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Tendencies and outcomes in endoscopic biliary sphincterotomies among people with or without type 2 diabetes mellitus in Spain, 2003-2013

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ABSTRACT

We aimed to compare incidence and outcomes for endoscopic biliary sphincterotomies in people with or without type 2 diabetes mellitus (T2DM) in Spain (2003-2013).

We collected all cases of endoscopic biliary sphincterotomies using national hospital discharge data and evaluated annual incidence rates stratified by T2DM status. We analyzed trends over time for in-hospital mortality (IHM) as the primary outcome and a composite of IHM or procedure-related complications (key secondary outcome). In multivariate analyses, we tested T2DM as an independent factor of IHM and IHM or complications.

We identified 126,885 endoscopic biliary sphincterotomies (23,002 [18.1%] in T2DM people). Crude incidence rates of endoscopic biliary sphincterotomies were > 3-fold higher in people with *vs* without T2DM ($85.5/10^5$ *vs* $26.9/10^5$ population, respectively). Annual incidence rates of endoscopic biliary sphincterotomies showed 11-year relative increments of 77.5% (from 60.0 to 106.5/105) in T2DM, and 53.7% (from 21.6 to 33.2/105) in non-T2DM people ($p < 0.001$). We found no significant changes in mortality trends over time for the populations with or without T2DM ($p = 0.15$ and $p = 0.21$, respectively). Rates of procedural pancreatitis decreased in people without T2DM ($p < 0.001$). In the multivariate analysis, older age, higher comorbidity and endoscopic biliary sphincterotomy during urgent admission were associated with a higher IHM. T2DM was associated with a lower IHM after an endoscopic biliary sphincterotomy (OR = 0.82 [0.74-0.92]). Time trend multivariate analyses 2003-2013 showed significant reductions in IHM over time only in people with T2DM (OR = 0.97 [0.94-1.00]).

Further studies are needed to confirm a lower IHM for endoscopic biliary sphincterotomies in people with T2DM.

Key words: Complications. Biliary tract disease. Mortality. Diabetes mellitus. Sphincterotomy.

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INTRODUCTION

Endoscopic biliary sphincterotomy is an effective procedure used to treat different pancreatobiliary medical conditions. It has therefore had a widespread acceptance for decades (1,2). On the one hand, it is possible that advancing technology and overall improved quality of medical care allow for better outcomes, but on the other hand, more aggressive approaches in the elderly and in those patients with higher numbers of medical coexisting conditions might confer a worse prognosis. Public reports of complications and mortality rates after endoscopic biliary sphincterotomies mainly belong to the last decades of the twentieth century (3-5). Recent literature on the topic mostly focuses on comparing the outcomes after endoscopic biliary dilation *vs* endoscopic biliary sphincterotomies alone (6-8), but in our own experience the numbers of patients undergoing one or another procedure are very dissimilar.

Type-2 diabetes (T2DM) is a prevalent chronic condition (9,10). To our knowledge, no recent reports compare rates of mortality and complications between people with or without diabetes. If we could detect that such a large population is differentially exposed to higher rates of procedure-related complications or mortality risk after endoscopic biliary sphincterotomies as compared to people without diabetes, this would add evidence to design specific strategies aimed to improve the outcomes in people with T2DM. Thus, our goal was to compare trends in incidence

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rates and outcomes like in-hospital mortality and other complications, for endoscopic biliary sphincterotomies in people with or without T2DM in Spain between 2003 and 2013 using national hospital discharge data.

METHODS

Participants

We conducted this cohort-based, retrospective, observational study using the Spanish National Hospital Database (MBDS, Minimum Basic Data Set). This database is managed by the Spanish Ministry of Health, Social Policy and Equality and compiles all the public and private hospital data, hence covering more than 95% of hospital discharges (11). The MBDS includes patient-related variables (sex, date of birth), date of admittance, urgent *vs* programmed admission, date of discharge, up to 14 discharge diagnoses, up to 20 procedures and whether the patient died during hospitalization. The Spanish Ministry of Health, Social Policy and Equality sets standards for registration and performs periodic audits. We analyzed the data between January 1st 2003 and December 31st 2013 (11-year time period).

