ORIGINAL RESEARCH

Impact of GOLD groups of chronic pulmonary obstructive disease on surgical complications

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Purpose: Chronic obstructive pulmonary disease (COPD) is associated with increased postoperative complications. Recently, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classified COPD patients into four groups based on spirometry results and the severity of symptoms. The objective of this study was to evaluate the impact of GOLD groups on postoperative complications.

Patients and methods: We reviewed the medical records of COPD patients who underwent preoperative spirometry between April and August 2013 at a tertiary hospital in Korea. We divided the patients into GOLD groups according to the results of spirometry and self-administered questionnaires that assessed the symptom severity and exacerbation history. GOLD groups, demographic characteristics, and operative conditions were analyzed.

Results: Among a total of 405 COPD patients, 70 (17.3%) patients experienced various postoperative complications, including infection, wound, or pulmonary complications. Thoracic surgery, upper abdominal surgery, general anesthesia, large estimated blood loss during surgery, and longer anesthesia time were significant risk factors for postoperative complications. Patients in high-risk group (GOLD groups C or D) had an increased risk of postoperative complications compared to those in low-risk group (GOLD groups A or B).

Conclusion: COPD patients in GOLD groups representing a high exacerbation risk have an increased risk of postoperative complications compared to those with low risk.

Keywords: chronic obstructive pulmonary disease, dyspnea, postoperative complications, risk assessment, spirometry

Introduction

Chronic obstructive pulmonary disease (COPD) is a disabling disease, of which the prevalence increases with age and causes significant morbidity and mortality.[1] It is the ninth leading cause of years of life lost according to World Health Organization Global Health Observatory data (http://www.who.int/gho/en/).

In the previous version of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, classification of COPD was based only on the forced expiratory volume in 1 second (FEV_1). In 2011, the GOLD guidelines emphasized the use of a combined COPD assessment based on exacerbation risk and patient symptoms, and a new classification of GOLD groups was suggested (http://www.goldcopd.com/). In recent studies, the capacity of this new COPD classification for predicting the clinical course of COPD has varied.[2–4]

As the numbers of COPD patients increase with longer life expectancy, more surgeons encounter surgical patients with underlying COPD. It is known that COPD is an independent risk factor for increased postoperative morbidity, mortality, and length of hospital stay.[5] It has been reported previously that such morbidities not only

include postoperative pulmonary complications, but also wound dehiscence, sepsis, and cardiac and renal complications. Therefore, accurate assessment of the status of COPD patients is important for guiding appropriate perioperative management.

To the best of our knowledge, the relationship between the COPD GOLD group and postoperative complications has not yet been studied. The aim of this study was to evaluate whether the COPD GOLD group classification is associated with the rate and type of postoperative complications.

Material and methods
Study design
We reviewed the medical records of COPD patients detected by preoperative spirometry at Seoul National University Hospital, between April 2013 and August 2013. This study was conducted in accordance with the amended Declaration of Helsinki, and was reviewed by the institutional review board at Seoul National University Hospital (protocol number H-1403-102-567, approval date April 22, 2014). During this period, self-administered questionnaires were collected in the pulmonary function test room of the hospital. Informed consent requirement was waived due to the retrospective study design, but patient records and information was anonymized and deidentified prior to analysis. Questions included those on comorbidities and the level of dyspnea (assessed using the COPD assessment test [CAT] and modified medical research scale [mMRC]). Details of the collection of COPD diagnostics have been described in our previous report in which we evaluated the prevalence of COPD among surgical candidates.[6] The data collected included demographic characteristics, comorbidities, spirometry results, operative conditions such as anesthesia time and estimated blood loss (EBL), and type of postoperative complications that occurred.

Definition
We defined COPD as a postbronchodilator FEV_1/FVC (forced vital capacity) ratio of <0.7 in patients ≥40 years of age. The COPD patients were classified into four groups according to the revised GOLD guidelines, based on the results of spirometry, symptom severity, and history of acute exacerbation reported on the questionnaire.

