



Prevalence of chronic obstructive pulmonary disease among 48,061 digestive tract cancer patients in Europe

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Background: Chronic obstructive pulmonary disease (COPD) shares common risk factors with digestive tract malignancies such as esophageal cancer. However, the prevalence and geographic distribution of COPD in patients with gastrointestinal (GI) cancer is only poorly understood.

Methods: We used the IQVIA's Oncology Dynamics (OD) database to identify a total of 48,061 patients with GI cancer (4,229 esophagus, 7,568 stomach, 27,300 colon, and 8,964 rectum cancer) from Germany, France, Italy, Spain and the UK.

Results: The prevalence of COPD among the 48,061 patients with GI cancer was 12.5% (5,983/48,061). We observed significant differences in frequencies of COPD between the different cancer sites with the highest COPD prevalence among patients with esophageal (25.5%) or gastric cancer (13.4%) and lowest prevalence in colon (11.0%) or rectal (9.8%) cancer patients. Moreover, rates of COPD strongly varied between digestive tract cancer patients from different countries. Interestingly, Spain (16.8%) and Germany (13.4%) had the highest COPD prevalence while prevalence of COPD was lowest in the UK (8.4%). Finally, we showed that the proportion of digestive tract cancer patients with COPD was highest among male patients (15%) and those >80 years (20.6%) when compared to all other patients.

Conclusions: In this analysis, we show that COPD is found at high frequencies in patients with digestive tract cancer in Europe. We demonstrate that prevalence varies according to digestive tract cancer sites and European countries.

Keywords: Cancer; chronic obstructive pulmonary disease (COPD); Europe; digestive tract

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Introduction

Both digestive tract cancers and chronic obstructive pulmonary disease (COPD) represent major global health burden associated with a dismal prognosis in many patients. Importantly, digestive tract cancers and COPD share many

different risk factors including alcohol and tobacco abuse, western diet and specific genetic aberrations. In the past, the relationship between digestive tract cancer and COPD has been extensively studied. As an example, it was suggested that cancer is more frequent in patients with COPD than

patients without COPD (1–4); HR 2.8 (95% CI: 2.6–3.1). Lung, liver, colorectal, breast, prostate and stomach were the most frequent malignancies overrepresented in COPD (1). In addition, COPD is a relevant driver for the development of complications in the context of necessary anti-cancer treatments (5,6). Just recently, elevate arterial blood pressure, myocardial infarction, COPD and asthma were comorbidities with a high risk for increased mortality in patients with colorectal cancer receiving surgery (7). Finally, besides other factors, COPD was identified as a factor reducing patients' adherence to cancer screening programs, potentially preventing cancer diagnosis in early disease stages (8). Despite these strong data showing an association between COPD and digestive tract cancers incidence as well as cancer-related morbidity, no comparative analyses regarding frequencies of COPD in digestive tract cancer patients from different countries have been published so far. We present the following article in accordance with the STROBE reporting checklist (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-200/rc>).

Methods

Database

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This retrospective study features a cross-sectional design. We analyzed the IQVIA's Oncology Dynamics (OD) database, which has been extensively described elsewhere (9–11). This database is an anonymized cross-sectional survey of oncologists using a standardized online questionnaire. This survey contains only questions about drug-treated cancer patients.

Patient selection and study outcome

Surveys were conducted in Germany, France, United Kingdom (UK), Spain, and Italy. Included were patients with one of the four gastrointestinal tumors: esophageal (ICD-10: C15), stomach (ICD10: C16), colon (ICD-10: C18), and rectum (ICD-10: C20), filled in the time between January 1st 2017 and March 31st 2021. The outcome of the study was the proportion of cancer patients with a documentation of COPD diagnosis (ICD-10: J40, J41, J42, J43, J44).

Statistical analysis

The prevalence of COPD was calculated as the proportion of patients with COPD on all patients. Multivariable logistic regression was used to evaluate the association between cancer type and country and COPD diagnosis adjusted for age, sex and facility. Cancers of colon and rectum were analyzed separately and additionally as one group (colorectal). For further details see (9–11).

