

# Time trends in coronary revascularization procedures among people with COPD: analysis of the Spanish national hospital discharge data (2001–2011)

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**Background:** People with COPD suffering from coronary artery disease are frequently treated with revascularization procedures. We aim to compare trends in the use and outcomes of these procedures in COPD and non-COPD patients in Spain between 2001 and 2011.

**Methods:** We identified all patients who had undergone percutaneous coronary interventions (PCIs) and coronary artery bypass graft (CABG) surgeries, using national hospital discharge data. Discharges were grouped into: COPD and no COPD.

**Results:** From 2001 to 2011, 428,516 PCIs and 79,619 CABGs were performed. The sex and age-adjusted use of PCI increased by 21.27% per year from 2001 to 2004 and by 5.47% per year from 2004 to 2011 in patients with COPD. In-hospital mortality (IHM) among patients with COPD who underwent a PCI increased significantly from 2001 to 2011 (odds ratio 1.11; 95% confidence interval 1.03–1.20). Among patients with COPD who underwent a CABG, the sex and age-adjusted CABG incidence rate increased by 9.77% per year from 2001 to 2003, and then decreased by 3.15% through 2011. The probability of dying during hospitalization in patients who underwent a CABG did not change significantly in patients with and without COPD (odds ratio, 1.06; 95% confidence interval 0.96–1.17).

**Conclusion:** The annual percent change in PCI procedures increased in COPD and non-COPD patients. We found a decrease in the use of CABG procedures in both groups. IHM was higher in patients with COPD who underwent a PCI than in those without COPD. However, COPD did not increase the probability of dying during hospitalization in patients who underwent a CABG.

**Keywords:** COPD, percutaneous coronary intervention, coronary artery bypass graft surgery, hospitalization, length of stay, in-hospital mortality

## Background

The association between COPD and coronary artery disease (CAD) is well known.<sup>1</sup> In studies of the general population, it has been shown an increased all-cause mortality as well as cardiovascular mortality in patients with COPD.<sup>2,3</sup> Patients with mild COPD seem to have even a higher risk of dying from cardiovascular causes than from respiratory insufficiency.<sup>4</sup>

COPD is highly prevalent among patients with CAD.<sup>5</sup> The causal connection between both diseases has historically been cigarette smoking.<sup>6</sup> However, a recent epidemiological study has shown that systemic inflammation plays a significant role in both atherogenesis and COPD.<sup>7</sup>

Other evidence that highlights the close relationship between COPD and CAD is the fact that this pulmonary disease is an independent factor of poor outcome and mortality

after coronary revascularization procedures.<sup>8</sup> The diagnosis of COPD was, together with other important clinical variables such as age, sex, and left ventricular ejection fraction, a predictor of mortality at 4 years of revascularization in the SYNTAX II score (index that punctuates the complexity of CAD by angiography and it helps to decide the optimal method of revascularization in patients with CAD complex).<sup>9</sup> As a result, treatment of CAD in patients with COPD can present therapeutic challenges. Given that COPD is associated with higher risk of adverse events after coronary artery bypass graft (CABG) surgery,<sup>10,11</sup> percutaneous coronary intervention (PCI) is now the most commonly used reperfusion procedure for COPD patients undergoing revascularization.<sup>6</sup> In fact, patients with COPD currently make up almost 10% of patients undergoing PCI.<sup>12</sup> Nonetheless, several studies have reported and elevated the risk of adverse outcomes among patients with COPD after PCI.<sup>5,12–14</sup>

Secular trends in the use of coronary revascularization procedures have been examined.<sup>15</sup> Culler et al<sup>16</sup> have identified, in a recent retrospective study, all Medicare beneficiaries undergoing a coronary revascularization procedure between 2008 and 2012. They have observed, on the one hand, that the total number of revascularization procedures peaked in 2010 and declined by >4% per year in 2011 and 2012, and second, that mortality rates remained between 2.1% and 2.2% annually during the study period. However, despite the poor prognosis of patients with COPD after PCI and CABG, no previous studies have evaluated the changes in utilization and outcomes of coronary revascularization procedures over time in these patients. It is possible that there have been advances in recent years, not only in surgical techniques, but also in monitoring and anesthesia, which they could have helped to improve results.<sup>17</sup>

In this study, we used national hospital discharge data to describe and compare trends in the use of coronary revascularization procedures in COPD and non-COPD patients between 2001 and 2011 in Spain. In particular, we analyzed trends in the use of CABG and PCI, patient comorbidities, and in-hospital outcomes such as length of stay (LOS) and in-hospital mortality (IHM).