Postoperative complications were defined as any deviation from the normal postoperative course, which included pulmonary, cardiac, infection, wound, and other complications.[7] Pneumonia was diagnosed based on typical clinical features (cough, fever, sputum production, or pleuritic chest pain), imaging findings, and laboratory results

such as leukocytosis and elevated C-reactive protein levels.[8,9] Wound complications were divided into major (Grades III and IV) and minor (Grades I and II) complications, according to whether further mechanical interventions were required such as drainage insertion or reoperation.[7]

Statistical analysis
Statistical analyses were performed using SPSS 22.0 (IBM Corporation, Armonk, NY, USA). Variables were compared between patients with and without postoperative complications using the Pearson χ^2 or Fisher's exact tests for categorical variables, and the Student's *t*- or Mann–Whitney *U*-tests for continuous variables in univariate analyses. Multivariate analysis using binary logistic regression was performed to evaluate factors related to postoperative complications.

Results
Baseline characteristics
A total of 474 COPD patients underwent preoperative spirometry. Among them, 69 patients did not undergo surgery for nonmedical reasons. Consequently, 405 patients were included in this study.

Of the 405 patients who underwent surgery, 58.7% were male, with a median age of 70 (range: 44–91) years. The overall body mass index (BMI) was 23.33±2.98 kg/m². Distribution of the GOLD groups was as follows: 62% (n=251) fell in group A, 32% (n=130) in group B, 3% (n=11) in group C, and 3% (n=13) in group D. The most common comorbidities were malignancy (51%), hypertension (51%), diabetes mellitus (19%), and cardiac diseases (13%) such as heart failure, angina, or arrhythmia (Table 1). Genitourinary (25%), upper abdominal (21%), and orthopedic operations (13%) were the most frequently performed surgeries.

Postoperative complications
Approximately 17.3% (n=70) of the patients experienced complications after surgery. The most common were infections (31%), wound (38%), and pulmonary complications (29%). Among the 22 patients who developed infectious complications, three patients had bloodstream infections and one had septic shock. Postoperative wound complications included wound dehiscence, seromas, intracavitary fluid collections, and superficial wound infections. Of the 27 patients with such complications, 17 (63.0%) had major complications that required further surgical or angiographic intervention. Pneumonia was the most common pulmonary complication, followed by pleural effusion and atelectasis (Table 2). No mortality was observed during hospitalization.

Table 1 Baseline characteristics of study patients

Variables	Patients without postoperative complications, n=335	Patients with postoperative complications, n=70	P-value
Age[a]	70 (46–91)	71 (44–88)	0.841
Male sex	281 (83.9)	66 (94.3)	0.024
BMI (kg/m²)[b]	23.51±2.90	22.44±3.18	0.006
Smoking history	239 (71.3)	64 (91.4)	<0.001
Underlying disease			
Hypertension	172 (51.3)	34 (48.6)	0.673
Diabetes mellitus	64 (19.1)	14 (20.0)	0.863
Tuberculosis	37 (11.0)	4 (5.7)	0.179
Liver disease	33 (9.9)	10 (14.3)	0.273
Heart disease	46 (13.7)	9 (12.9)	0.846
Renal disease	16 (4.8)	4 (5.7)	0.761
Neurologic disease	37 (11.0)	10 (14.3)	0.441
Malignancy	158 (47.2)	47 (67.1)	0.002
ASA physical status			0.998
1	38 (11.3)	8 (11.4)	
2	269 (80.3)	56 (80.0)	
3	28 (8.4)	6 (8.6)	
PFT values			
FVC, % predicted[b]	103.64±15.86	102.10±15.63	0.461
FEV$_1$, % predicted[c]	94 (84–106)	90 (94.5–102.25)	0.044
FEV$_1$/FVC, %[c]	64 (59–67)	63 (53.5–68)	0.226

Notes: Data are presented as numbers (%) unless otherwise indicated. [a]Median (range), [b]mean ± SD, [c]median (interquartile range).
Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; PFT, pulmonary function test; FEV$_1$, forced expiratory volume in 1 second; FVC, forced vital capacity.

Comparison between patients with and without postoperative complications

On the basis of the univariate analysis, patients with postoperative complications were more likely to be male (P=0.024), have lower BMI (P=0.006), have history of smoking (P<0.001), and have lower FEV$_1$ values (P=0.044; Table 1). Thoracic surgery (P=0.021) and upper abdominal surgery (P<0.001) were significantly related to increased risk of postoperative complications. General anesthesia (P<0.001), longer anesthesia time (P<0.001), and a larger amount of EBL (P<0.001) were also significantly related to postoperative complications (Table 3).