Results

Baseline characteristics

Overall, 48,061 people with a malignancy of the digestive tract (4,229 esophageal, 7,568 stomach, 27,300 colon, and 8,964 rectal cancer) documented by 811 physicians were analysed (*Table 1*). There was a significant difference in age from 64.1 years in patients with esophagus cancer to 66.0 years in colon cancer patients. Esophageal cancer was associated with highest frequency of males (73.7%), lowest rates were found in subjects having colon cancer (61.0%).

Prevalence of COPD

Rates of COPD were highest among patients with esophageal (25.5%) and lowest in patients with rectal malignancies (9.8%). Patients with stomach and colon cancer had a COPD prevalence of 13.4% and 11.0%, respectively. In a multivariate regression model, esophageal cancer (OR: 3.88, 95% CI: 3.50–4.30, $P < 0.001$), stomach cancer (OR: 1.49, 95% CI: 1.35–1.64, $P < 0.001$) and colon cancer (OR: 1.12, 95% CI: 1.03–1.21, $P = 0.008$) were significantly linked with a higher odd of COPD compared to rectal cancer as reference group (*Table 2*). In the sensitivity analyses using colorectal cancer as reference group, esophageal cancer (OR: 3.50, 95% CI: 3.22–3.78, $P < 0.001$), stomach cancer (OR: 1.36, 95% CI: 1.26–1.46, $P < 0.001$) were also linked to a higher odd of COPD.

Geographical variation

Among all cancer types, COPD prevalence was highest in Spain (16.8%; *Figure 1*), followed by Germany (13.4%). The highest COPD prevalence was among patients with esophageal cancer (34.6% in France, 34.0% in Germany, and 32.7% in Spain). The lowest prevalence of COPD was

Table 1 Baseline characteristics of study patients

Variable	Esophagus	Stomach	Colon	Rectum	P value
N	4,229	7,568	27,300	8,964	
Age, year (mean, SD)	64.1 (9.3)	64.4 (10.9)	66.0 (10.6)	64.8 (10.7)	<0.001
Males (%)	73.7	64.5	61.0	62.5	<0.001
Facility (%)					
Hospital	78.7	51.7	51.7	58.2	<0.001
Office based oncologist	8.9	12.8	12.6	18.4	
Unknown	12.4	35.5	35.7	23.4	
Country (%)					
Germany	21.0	23.0	18.0	25.4	<0.001
France	17.0	13.0	15.2	14.2	<0.001
Italy	12.4	35.5	35.7	23.4	<0.001
Spain	13.2	15.0	16.4	22.4	<0.001
UK	36.4	13.5	14.6	14.6	<0.001

SD, standard deviation.

among rectum cancer patients with 14.7% in Spain, 9.1% in France, and 8.4% in Germany. In multivariate regression analysis, the odds for COPD was at highest in Spain (OR: 2.65, 95% CI: 2.39–2.94, $P<0.001$), followed by Germany (OR: 1.95, 95% CI: 1.76–2.16, $P<0.001$), Italy (OR: 1.77, 95% CI: 1.60–1.96, $P<0.001$) and France (OR: 1.65, 95% CI: 1.47–1.84, $P<0.001$), when compared to the UK (Table 2).

Discussion

In our analyses, we show that COPD is not not equally distributed between different tumor entities and largely varies between different countries and age groups. This adds a country-specific component to the previously available results from epidemiologic and clinical analyses, allowing the identification of previously unrecognized aspects regarding the role of COPD in patients with digestive tract cancer.

Digestive tract cancers belong to the most important malignancies worldwide with continuously rising prevalence rates (12). Similarly, COPD is an extremely common disease, causing a significant morbidity and mortality in almost all countries worldwide (11). COPD and digestive tract cancers share a variety of features and risk factors such as smoking and alcohol abuse. We therefore used

the IQVIA Oncology Dynamics (OD) database to analyze potential associations between these cancers and COPD in five different countries. We clearly show that COPD rates are highest in patients with esophageal cancer, while COPD prevalence was lowest among patients with rectal cancer. Unfortunately, our database does not allow to distinguish between the different histological entities of esophageal cancer. However, given the relatively low COPD rates in gastric cancer and the widely overlapping risk profiles of COPD and squamous cell carcinoma (SCC) of the esophagus (13), it seems likely that the effect is driven by this cancer subtype rather than adenocarcinoma of the esophagus. Notably, the distribution of COPD was very heterogeneous between different European countries. Interestingly, Spain and Germany displayed higher frequencies of COPD in digestive tract cancer patients while the association was rather weak in the UK. On the one hand, this finding might reflect the different distribution of COPD in the different countries, on the other hand it might also reflect the different relevance of COPD as a risk factor in the different countries. In addition, these data also raise the question of other risk factors in the context of COPD that could influence the role as a factor in the development of cancer. Conceivable, for example, would be certain genetic alterations that are distributed differently in different countries. In line with

