesized that newer GOLD guidelines would frequently lead to a differnent initital treatment choice.
Aims and objectives: To demonstrate the magnitude of difference in recommended initial treatments in COPD patients based on past and recent GOLD revisions.
Methods: We retrospectively analyzed 52 patients with first diagnosed stable COPD. Spirometry, COPD Assessment Test and evaluation of exacerbations were done. Patients were allocated to the most appropriate treatment according to GOLD 2006 and 2011 management scheme.
Results: According to GOLD 2006 criteria 32 (61,5%), 18 (34,6%) and 2 (3,8%) patients were stage II, III and IV, respectively. Forty (76,9%) patients should be prescribed monotherapy with LABA or LAMA and 12 (23,1%) required ICS/LABA therapy. According to GOLD 2011 6 (11,5%), 19 (36,5%), 2 (3,8%) and 25 (48,1%) patients were Group A, B, C and D, respectively. Thus, 6 (11,5%) patients would not be prescribed long-acting bronchodilators (BD) as initial therapy, 20 (38,5%) patients required monotherapy with long-acting BD and 26 (50,0%) required therapy with ICS/LABA. In accordance with GOLD 2011 treatment scheme, initial therapy was required to be changed in 21 (40,4%) patients (13 (40,6%) stage II and 8 (40,0%) stage III-IV). In 6 (11,5%) cases we had to administer more "light" therapy (with short-acting BD instead of long-acting BD), and 14 (26,9%) patient required more intensive treatment, usually LABA/ICS instead of monotherapy.
Conclusions: In significant proportion of COPD patients GOLD 2011 treatment scheme leads to another, generally more intensive, initial treatment.

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GOLD assessment of COPD patients: Impact of symptoms assessment choice

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Background: The 2011 GOLD guidelines recommend combined COPD assessment using *symptoms* (modified Medical Research Council Dyspnoea [mMRC] ≥2 or COPD Assessment Test [CAT] ≥10) combined with a *history of exacerbations in the past 12mo* {0,1} vs 2+ and *spirometric classification* GOLD I/II vs III/IV. Four groups are identified, A: low symptoms + low risk; B: high symptoms + low risk; C: low symptoms + high risk; D: high symptoms + high risk.
Objectives: Characterize the 4 groups using the ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints) cohort.
Methods: 2028 COPD patients, FEV1<80%pred, provided baseline mMRC, SGRQ and previous 12mo history of exacerbations. SGRQ score ≥25 was used to replace the CAT ≥10, using a validated conversion (Jones: BMCPulmMed 2011).
Results: The 4 groups were comparable on age and gender, but had different characteristics. Size of patient groups classified by mMRC were A: 23%, B: 14%, C: 23%, D: 40%; by SGRQ, A: 9%, B: 28%, C: 3%, D: 60%. Compared to the SGRQ, patients classified as 'low symptoms' (GOLD A & C) using mMRC had worse health status, more fatigue and lower exercise capacity (6MWD). Categorising mMRC as 0 vs. ≥1 produced groups of similar size to those classified by SGRQ: A: 9%, B: 29%, C: 4%, and D: 59%. The kappa of agreement for group membership defined by SGRQ and mMRC increased from 0.2 (mMRC ≤1 vs ≥2) to 0.5 (mMRC 0 vs ≥1).
Conclusions: The new assessment permits classification of COPD patients beyond airflow obstruction. GOLD recommends either CAT ≥10 or mMRC ≥2 as the symptomatic cut-point, but this analysis suggests that mMRC ≥1 will classify patients more closely to using the CAT.
Clinicaltrials.gov NCT00292552; GSK study SCO104960.

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Comparison of modified Medical Research Council (mMRC) dyspnoea scale cut point ≥1 with COPD assessment test (CAT) ≥10 to differentiate low and high symptom COPD patients

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The GOLD 2011 guidelines recommend categorising patents into: A: low risk, less symptoms; B: low risk, more symptoms; C: high risk, less symptoms; D: high risk, more symptoms. A CAT score ≥10 or mMRC score ≥2 are proposed for categorising symptoms. A recent analysis suggests that the mMRC places more severe patients in the 'less symptom' categories than the CAT (Adamek *et al*, ERS 2012). This analysis compared health status scores split by CAT ≥10 or mMRC ≥1, using St George's Respiratory Questionnaire (SGRQ) and short form health survey (SF-12) Physical Component (PC) scores, in a primary care population from the Health-Related Quality of Life in European COPD Study.

Data from 1817 patients (mean [SD] FEV_1 1.6 [0.6] L; age 64.9 [9.6] years; males 72%) were used. The CAT classified 17.2% of patients as low symptom (GOLD A+C) vs. 18.9% by mMRC. SGRQ scores in the mMRC low symptom groups were slightly higher than those classified by CAT. The distribution of low symptom patients into low risk and high risk categories differed.

	CAT (≥ 10)			mMRC (≥ 1)		
Patient Group	Patients n (%)	SGRQ mean±SD	SF-12 PC mean±SD	Patients n (%)	SGRQ mean±SD	SF-12 PC mean±SD
A	40 (2.2)	25.0±9.3	45.1±7.4	38 (2.1)	36.3±16.5	42.6±8.1
B	227 (12.5)	50.0±15.9	35.6±7.8	230 (12.7)	48.2±17.0	36.0±8.3
C	272 (15.0)	21.6±10.7	46.0± 7.7	306 (16.8)	27.6±14.7	44.7±8.1
D	1271 (70.0)	49.4±17.6	36.0± 8.5	1241 (68.3)	48.7±18.5	36.1±8.6
Missing	7 (0.4)	-	-	2 (0.1)	-	-

The mMRC cut-point of ≥1 identifies a group of low symptom patients who have similar health status to those classified by CAT but are not directly equivalent. The small differences in classification of patients using CAT or MRC ≥1 may influence treatment in only a very small proportion of patients.