Patients with postoperative complications had a higher GOLD grade than those without complications (P=0.020). However, the COPD GOLD group distribution according to the combined assessment did not show significant difference between patients with and without postoperative complications (P=0.056). When patients were divided into two groups based on the risk evaluation, there was a significant association between the patients with a high risk (GOLD groups C or D) and postoperative complications (P=0.047), compared to those with a low risk (GOLD groups A or B). In contrast, the level of subjective dyspnea (GOLD groups A or C versus B or D) was not related to the risk of postoperative complications (P>0.999; Table 4).

On the basis of multivariate analysis, we observed a significant association between postoperative complications and patients in high-risk group (GOLD groups C or D; odds ratio [OR] =4.023, 95% confidence interval [CI] =1.312–12.335, P=0.015). In addition, a larger amount of EBL (L) (OR =1.788, 95% CI =1.076–2.972, P=0.025), and longer anesthesia time (hours) (OR =1.445, 95%

Table 2 Types of postoperative complications

Category	Postoperative complication	n (%)
Pulmonary		20 (4.9)
	Pneumonia	11 (2.7)
	Pleural effusion	9 (2.2)
	Atelectasis	4 (1.0)
Infection		22 (5.4)
	Organ specific infection	19 (4.7)
	Bloodstream infection	3 (0.7)
	Septic shock	1 (0.2)
Renal		6 (1.5)
	Acute kidney injury	6 (1.5)
	Dialysis	2 (0.5)
Cardiac		4 (1.0)
	Arrhythmia	4 (1.0)
Wound		27 (6.7)
	Major	17 (4.2)
	Minor	10 (2.5)
Others		13 (3.2)
	Acute urinary retention	7 (1.7)
	Delirium	6 (1.5)

Note: More than one postoperative complication could occur in each patient.

Table 3 Surgical information of patients with and without complications

Variables	Patients without postoperative complications, n=335	Patients with postoperative complications, n=70	P-value
Surgery site			
Brain	13 (3.9)	0 (–)	0.137
Head and neck	44 (13.1)	3 (4.3)	0.036
Thorax	8 (2.4)	6 (8.6)	0.021
Upper abdomen	54 (16.1)	29 (41.4)	<0.001
Lower abdomen	36 (10.7)	9 (12.9)	0.675
Genitourinary	94 (28.1)	11 (15.7)	0.032
Orthopedic	45 (13.4)	7 (10.0)	0.435
General anesthesia	268 (80.0)	69 (98.6)	<0.001
Emergency operation	7 (2.1)	0 (–)	0.610
Anesthesia time (hours)[a]	1.92 (1.17–3.33)	4.62 (3.17–5.83)	<0.001
EBL (L)[a]	0.02 (0.00–0.15)	0.40 (0.15–0.96)	<0.001

Notes: Data are presented as numbers (%) unless otherwise indicated. [a]Median (interquartile range).
Abbreviation: EBL, estimated blood loss.

Table 4 Distribution of postoperative complications based on the COPD group

Comparison	Patients without complications, n=335	Patients with complications, n=70	P-value
GOLD grade[a]			0.020
1	272 (81.2)	48 (68.6)	
2	54 (16.1)	17 (24.3)	
3	9 (2.7)	4 (5.7)	
4	0 (–)	1 (1.4)	
GOLD group			0.056
A	210 (62.7)	41 (58.6)	
B	110 (32.8)	20 (28.6)	
C	7 (2.1)	4 (5.7)	
D	8 (2.4)	5 (7.1)	
Risk assessment			0.047
Low risk (A or B)	319 (95.2)	62 (88.6)	
High risk (C or D)	16 (4.8)	8 (11.4)	
Level of symptoms			>0.999
Less symptoms (A or C)	217 (64.8)	45 (64.3)	
More symptoms (B or D)	118 (35.2)	25 (35.7)	

Notes: Data are presented as numbers (%). [a]GOLD grade is defined as: 1, FEV_1 ≥80% predicted; 2, 50% ≤ FEV_1 <80% predicted; 3, 30% ≤ FEV_1 <50% predicted; 4, FEV_1 <30% predicted.
Abbreviations: COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

CI =1.205–1.732, P<0.001) were related to postoperative complications (Table 5).

Postoperative complications analysis

We analyzed each type of postoperative complications to evaluate if the GOLD group was significantly associated with any particular one.