## Methods

A retrospective, descriptive, epidemiological study was conducted using the Spanish National Hospital Database (CMBD, Conjunto Mínimo Básico de Datos), which compiles all public and private hospital data, hence covering more than 95% of hospital discharges.<sup>18</sup> The CMBD database is managed by the Spanish Ministry of Health, Social Services

and Equality and includes patient variables (sex and date of birth), date of admittance, date of discharge, up to 14 discharge diagnoses, and up to 20 procedures performed during hospitalization. The Spanish Ministry of Health, Social Services and Equality sets recording standards and performs periodic audits.<sup>18</sup>

We selected all surgical admissions of patients who underwent coronary revascularization procedures using the International Classification of Diseases – Ninth Revision, Clinical Modification (ICD-9-CM). The procedure codes used were 36.10–36.19 for CABG and 36.06, 36.07, 36.09, and 0.66 for PCI. Discharges were grouped by COPD status as follows: no COPD and COPD (ICD-9-CM codes: 490–492 and 495–496, respectively). Patients who underwent both CABG and PCI during their hospitalization were excluded.

The outcomes of interest included the percentage of patients who died during hospitalization, defined as IHM and the mean LOS.

Clinical characteristics included information on overall comorbidity at the time of surgery, which was assessed by computing the Charlson comorbidity index (CCI). The index applies to 17 disease categories whose scores are totaled to obtain an overall score for each patient.<sup>19</sup> The 17 diseases included in the CCI are myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, COPD, connective tissue disease, ulcer disease, diabetes, renal disease, hemiplegia, any tumor, leukemia, lymphoma, liver disease, metastatic solid tumor, and AIDS. The index is subsequently categorized into three levels: 0, no disease; 1, one or two diseases; and 2, three or more diseases.<sup>20</sup> To calculate the CCI, we used 17 disease categories, excluding COPD and acute myocardial infarction, as described by Thomsen et al.<sup>20</sup>

## Statistical analysis

A descriptive statistical analysis was performed. Rates for COPD and non-COPD patients for each coronary revascularization procedure were calculated in terms of 100,000 inhabitants. We also calculated the yearly age- and sex-specific incidence rates for COPD and non-COPD patients, dividing the number of cases per year, sex, and age group by the corresponding number of people in that population group, according to data from the Spanish National Institute of Statistics, as reported on December 31 of each year.<sup>21</sup>

In our study, we used joinpoint log-linear regression to identify the years in which changes in tendency occurred in the use of PCI and CABG in patients with and without COPD, as well as to estimate the annual percent change (APC) in each

of the periods delimited by the points of change. The analysis started with the minimum number of joinpoints and tested whether the inclusion of one or more joinpoints was statistically significant.<sup>22</sup> In the final model, each joinpoint indicated a significant change in the tendency, and the APC was obtained in each of the segments delimited by the joinpoints, using the weighted least squares technique. The Joinpoint Regression Program Version 4.0.4 was used for the analysis.<sup>23</sup>

In order to test the time trend for IHM, logistic regression analyses were performed with mortality as a binary outcome, using year of discharge, sex, age, and CCI as independent variables. Models were generated for COPD and non-COPD subjects and for the entire population, in order to compare the IHM of those who have the disease and those who do not. Statistical analyses were performed using Stata version 10.1 (StataCorp LP, College Station, TX, USA). Statistical significance was set at  $P < 0.05$  (two-tailed).

## Ethical aspects

Data confidentiality was maintained at all times according to Spanish legislation. Patient identifiers were deleted before the database was provided to the authors, in order to maintain patient anonymity. It is not possible to identify patients at individual levels, either in this article or in the database. Given the anonymous and mandatory nature of the dataset, it was not necessary to obtain informed consent. The study protocol was approved by the ethics committee of the Rey Juan Carlos University.

## Results

From 2001 to 2011, a total of 508,135 admissions of patients who underwent scheduled or unscheduled coronary revascularization procedures were recorded in Spain. Over the study period, 7.17% ( $n=36,478$ ) of all patients who underwent coronary revascularization procedures had COPD. There were a total of 428,516 PCIs (6.91% [ $n=29,630$ ] in patients with COPD) and 79,619 CABGs (8.6% [ $n=6,848$ ] in patients with COPD).

## Percutaneous coronary intervention

In patients who underwent a PCI, there was a significant male predominance in patients both with and without COPD (92.82% and 75.54%, respectively). Mean age was 69.78 years (standard deviation [SD], 9.55 years) in patients with COPD and 65.02 years (SD, 11.37 years) in those without COPD ( $P < 0.01$ ).

Patients with COPD who underwent PCIs had higher CCI values compared with those without COPD (56.79% vs 43.75% with one or more coexisting conditions, respectively).

Among those who received a PCI, the median LOS was significantly higher in patients with COPD (7.00 days [interquartile range (IQR) 8.00 days]) compared with those without COPD (6.00 days [IQR 7.00 days]). Also, IHM was significantly higher in patients with COPD (2.97%) compared with patients without COPD (2.12%).

According to the results of the joinpoint analysis, we found that the sex and age-adjusted use of PCI increased by 21.27% per year from 2001 to 2004 and by 5.47% per year from 2004 to 2011 in patients with COPD (Figure 1A). In patients without COPD, the use of PCI increased by 14.7% per year from 2001 to 2005. From 2005 to 2008, it increased by 5.21% per year, and from 2008 to 2011 it also increased by 0.48% per year, but not significantly in both cases (Figure 1B).