Table 2 Association between GI cancer type, country and the prevalence of COPD in GI cancer patients (multivariable logistic regression model)

Variable	Proportion of patients with COPD (%)	OR (95% CI)	P value
Age, year			
≤50	3.3	Reference	
50–60	8.0	2.34 (1.94–2.84)	<0.001
60–70	12.4	3.93 (3.28–4.70)	<0.001
70–80	17.2	6.02 (5.02–7.21)	<0.001
>80	20.6	8.05 (6.61–9.80)	<0.001
Sex			
Male	15.0	1.87 (1.76–2.00)	<0.001
Female	8.2	Reference	
Cancer type			
Esophagus	25.5	3.88 (3.50–4.30)	<0.001
Stomach	13.4	1.49 (1.35–1.64)	<0.001
Colon	11.0	1.12 (1.03–1.21)	0.008
Rectum	9.8	Reference	
Country			
Germany	13.4	1.95 (1.76–2.16)	<0.001
France	11.9	1.65 (1.47–1.84)	<0.001
Italy	11.9	1.77 (1.60–1.96)	<0.001
Spain	16.8	2.65 (2.39–2.94)	<0.001
UK	8.4	Reference	

GI, gastrointestinal; COPD, chronic obstructive pulmonary disease; OR, odds ratio.

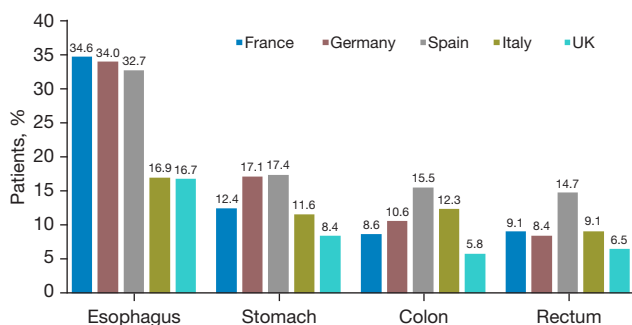


Figure 1 Prevalence of COPD among patients with GI cancers in five countries of Europe. COPD, chronic obstructive pulmonary disease; GI, gastrointestinal.

this hypothesis, we demonstrate that the cancer promoting effect of COPD varies between male and female patients as well as different age groups. Finally, differences between the respective health care systems could also be conceivable as specific factors that could explain the observed differences.

Using of data from a large cohort of patients from different European countries, helped us to better understand the intercountry variation of COPD rates in digestive tract cancer. However, our study has important limitations that needs to be considered in the interpretation of the results. Most importantly, the original questionnaire was intended for use as a research tool. Moreover, different

factors that may influence carcinogenesis in COPD patients such as the genetic and/or socioeconomic status as well as smoking behavior and alcohol were not part of the questionnaire. Next, due to the cross-sectional design, there is no information on the order of event enabling to identify if cancer or COPD was diagnosed first, therefore no causal relationships but only associations can be given from the data presented here. Finally, no data regarding lung function were recording within the database. Nevertheless, the database was used for many different studies and has demonstrated a cancer type distribution similar to the comparator sources (14).

In summary, our data demonstrate that COPD is differentially associated with digestive tract cancers. Notably, despite showing some variation, this association was observed in five different European countries, underlining the role of COPD as a potential cancer promoting factor in gastrointestinal malignancies. Results from this study clearly demonstrate that along with pulmonary cancers also digestive tract cancers should be considered in patients with COPD to improve long-term prognosis.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://apm.amegroups.com/article/view/10.21037/apm-22-200/rc>

Data Sharing Statement: Available at <https://apm.amegroups.com/article/view/10.21037/apm-22-200/dss>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-200/coif>). Karel Kostev and Laura Hoyer are employees of IQVIA. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). An individual consent form was not

obtained following the national and European legislation, as the used database contains only fully anonymized data.

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