We chose disease and procedure criteria according to the International Classification Diseases-Ninth Revision, Clinical Modification (ICD-9-CM codes) (12), which is used in the Spanish MBDS. We selected all admissions during which an endoscopic biliary sphincterotomy (papillotomy) was performed (code 51.85), identified based on any procedural field. We additionally registered whether endoscopic dilatation of the ampulla of Vater or the biliary tract (code 51.84), or endoscopic biliary stenting (code 51.87) were performed. We discarded cases with nontherapeutic procedures, namely diagnostic endoscopic retrograde cholangiographies for diagnostic purposes only (codes 51.10, 51.11 and 52.13).

We grouped discharge diabetes status as follows: people with no diabetes *vs* people with T2DM. We identified T2DM with the ICD-9-CM codes: 250.x0 and 250.x2. We excluded people with type 1 diabetes mellitus (ICD-9-MC codes: 250.x1; 250.x3), cases with a diagnosis of gallbladder or pancreas cancer (ICD-9-MC codes: 156.x and 157.x, respectively) and people younger than 18 years old. Clinical characteristics included information on overall comorbidity at the time of diagnosis based on the Charlson comorbidity index (CCI) (13,14). The index applies to 17 disease categories whose scores are totaled to obtain an overall score for each case. The index is subsequently categorized into three levels: 0, no disease; 1, one or two diseases; and 2, three or more than three diseases. We used 16 disease categories after excluding diabetes to calculate our modified CCI.

We considered other risk factors in the data analysis: obesity (ICD-9-MC codes: 278.0, 278.0x, 278.1, 278.8), and whether or not the procedure was performed during an urgent admission. The primary outcome was the proportion of participants who died during admission, defined as in-hospital mortality (IHM). The key secondary outcome was a composite of IHM and procedural-related complications, as defined by codes 997.4, 996.59 and 996.7. These complications included procedure-related cholangitis (code 576.1), acute pancreatitis (code 577.0), biliary perforation or fistula (codes 567.81/575.4/575.5/576.3/576.4) and gastrointestinal bleeding (codes 578.0/578.1/578.9/998.11/998.12).

Statistical methods

The incidence of endoscopic biliary sphincterotomies for the populations with and without T2DM per 100,000 inhabitants was estimated. The yearly age-, sex-specific incidence rates for diabetic patients were calculated dividing the number of cases per year, sex, and age group by the corresponding estimated number of people in that population group with diabetes according to data from the Spanish National Institute of Statistics, as reported on December 31st of each year (15). The estimated prevalence of diabetes for sex and age groups was obtained from data from the Spanish Di@bet.es Study and the National Health Surveys conducted in 2003/4, 2006/7, 2009/10 and 2011/12 (10,16). In a similar fashion, we also calculated the yearly age-, sex-specific incidence rates for non-T2DM patients dividing the number of cases per year, sex, and age group by the corresponding number of people in that population group without diabetes according to the same sources.

We obtained the values for the variables as proportions or rates, means with standard deviations or medians with interquartile ranges, as was the case for length of hospital stay (LOHS). Bivariate analyses of the variables according to the year were conducted using binary logistic regression (proportions), ANOVA (means) and Kruskall-Wallis test (medians) as appropriate. In order to test the time trend for IHM adjusted by potential confounding variables, we performed logistic regression analyses with mortality as a the primary binary outcome, and the composite of mortality and procedural complications as the key secondary binary outcome, entering age, gender, CCI, obesity, urgent admission procedure, additional biliary dilatation and year of discharge as independent variables in both models. Models for subjects with and without diabetes and for the entire population were generated in order to compare the IHM and the composite of IHM and procedural complications between those with and without the disease. Statistical analyses were performed using Stata version 10.1 (Stata, College Station, Texas, USA). Nominal statistical significance was set at $p < 0.05$ (2-tailed).