Higher-risk group (GOLD groups C or D) was significantly associated with postoperative infection (OR =3.755, 95% CI =1.053–13.387, P=0.041) or wound complications (OR =5.883, 95% CI =1.642−21.082, P=0.007) compared to a lower-risk group (GOLD groups A or B) based on multivariate binary logistic regression analysis. On the other hand, higher-risk group was not significantly associated with postoperative pulmonary complications (OR =1.103, 95% CI =0.187−6.510, P=0.914).

Table 5 Multivariable analysis for factors related to postoperative complications

Variables	OR	95% CI	P-value
High-risk group[a]	4.023	1.312–12.335	0.015
Male sex	0.620	0.134–2.871	0.541
BMI (kg/m²)	0.962	0.864–1.072	0.484
Smoking history	6.079	1.704–21.687	0.005
Underlying malignancy	1.112	0.552–2.243	0.766
Thoracic surgery	2.069	0.555–7.714	0.279
Upper abdominal surgery	1.883	0.927–3.827	0.080
Estimated blood loss (L)	1.788	1.076–2.972	0.025
General anesthesia	4.547	0.566–36.541	0.154
Anesthesia time (hours)	1.445	1.205–1.732	<0.001

Note: [a]GOLD groups C or D.
Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

Upper abdominal surgery and a larger amount of EBL during surgery were related to an increased risk of postoperative pulmonary complications, while lower BMI and larger EBL were related to increased risk of postoperative infection. Larger EBL, smoking history, and upper abdominal surgery increased the risk of wound complications in COPD patients in high-risk group (Table S1).

Discussion

Of the 405 COPD patients who underwent surgery, 70 patients (17.3%) experienced postoperative complications, similar to those previously reported,[5,10,11] High-risk GOLD groups (GOLD groups C or D) were significantly associated with postoperative complications, as compared to low-risk GOLD groups (GOLD groups A or B). Most common postoperative problems included infection, wound, and pulmonary complications.

Because of the increased life expectancy associated with various comorbidities, surgeons, anesthesiologists, and respiratory physicians need to deal with large numbers of high-risk respiratory patients. COPD is considered as an independent risk factor for postoperative mortality and cardiopulmonary complications.[12] It is now believed that COPD is also a risk factor for various postoperative morbidities, such as stroke, acute kidney injury, ascites, and wound dehiscence, in cardiopulmonary surgery, as well as genitourinary, orthopedic, plastic surgery, and others.[5]

In this study, the high-risk GOLD groups (GOLD groups C or D) and postoperative complications were significantly associated. The level of airflow limitation (FEV_1% predicted)

had a significant influence on postoperative complications; this was compatible with previous findings that severe airflow limitation leads to increased risk of postoperative respiratory complications after upper abdominal and thoracic surgery.[13–15]

On the other hand, severe dyspnea (GOLD groups B or D) was not related to postoperative complications. We further analyzed the results based on mMRC and CAT scores because classification of the patients could differ depending on the scoring system used (Table S2), given that the mMRC is a one-dimensional measurement for quantifying dyspnea only, while the CAT score is a multidimensional method that assesses eight categories.[16] Neither the mMRC nor the CAT scores showed a significant relationship between postoperative complications.

Very few reports are available about the relationship between the level of dyspnea and postoperative complications. A previous study of 269 COPD patients undergoing total aortic arch replacement showed that the patient's subjective dyspnea was significantly related to postoperative pulmonary complications.[17] However, this report only included aortic arch replacement surgery and related pulmonary complications, which differs from our study.

In addition to the high-risk GOLD groups (GOLD groups C or D), male sex, lower BMI, underlying malignancy, thoracic and upper abdominal surgery, general anesthesia, longer anesthesia time, and a larger EBL during surgery were also related to an increased risk of postoperative complications. A lower BMI represents a poor nutritional status, which could affect postoperative outcomes.[18,19] Thoracic and upper abdominal surgeries, longer anesthesia time, and general anesthesia have previously been reported to be related to postoperative complications.[12,17,20] Anesthetic agents and muscle relaxants, as well as mechanical ventilation during general anesthesia, interfere with the respiratory system and therefore affect postoperative recovery.[12]

In our study, age was not related to postoperative morbidities. Several previous studies have shown advanced age as a risk factor for selected types of complications in limited circumstances.[21,22] However, opposite results do exist suggesting that advanced age is not directly related to, or even protective against postoperative events.[23,24] The aforementioned studies were based on specific types of surgeries and complications, which lack various postoperative morbidities such as wound dehiscence, renal failure, delirium, and so on. Our study focused on a variety of surgery types and postoperative events, which leads to the current result that age has no significant impact on all-cause postoperative complications.