Table 1 shows time trend outcomes in annual PCIs in patients with and without COPD in Spain, from 2001 to 2011. We found that the mean age of patients with COPD who underwent a PCI was  $68.43 \pm 8.95$  years in 2001 and increased to  $70.61 \pm 19.85$  years in 2011 ( $P < 0.05$ ). The proportion of men decreased significantly from 95.1% in 2001 to 92.05% in 2011. The prevalence of those with a CCI of one or more increased from 46.95% in 2001 to 62.10% ( $P < 0.05$ ).

LOS after PCI decreased significantly over the study period in both groups of patients ( $P < 0.001$ ), showing higher values among those with COPD in all years analyzed (Table 1).

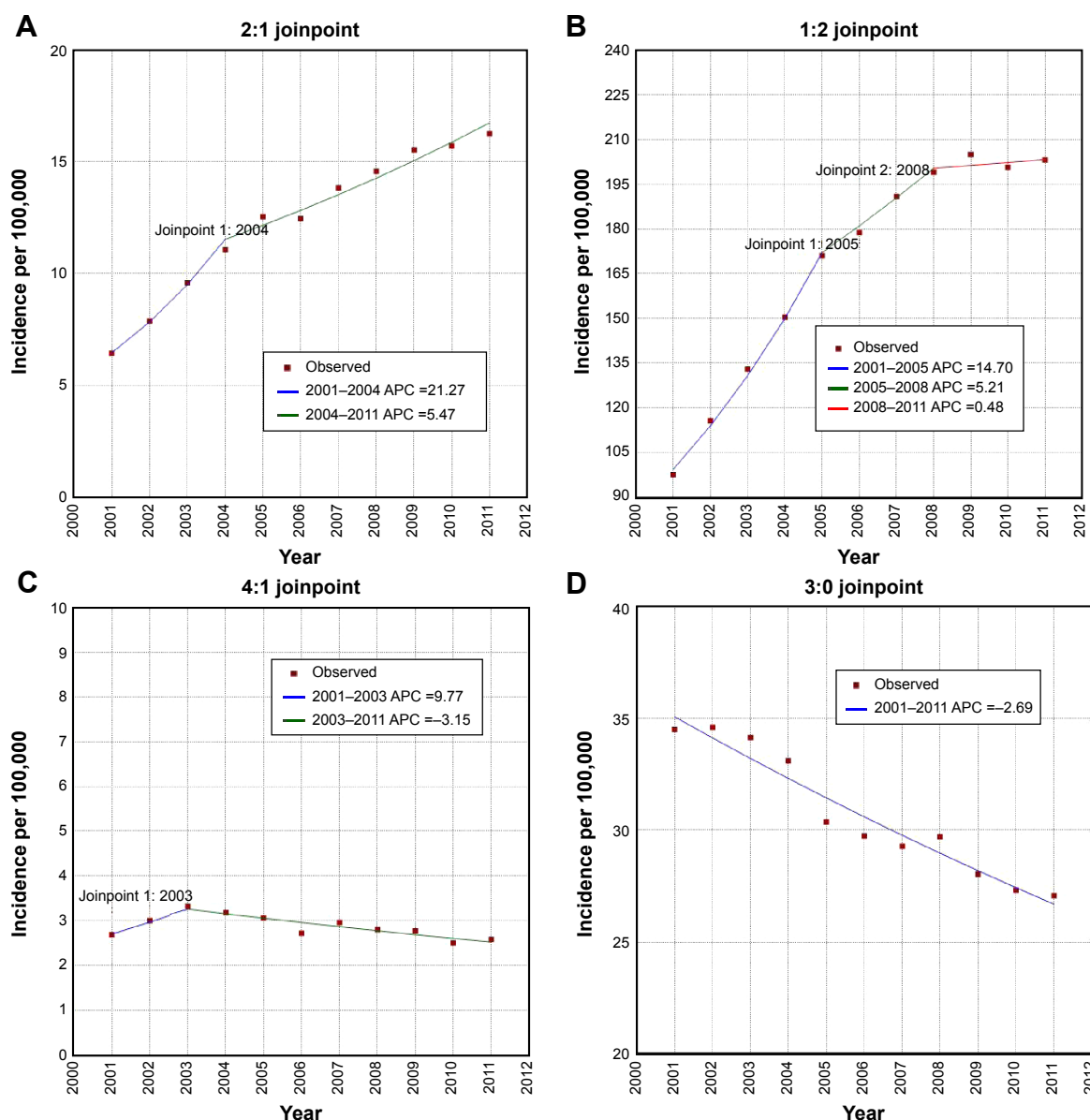
The IHM among those who underwent a PCI increased for those without COPD (from 1.94% in 2001 to 2.42% in 2011,  $P < 0.001$ ). This parameter also increased in patients with COPD (from 2.37% in 2001 to 2.83% in 2011,  $P < 0.01$ ) (Table 1).