Ethical aspects

We maintained data confidentiality at all times according to Spanish legislation. Participants' identifiers had been deleted before the database was provided to the authors in order to maintain people anonymity. Given the anonymous and mandatory nature of the dataset, it was deemed not necessary to obtain informed consent.

RESULTS

The total number of people having an endoscopic biliary sphincterotomy in the entire 11-year period was 126,885. Among them, 23,002 (18.1%) had T2DM.

Incidence rates for endoscopic biliary sphincterotomies in people with and without T2DM

There was an overall increase in endoscopic biliary sphincterotomies over time (Table I). The crude incidence

of endoscopic biliary sphincterotomies was > 3-fold higher among T2DM people than among non-T2DM people for the full 11-year period (85.5 *vs* 26.9 cases/10^5 population). Annual incidence rates of endoscopic biliary sphincterotomies increased during the 11-year period: crude incidence rates raised from 60.0 to 106.5 cases/10^5 total population, a 77.5% 11-year relative increment, in people with T2DM and from 21.6 to 33.2 cases/10^5 total population, a 53.7% 11-year relative increment, in people without T2DM (all p values < 0.001; calculated from data shown in table I).

Characteristics of the patients undergoing endoscopic biliary sphincterotomies

People without T2DM who had endoscopic biliary sphincterotomies were progressively older (p = 0.005), but people with T2DM were not (p = 0.06; table I). People with T2DM were older than people without T2DM (mean, 75.1 ± 10.5 *vs* 69.1 ± 16.9 years old). The number of coexisting medical conditions increased over time (p < 0.001). Obesity was more prevalent among cases with T2DM (7.4 *vs* 3.7%). Over time, there was an overall trend to perform a lower percentage of procedures during urgent medical admissions. We found increasing numbers of biliary stent insertions and biliary dilatations (all p values < 0.001). LOHS significantly decreased over time for the populations with and without T2DM (p < 0.001).

Outcomes: in-hospital mortality and procedural complications

Crude mortality rates did not differ among people with and without T2DM (1.8% and 1.7%, respectively; table I). Moreover, we found no significant changes in mortality trends over time for any of both populations. Crude incidence rates for procedural pancreatitis were lower in people with T2DM than in people without T2DM (15.9% *vs* 18.3%, respectively). Over time, we found decreasing numbers of procedural pancreatitis, but this trend reached statistical significance only for people without T2DM. Procedural gastrointestinal bleeding increased over time only in people without T2DM (p < 0.001).

Factors associated with in-hospital mortality (primary outcome)

Older age, higher comorbidity and having an endoscopic biliary sphincterotomy during an urgent admission were associated with a higher IHM (Table II). T2DM was associated with a lower IHM after an endoscopic biliary sphincterotomy (odds ratio [OR] = 0.82 [0.74-0.92]). Time trend analyses 2003-2013 showed significant reductions in IHM over time only in people with T2DM (OR = 0.97 [0.94-1.00]).

Factors associated with in-hospital mortality or procedural complications (key secondary outcome)

Female sex, higher comorbidity, obesity and having an endoscopic biliary sphincterotomy during an urgent admission were associated with higher rates of mortality or combined procedural complications, whereas older age and undergoing biliary dilatation were associated with lower rates (Table III). T2DM was associated with a lower risk of IHM or procedural complications combined after an endoscopic biliary sphincterotomy (OR = 0.85 [0.82-0.88]). The time trend analyses 2003-2013 showed slight reductions in IHM or procedural complications combined over time (OR = 0.99 [0.98-1.00]).

DISCUSSION

In this observational, retrospective, national-based study, we found increasing annual incidence rates of endoscopic biliary sphincterotomies, especially in people with T2DM. The crude annual incidence rates of endoscopic biliary sphincterotomies were higher among people with T2DM than in people without T2DM for all the years analyzed. We must underscore that these figures were referred to the census overall population; so, the apparently increasing rates may have partially obeyed to the higher prevalence of T2DM in the population. However, we believe that having had access to precise estimations of the prevalence rates of T2DM from the Spanish Di@bet.es Study and the National Health Surveys conducted in 2003/4, 2006/7, 2009/10 and 2011/12 give strength to our results (10,16). Gallbladder stones are indeed more prevalent in people with T2DM (17). Moreover, other studies have reported similar crude incidence rates (18).