We also analyzed the variables for each type of postoperative complication. High-risk groups (GOLD groups C or D) were significantly associated with an increased risk of postoperative infection and wound complications. COPD patients have lower partial pressure of oxygen in arterial blood than non-COPD patients as reported in our previous study.[6] Such limited oxygen within the healing tissues leads to impaired wound healing, susceptibility to bacterial infections, and dehiscence of surgical anastomosis. This is also exacerbated by the antiproliferative effects of nicotine on red blood cells, fibroblasts, and macrophages in smokers with COPD.[12,25] Decreased oxygen delivery can also delay wound-healing processes such as re-epithelialization as proven in animal studies.[26] A previous study of patients undergoing abdominal surgery reported that the major independent risk factors for wound dehiscence include chronic pulmonary disease and postoperative coughing, which can lead to delayed wound healing due to the mechanical movement at the site of surgery.[27]

To the best of our knowledge, this is the first study evaluating the relationship between the COPD GOLD group and postoperative complications. However, this study had several limitations. First, this is a retrospective study performed at a single center. Second, the small number of patients in GOLD groups C and D affected the statistical power of the comparisons in this study. GOLD groups A and B comprised 251 and 130 patients each, while GOLD groups C and D comprised only eleven and 13 patients, respectively. Third, study population was outpatient based, with relatively good performance status; therefore, caution is needed to generalize this result on other populations.

Conclusion

In conclusion, 17.3% of COPD patients experienced postoperative complications. Using the GOLD definition, high-risk groups (GOLD groups C or D) were more significantly associated with postoperative complications than low-risk groups (GOLD groups A or B). While the severity of dyspnea does not show significant correlation with postoperative complications, lower value of FEV_1 has much influence on increased risk of surgical complications.

Author contributions

SMC and HJK contributed to conception and design of the study, and acquisition, and analysis of data. JL, YSP, CHL, SML, JJY, CGY, YWK, and SKH contributed to study design and interpretation of data. SMC and HJK drafted the manuscript. JL, YSP, CHL, SML, JJY, CGY, YWK, and SKH revised the manuscript. All authors had access

to the final version of the manuscript, and approved the version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosure

The authors report no conflicts of interest in this work.

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Supplementary materials

Table S1 Multivariate analysis of postoperative pulmonary complications, infection, and wound complications

Variables	OR	95% CI	P-value
Postoperative pulmonary complication[a]			
High-risk group[b]	1.103	0.187–6.510	0.914
Upper abdominal surgery	3.155	1.208–8.238	0.019
EBL (L)	1.591	1.051–2.409	0.028
Postoperative infection[c]			
High-risk group[b]	3.755	1.053–13.387	0.041
BMI (kg/m^2)	0.847	0.727–0.987	0.034
EBL (L)	1.909	1.285–2.836	0.001
Postoperative wound complication[d]			
High-risk group[b]	5.883	1.642–21.082	0.007
EBL (L)	1.593	1.014–2.503	0.043
Smoking history	11.532	1.393–95.472	0.023
Upper abdominal surgery	3.846	1.607–9.209	0.002

Notes: [a]Adjusted for underlying heart disease, underlying malignancy, upper abdominal surgery, EBL, and general anesthesia; [b]GOLD groups C and D; [c]adjusted for BMI, underlying malignancy, upper abdominal surgery, EBL, and general anesthesia; [d]adjusted for BMI, underlying malignancy, smoking history, upper abdominal surgery, EBL, and general anesthesia.
Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index; EBL, estimated blood loss.

Table S2 Relationship between dyspnea and postoperative complications

Symptom assessment	Patients without postoperative complications, n=335	Patients with postoperative complications, n=70	P-value
mMRC			0.724
<2	278 (83.0)	60 (85.7)	
≥2	57 (17.0)	10 (14.3)	
CAT			0.885
<10	238 (71.0)	49 (70.0)	
≥10	97 (29.0)	21 (30.0)	

Note: Data are presented as numbers (%).
Abbreviations: mMRC, modified medical research scale; CAT, COPD assessment test.