As can be seen in Table 2, after multivariate adjustment, the IHM among patients with COPD who underwent a PCI increased significantly from 2001 to 2011 (odds ratio [OR] 1.11; 95% confidence interval [CI] 1.03–1.20).

By contrast, the IHM did not change significantly according to sex. On the other hand, the IHM was significantly higher in those with one or two (OR 1.93; 95% CI 1.65–2.26) or three or more (OR 3.26; 95% CI 2.54–4.18) comorbidities associated with COPD.

## Coronary artery bypass graft

We found that, in patients who underwent a CABG, the mean age was significantly higher in patients with COPD than in those without COPD (68.48 years [SD 8.42 years] vs 66.72 years [SD 9.55 years]) and there was higher proportion of males undergoing CABG procedures in both groups (93.17% in patients with COPD vs 76.49% in patients without COPD,  $P < 0.05$ ).



**Figure 1** Joinpoint analyses.

**Notes:** Joinpoint analysis in annual PCI in patients with (A) and without (B) COPD in Spain, from 2001 to 2011. Joinpoint analysis in annual CABG in patients with (C) and without (D) COPD in Spain, from 2001 to 2011. Annual percent change (APC) (based on rates that were sex and age-adjusted using the Spanish National Statistics Institute Census projections) calculated by using joinpoint regression analysis. APC is significantly different from zero (two-sided  $P < 0.05$ ).

**Abbreviation:** PCI, percutaneous coronary intervention.

In our study, patients with COPD who underwent a CABG had higher CCI values than those without COPD (58.15% vs 51.84% with one or more comorbidities).

In patients with COPD, the IHM was significantly higher than in those without COPD (7.75% vs 7.17%); however, the median LOS was significantly higher in patients with COPD (17.00 days [IQR 17.00 days]) compared with those without COPD (15.00 days [IQR 14.00 days]).

Among patients with COPD who underwent CABG, the sex and age-adjusted CABG incidence rate increased by 9.77% per year from 2001 to 2003, then decreased by 3.15% through 2011 (Figure 1C). In patients without COPD, the

incidence rate decreased at a constant rate of 2.69% per year over the entire period of study (Figure 1D).

As can be seen in Table 3, over the 11-year study period, the mean age of patients with COPD who underwent CABG was  $66.82 \pm 8.34$  years in 2001 and  $69.3 \pm 8.45$  years in 2011. Significant differences in age were observed ( $P < 0.001$ ). The proportion of men was 94.24% in 2001 and 91.68% in 2011 (no significant differences).

In our study, LOS in patients with COPD decreased significantly from 18 days (IQR, 19 days) in 2001 to 16 days (IQR, 16 days) in 2011 ( $P < 0.01$ ). In patients without COPD, LOS also decreased significantly over the period of study (Table 3).

**Table 1** Characteristics and outcomes of hospital discharges after percutaneous coronary intervention among patients with and without COPD in Spain, from 2001 to 2011