Crude incidence rates for procedural pancreatitis were lower in people with T2DM than in people without T2DM, but we found a significant downward trend over time in people without T2DM only, perhaps due to a much larger denominator for this population. Older studies have reported lower rates of pancreatitis (19,20), but in our study we are possibly including many more cases of asymptomatic, biochemical pancreatitis that are diagnosed on the basis of routine determination of blood values of pancreatic enzymes after the procedure (21).

Crude mortality rates did not differ between people with or without T2DM. Mortality rates during admissions in which endoscopic biliary sphincterotomies were done remained under 2%; this figure is similar to other previously published results (22). Additionally, we found no significant changes in mortality trends over time for any of both populations, which could be influenced by the low number of fatalities.

In the multivariate analyses, T2DM was associated with an 18% lower IHM after an endoscopic biliary sphincterotomy. The time trend analyses 2003-2013 showed sig-

Table I. Incidence, clinical characteristics and outcomes of patients with and without type 2 diabetes mellitus that underwent an endoscopic biliary sphincterotomy in Spain, 2003-2013

Biliary sphincterotomy	*2003*	*2004*	*2005*	*2006*	*2007*	*2008*	*2009*	*2010*	*2011*	*2012*	*2013*	*Total*
No diabetes mellitus												
N ([a]Incidence/10^5); $p < 0.001$	7,178 (21.6)	7,567 (22.8)	7,856 (23.0)	8,023 (22.8)	8,483 (24.2)	9,615 (27.1)	10,286 (28.6)	10,561 (29.4)	11,030 (30.8)	11,367 (31.7)	11,917 (33.2)	103,883 (26.9)
Age, mean ([b]SD); $p = 0.005$	68.7 (16.5)	68.7 (16.5)	69.0 (16.4)	68.9 (16.7)	69.2 (16.8)	68.8 (17.1)	69.3 (16.9)	69.5 (17.1)	69.1 (17.2)	69.2 (17.3)	69.5 (17.0)	69.1 (16.9)
Male, n (%); $p < 0.001$	3,116 (43.4)	3,252 (43.0)	3,368 (42.9)	3,531 (44.0)	3,771 (44.5)	4,299 (44.7)	4,638 (45.1)	4,862 (46.0)	5,035 (45.7)	5,231 (46.0)	5,562 (46.7)	46,665 (44.9)
[c]CCI = 0, n (%); $p < 0.001$	5,160 (71.9)	5,438 (71.9)	5,585 (71.1)	5,676 (70.8)	5,889 (69.4)	6,685 (69.5)	7,002 (68.1)	7,038 (66.6)	7,269 (65.9)	7,484 (65.8)	7,581 (63.6)	70,807 (68.2)
CCI = 1, n (%)	1,612 (22.5)	1,669 (22.1)	1,776 (22.6)	1,848 (23.0)	2,005 (23.6)	2,262 (23.5)	2,546 (24.8)	2,667 (25.3)	2,866 (26.0)	2,955 (26.0)	3,266 (27.4)	25,472 (24.5)