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	P-value
<b>No COPD</b>												
N	18,960	22,737	26,703	30,811	35,774	38,212	41,636	44,289	46,394	46,067	47,303	0.000
Incidence	97.48	115.63	133.04	150.34	171.01	178.78	190.86	199.02	204.97	200.7	203.11	
Age, mean (SD)	63.75 (10.74)	64 (10.93)	63.93 (11)	64.37 (11.05)	64.75 (11.06)	65.03 (11.21)	65.22 (11.36)	65.49 (11.51)	65.47 (11.6)	65.51 (11.71)	65.69 (11.77)	0.000
Male, n (%)	14,578 (76.89)	17,405 (76.55)	20,454 (76.55)	23,386 (75.9)	27,005 (75.49)	28,762 (75.27)	31,326 (75.24)	33,206 (74.98)	34,931 (75.29)	34,729 (75.39)	35,562 (75.18)	0.000
CCI 0, <sup>a</sup> n (%)	12,443 (65.63)	14,145 (62.21)	16,011 (59.96)	18,079 (58.68)	20,476 (57.24)	21,654 (56.67)	23,046 (55.35)	24,167 (54.57)	24,925 (53.72)	24,505 (53.19)	24,913 (52.67)	0.000
CCI 1–2, <sup>a</sup> n (%)	6,314 (33.3)	8,278 (36.41)	10,241 (38.35)	12,204 (39.61)	14,537 (40.64)	15,814 (41.38)	17,603 (42.28)	18,888 (42.65)	20,034 (43.18)	20,027 (43.47)	20,769 (43.91)	
CCI ≥3, <sup>a</sup> n (%)	203 (1.07)	314 (1.38)	451 (1.69)	528 (1.71)	761 (2.13)	744 (1.95)	987 (2.37)	1,234 (2.79)	1,435 (3.09)	1,535 (3.33)	1,621 (3.43)	
LOS, median (IQR)	6 (9)	6 (9)	6 (8)	6 (8)	6 (8)	6 (7)	6 (7)	5 (7)	5 (7)	5 (6)	5 (6)	0.000
IHM, n (%)	368 (1.94)	426 (1.87)	522 (1.95)	577 (1.87)	728 (2.03)	743 (1.94)	849 (2.04)	973 (2.2)	1,051 (2.27)	1,069 (2.32)	1,143 (2.42)	0.000
<b>COPD</b>												
N	1,265	1,569	1,945	2,290	2,647	2,689	3,044	3,260	3,526	3,611	3,784	0.000
Incidence	6.43	7.88	9.59	11.07	12.55	12.46	13.83	14.57	15.54	15.71	16.25	
Age, mean (SD)	68.43 (8.95)	68.7 (9.1)	68.7 (9.22)	68.8 (9.32)	69.4 (9.54)	69.8 (9.22)	69.91 (9.52)	70.11 (9.58)	70.16 (9.76)	70.55 (9.76)	70.61 (9.85)	0.000
Male, n (%)	1,203 (95.1)	1,480 (94.33)	1,803 (92.7)	2,130 (93.01)	2,477 (93.58)	2,490 (92.6)	2,817 (92.54)	3,019 (92.61)	3,259 (92.43)	3,342 (92.55)	3,483 (92.05)	0.011
CCI 0, <sup>a</sup> n (%)	671 (53.04)	850 (54.17)	928 (47.71)	1,050 (45.85)	1,233 (46.58)	1,174 (43.66)	1,335 (43.86)	1,310 (40.18)	1,405 (39.85)	1,414 (39.16)	1,434 (37.9)	0.000
CCI 1–2, <sup>a</sup> n (%)	564 (44.58)	669 (42.64)	949 (48.79)	1,143 (49.91)	1,302 (49.19)	1,396 (51.92)	1,556 (51.12)	1,746 (53.56)	1,936 (54.91)	1,979 (54.8)	2,109 (55.73)	
CCI ≥3, <sup>a</sup> n (%)	30 (2.37)	50 (3.19)	68 (3.5)	97 (4.24)	112 (4.23)	119 (4.43)	153 (5.03)	204 (6.26)	185 (5.25)	218 (6.04)	241 (6.37)	
LOS, median (IQR)	9 (10)	8 (9)	8 (10)	8 (9)	8 (9)	7 (8)	7 (8)	7 (8)	7 (7)	7 (7)	6 (6)	0.000
IHM, n (%)	30 (2.37)	40 (2.55)	60 (3.08)	77 (3.36)	81 (3.06)	77 (2.86)	67 (2.2)	117 (3.59)	132 (3.74)	92 (2.55)	107 (2.83)	0.007

**Notes:** <sup>a</sup>CCI (Charlson comorbidity index); comorbidities included in the CCI, except COPD and AMI. Incidence per 100,000. Incidence was calculated using the Spanish National Statistics Institute census projections, adjusted by sex and age.<sup>21</sup>

**Abbreviations:** AMI, acute myocardial infarction; n, number of procedures; IHM, in-hospital mortality; LOS, length of stay; SD, standard deviation; IQR, interquartile range.

**Table 2** Multivariate analysis of the factors associated with in-hospital mortality after coronary revascularization procedures among patients with and without COPD in Spain, from 2001 to 2011

	In-hospital mortality (OR) <sup>a</sup> COPD		In-hospital mortality (OR) <sup>a</sup> No COPD		In-hospital mortality (OR) <sup>a</sup> All	
	PCI	CABG	PCI	CABG	PCI	CABG
Age (years)						
40–59	1	1	1	1	1	1
60–69	2.00 (1.46–2.73)	1.77 (1.21–2.60)	1.42 (1.32–1.53)	1.51 (1.37–1.67)	1.46 (1.36–1.57)	1.52 (1.39–1.68)
70–79	2.82 (2.10–3.78)	3.22 (2.25–4.60)	2.42 (2.26–2.59)	2.54 (2.32–2.79)	2.45 (2.30–2.61)	2.59 (2.37–2.83)
≥80	4.29 (3.14–5.84)	5.84 (3.76–9.06)	4.40 (4.08–4.73)	3.87 (3.42–4.39)	4.37 (4.07–4.70)	4.00 (3.55–4.51)
Sex						
Male	1	1	1	1	1	1
Female	0.87 (0.66–1.14)	1.32 (0.96–1.80)	1.21 (1.15–1.27)	1.39 (1.30–1.48)	1.19 (1.14–1.25)	1.38 (1.30–1.47)
Charlson index						
0	1	1	1	1	1	1
1–2	1.93 (1.65–2.26)	1.47 (1.21–1.78)	2.31 (2.20–2.42)	1.67 (1.57–1.78)	2.28 (2.18–2.39)	1.65 (1.56–1.75)
≥3	3.26 (2.54–4.18)	2.58 (1.78–3.72)	5.56 (5.11–6.05)	3.60 (3.17–4.08)	5.25 (4.85–5.70)	3.48 (3.08–3.92)
COPD						
No	NA	NA	NA	NA	1	1
Yes	NA	NA	NA	NA	1.11 (1.03–1.20)	1.06 (0.96–1.17)
Year	0.98 (0.96–1.00)	0.93 (0.90–0.96)	0.99 (0.99–1.01)	0.94 (0.93–0.95)	0.99 (0.99–1.00)	0.94 (0.93–0.95)

**Notes:** <sup>a</sup>Calculated using logistic regression models: odds ratio (OR). The logistic regression multivariate model was built using “death (yes/no)” as dependent variables and year, sex, Charlson comorbidity index, and age as independent variables.

**Abbreviations:** CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; IQR, interquartile range; NA, not available.

The IHM decreased significantly for those with and without COPD during the 11-year study period (10.59% in 2001 vs 5.99% in 2011 and 8.85% vs 5.92%, respectively) (Table 3).

After multivariate adjustment, the IHM among patients with COPD who underwent a CABG decreased significantly over the entire study period (OR 0.93; 95% CI 0.90–0.96). On the other hand, it did not change significantly according to sex. Finally, the IHM was significantly higher in patients with COPD with one or two (OR 1.47; 95% CI 1.21–1.78) and with three or more (OR 2.58; 95% CI 1.78–3.72) comorbidities. The probability of dying during hospitalization in patients who underwent a CABG did not change significantly in patients with and without COPD (Table 2).

## Discussion

In the present study, we found different trends over the last 11 years in the hospitalizations of subjects with and without COPD who underwent coronary revascularization procedures. Our results reveal that patients with COPD account for 7.17% of all revascularization procedures in Spain. We found an increase in PCI procedure rates from 2001 to 2011; and a decline in hospital admissions for CABG in patients with COPD from 2003 to 2011.

Although there are no previous studies that have assessed the trends in coronary revascularization procedure for COPD over time, our results are consistent with studies conducted in patients with other chronic diseases. So, for example, in

patients with diabetes, it has been observed that PCI rates have increased significantly due to advances in stent device technology and adjunctive pharmacology. By contrast, CABG rates have declined due to the fact that this procedure is more invasive than PCI procedures.<sup>24,25</sup>

In Spain, as other countries, the indications for PCI have become wider over the last years; more hospitals have included units where PCI procedures are conducted; PCI have improved in effectiveness in the last years and have very low morbidity, mortality, and cost compared with CABG. These tendencies have been found in studies conducted elsewhere.<sup>26–28</sup>

We found that IHM increased significantly over time among COPD patients after PCI. In addition, the IHM was significantly higher in those with one or more comorbidities associated with COPD. Data on patients with COPD undergoing PCI are limited. Previous studies that focused on mortality in patients undergoing PCI suggested worse prognosis in patients with COPD.<sup>12,13</sup> More recently, Konecny et al<sup>5</sup> have shown that there is a clearly increased mortality rate with each additional level of COPD severity; namely, patients with mild or moderate COPD did better than those with severe COPD who, in turn, did better than those with very severe COPD. Patients without COPD had better survival than those with any level of COPD. In another study in which it was assessed the incidence of COPD in patients with acute ST-segment elevation myocardial infarction undergoing primary PCI and the impact of COPD on the prognostic outcome of this patient population, it was

**Table 3** Characteristics and outcomes of hospital discharges after coronary artery bypass graft among patients with and without COPD in Spain, from 2001 to 2011

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	P-value
<b>No COPD</b>												
N	6,845	6,948	7,000	6,915	6,471	6,462	6,470	6,672	6,389	6,293	6,306	0.000
Incidence	34.5	34.61	34.15	33.1	30.37	29.75	29.29	29.72	28.04	27.32	27.08	
Age, mean (SD)	65.68 (9.42)	65.78 (9.32)	66.01 (9.32)	66.44 (9.41)	66.79 (9.26)	67.22 (9.49)	66.96 (9.65)	67.07 (9.62)	67.19 (9.72)	67.32 (9.9)	67.68 (9.7)	0.000
Male, n (%)	5,259 (76.83)	5,325 (76.64)	5,306 (75.8)	5,239 (75.76)	4,880 (75.41)	4,976 (77)	4,959 (76.65)	5,102 (76.65)	4,930 (77.16)	4,779 (75.94)	4,905 (77.78)	0.052
CCI 0-3 n (%)	3,949 (57.69)	3,848 (55.38)	3,612 (51.6)	3,504 (50.67)	3,080 (47.6)	2,929 (45.33)	3,002 (46.4)	2,963 (44.41)	2,716 (42.51)	2,727 (43.33)	2,713 (43.02)	0.000
CCI 1-2, n (%)	2,800 (40.91)	2,964 (42.66)	3,226 (46.09)	3,248 (46.97)	3,193 (49.34)	3,322 (51.41)	3,279 (50.68)	3,460 (51.86)	3,423 (53.58)	3,293 (52.33)	3,370 (53.44)	
CCI ≥3, n (%)	96 (1.4)	136 (1.96)	162 (2.31)	163 (2.36)	198 (3.06)	211 (3.27)	189 (2.92)	249 (3.73)	250 (3.91)	273 (4.34)	223 (3.54)	
LOS, median (IQR)	17 (16)	17 (16)	16 (16)	15 (14)	16 (16)	16 (14)	16 (15)	15 (14)	15 (13)	15 (12)	14 (14)	0.000
IHM, n (%)	606 (8.85)	581 (8.36)	520 (7.43)	496 (7.17)	478 (7.39)	465 (7.2)	452 (6.99)	472 (7.07)	383 (5.99)	395 (6.28)	373 (5.92)	0.000
<b>COPD</b>												
N	538	607	683	669	658	595	658	631	632	576	601	0.000
Incidence	2.69	3	3.32	3.18	3.06	2.72	2.96	2.8	2.77	2.5	2.58	
Age, mean (SD)	66.82 (8.34)	67.44 (8.59)	68.17 (8.38)	68.55 (8.08)	68.83 (8.5)	68.7 (8.31)	68.65 (8.21)	68.78 (8.54)	68.7 (8.49)	69.14 (8.56)	69.3 (8.45)	0.000
Male, n (%)	507 (94.24)	564 (92.92)	640 (93.7)	626 (93.57)	610 (92.71)	555 (93.28)	618 (93.28)	590 (93.5)	583 (92.25)	536 (93.06)	551 (91.68)	0.864
CCI 0-3 n (%)	296 (55.02)	300 (49.42)	302 (44.22)	298 (44.54)	279 (42.4)	241 (40.5)	281 (42.71)	230 (36.45)	217 (34.34)	211 (36.63)	211 (35.11)	0.000
CCI 1-2, n (%)	227 (42.19)	289 (47.61)	356 (52.12)	339 (50.67)	354 (53.8)	334 (56.13)	346 (52.58)	380 (60.22)	385 (60.92)	331 (57.47)	344 (57.24)	
CCI ≥3, n (%)	15 (2.79)	18 (2.97)	25 (3.66)	32 (4.78)	25 (3.8)	20 (3.36)	31 (4.71)	21 (3.33)	30 (4.75)	34 (5.9)	46 (7.65)	
LOS, median (IQR)	18 (19)	18 (18)	19 (18)	17 (18)	18 (18)	19 (18)	17 (17)	18 (16)	16 (16)	16 (15)	16 (16)	0.001
IHM, n (%)	57 (10.59)	51 (8.4)	64 (9.37)	45 (6.73)	48 (7.29)	49 (8.24)	54 (8.21)	53 (8.4)	38 (6.01)	36 (6.25)	36 (5.99)	0.056

**Notes:** CCI (Charlson comorbidity index); Comorbidities included in the CCI, except COPD and AMI. Incidence per 100,000. Incidence was calculated using the Spanish National Statistics Institute census projections, adjusted by sex and age.<sup>21</sup>

**Abbreviations:** AMI, acute myocardial infarction; n, number of procedures; IHM, in-hospital mortality; LOS, length of stay; SD, standard deviation; IQR, interquartile range.

demonstrated that COPD was not an independent predictor of short-term and medium-term mortality.<sup>29</sup> Although the inconsistent findings between this study and previous reports remain poorly explained, there are some reasons that may explain the discrepancy. First, the enrollment and exclusion criteria and the diagnosis of COPD may not be identical between the different studies. Second, primary PCI, which was not a criterion for study enrollment in the majority of the recent studies, was performed in all patients in the last study.<sup>29</sup> In any case, there are no previous studies that have evaluated the evolution of mortality in these patients over time.

Incomplete revascularization is the frequent final outcome in patients with multivessel coronary disease who undergo PCI. However, the IHM among patients with COPD who underwent a CABG decreased significantly over the entire study period. It did not change significantly according to sex. On the other hand, the IHM was significantly higher in patients with COPD with comorbidities. Leavit et al<sup>30</sup> also showed, to assess the long-term survival of patients with COPD undergoing CABG, that the presence of COPD and  $\geq 1$  other comorbidity significantly reduced the 10-year survival. In COPD patients with  $\geq 1$  other comorbidity, the 10-year survival was 30%, and the incidence rate of death was 9.4 deaths per 100 person years of follow-up.

The probability of dying during hospitalization in patients who underwent a CABG did not change significantly in patients with and without COPD in our study. There are conflicting reports on the impact of COPD on patient outcomes after CABG. Several studies have also demonstrated similar IHM in CABG patients with and without COPD.<sup>31–34</sup> Manganas et al<sup>34</sup> found no evidence of increased post-CABG mortality in patients with COPD, although these patients demonstrated an increased incidence of postoperative chest infections and atrial fibrillation, and required longer hospital stay. In a large retrospective analysis, Angouras et al<sup>35</sup> did not find any difference IHM and major morbidities between patients with and without COPD, although those with COPD had a longer hospital stay and a higher long-term mortality rate. By contrast, other studies have reported an increased risk for long-term mortality and lower survival in COPD patients.<sup>30,36,37</sup> So, Saleh et al<sup>38</sup> found, in a large retrospective study, that the severity of COPD proved to be a prognostic marker in patients undergoing CABG. More advanced stages of COPD, rather than mild or moderate forms, were found to be significantly associated with early mortality following CABG. To improve the outcomes, it has been suggested that off-pump coronary artery bypass grafting may be more suitable for patients with pulmonary diseases with a lower mortality and morbidity risk as compared with

conventional CABG. However, Almassi et al<sup>39</sup> did not find benefit to use an off-pump coronary artery bypass approach rather than conventional CABG in COPD patients.

In our investigation, the median LOS for PCI decreased from 9 days in 2001 to 6 days in 2011, among COPD patients, and from 6 to 5 days among non-COPD patients. With regard to CABG, the median was 18 days in 2001 and 16 days in 2011 for those with COPD, with equivalent figures of 17 and 14 days for those without COPD. Postoperative respiratory complications can increase hospital LOS as well as mid-term mortality of CABG patients with severe left ventricular dysfunction.<sup>40</sup> These, together with prolonged mechanical ventilation time, have been also identified as independent risk factors of postoperative acute renal failure requiring renal replacement therapy after cardiac surgery in patients with preoperatively normal renal functions, a complication that increases hospital LOS and IHM.<sup>41</sup>

In patients without COPD who had undergone either a PCI or a CABG, women had worse outcomes than men. However, we have not found differences by sex in patients with COPD. These results contrast with those obtained in other chronic diseases such as diabetes where it has been suggested that the worse effect of diabetes on outcomes in women might be related to the onset mechanism for cardiovascular disease, the success of the revascularization coronary procedure, and the higher burden of cardiovascular risk factors.<sup>42,43</sup>

We should recognize strength and limitations of the current study. The main strength lies in its large sample size, its 11-year follow-up period, and its standardized methodology maintained constant along the study period. Nevertheless, several limitations warrant consideration. First, a potential source of bias comes from the use of ICD-9-CM diagnosis codes for identifying patients hospitalized for COPD.<sup>44,45</sup> It might generate underdiagnosis of COPD, because all patients receiving PCI or CABG did not perform pulmonary function tests. However, the ICD-9-CM codes have been previously used for epidemiological investigations and proved to be a valid method to identify patients suffering from this disease.<sup>46,47</sup> In relation to CAD, we have not provided information of this diagnosis, such as ST-elevation myocardial infarction, non-ST-elevation acute coronary syndrome, or stable angina. By contrast, we have provided the entire CAD grouped to have enough statistical power. If we stratify CAD, we would lose power because some clinical categories would have a very small number of subjects. On the other hand, this study and its outcomes were limited to the variables coded which do not include relevant data such as the extent of the coronary disease, the severity of COPD, or the pharmacologic

treatment. In addition, the endpoint of this study is limited to short-term mortality and we cannot provide information of long-term mortality. Another limitation of this database is its anonymity (no identifying items such as clinical history number), which makes it impossible to detect whether the same patient was admitted more than once during the same year. In addition, patients who moved from one hospital to another would appear twice.

Nevertheless the administrative database used in our study was introduced in Spain in 1982, is a mandatory register, and its coverage is estimated to be greater than 95%.<sup>18</sup> Concerns have been raised about the accuracy of routinely collected datasets; however, these datasets are periodically audited. Consequently, the quality and validity of our dataset have been assessed and shown to be useful for health research.<sup>48</sup> Another limitation of our study is the missing causal relationship between IHM and CABG/PCI as patients admitted for cancer and non-cardiovascular were also included, the mortality of whom may not have been affected by the CABG/PCI.

## Conclusion

Our results show that the APC in PCI procedures increased over study period in COPD and non-COPD patients. The IHM among patients with COPD who underwent a PCI increased significantly. Other outcome such as LOS was worse among individuals with COPD than those without COPD for PCI although they improved over the entire study period for both groups. Higher comorbidity was associated with higher IHM in PCI procedures in both groups of patients. On the other hand, we found a decrease in the use of CABG procedures in patients with and without COPD. The IHM did not change according to the existence, or not, of COPD among patients who underwent a CABG. These findings emphasize the need for further improvement in the control of cardiovascular risk factors in people with COPD.

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## Author contributions

All authors contributed toward data analysis, drafting and critically revising the paper, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

## Disclosure

Dr Bueno reports having received consulting/speaking fees from Abbott, AstraZeneca, Bayer, BMS-Pfizer, Daiichi Sankyo, Eli Lilly, Ferrer, Menarini, Novartis, Sanofi, Servier, and research grants from AstraZeneca. The other authors report no conflicts of interest in this work.

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