CCI ≥ 2, n (%)	406 (5.7)	460 (6.1)	495 (6.3)	499 (6.2)	589 (6.9)	668 (7.0)	738 (7.2)	856 (8.1)	895 (8.1)	928 (8.2)	1,070 (9.0)	7,604 (7.3)
Obesity, yes (%); $p < 0.001$	177 (2.5)	216 (2.9)	203 (2.6)	253 (3.2)	247 (2.9)	286 (3.0)	391 (3.8)	427 (4.0)	466 (4.2)	535 (4.7)	622 (5.2)	3,823 (3.7)
Urgent admission procedure, yes (%); $p < 0.001$	5,107 (71.2)	5,332 (70.5)	5,591 (71.2)	5,745 (71.6)	5,893 (69.5)	6,549 (68.1)	7,123 (69.3)	7,250 (68.7)	7,260 (65.8)	7,576 (66.7)	7,993 (67.1)	71,419 (68.8)
Biliary stent insertion, n (%); $p < 0.001$	520 (7.2)	677 (9.0)	793 (10.1)	949 (11.8)	1,012 (11.9)	1,298 (13.5)	1,398 (13.6)	1,567 (14.8)	1,632 (14.8)	1,756 (15.4)	1,909 (16.0)	13,511 (13.0)
Biliary dilatation, n (%); $p < 0.001$	50 (0.7)	60 (0.8)	81 (1.0)	127 (1.6)	148 (1.7)	196 (2.0)	259 (2.5)	303 (2.9)	360 (3.3)	405 (3.6)	436 (3.7)	2,425 (2.3)
Biliary fistula or perforation, n (%); $p = 0.144$	119 (1.7)	120 (1.6)	139 (1.8)	127 (1.6)	133 (1.6)	170 (1.8)	174 (1.7)	194 (1.8)	187 (1.7)	237 (2.1)	229 (1.9)	1,829 (1.8)
Cholangitis, n (%); $p = 0.540$	0 (0)	1 (0)	1 (0)	0 (0)	2 (0)	0 (0)	0 (0)	2 (0)	1 (0)	2 (0)	0 (0)	9 (0)
Pancreatitis, n (%); $p < 0.001$	1,499 (20.9)	1,492 (19.7)	1,518 (19.3)	1,484 (18.5)	1,520 (17.9)	1,704 (17.7)	1,812 (17.6)	1,942 (18.4)	1,925 (17.5)	1,983 (17.5)	2,172 (18.2)	1,9051 (18.3)
Gastrointestinal bleeding, n (%); $p < 0.001$	354 (4.9)	369 (4.9)	437 (5.6)	415 (5.2)	444 (5.2)	492 (5.1)	560 (5.4)	495 (4.7)	616 (5.6)	698 (6.1)	685 (5.8)	5,565 (5.4)
[d]LOHS, median ([e]IQR); $p < 0.001$	9 (12)	9 (12)	9 (12)	9 (12)	9 (12)	9 (12)	9 (12)	8 (11)	8 (11)	8 (10)	8 (10)	8 (12)
[f]IHM, n (%); $p = 0.213$	112 (1.6)	95 (1.3)	123 (1.6)	134 (1.7)	135 (1.6)	166 (1.7)	193 (1.9)	180 (1.7)	189 (1.7)	201 (1.8)	193 (1.6)	1,721 (1.7)
Type 2 diabetes mellitus												
N (incidence/10^5); $p < 0.001$	1,257 (60.0)	1,427 (68.2)	1,506 (68.5)	1,590 (69.0)	1,746 (75.7)	2,098 (87.8)	2,305 (93.1)	2,486 (100.4)	2,732 (95.6)	2,810 (98.3)	3,045 (106.5)	23,002 (85.5)
Age, mean (SD); $p = 0.061$	74.3 (10.5)	74.8 (10.0)	74.9 (10.6)	75.1 (10.3)	75.1 (10.1)	75.4 (10.6)	74.9 (10.8)	75.0 (10.6)	75.6 (10.3)	75.0 (10.7)	75.3 (10.7)	75.1 (10.5)
Male, n (%); $p < 0.001$	539 (42.9)	643 (45.1)	641 (42.6)	725 (45.6)	769 (44.0)	932 (44.4)	1,090 (47.3)	1,202 (48.4)	1,368 (50.1)	1,410 (50.2)	1,521 (50.0)	10,840 (47.1)

[a]Crude incidence per-estimated population; [b]SD: Standard deviation; [c]CCI: Modified Charlson Comorbidity Index excludes diabetes; [d]LOHS: Length of hospital stay.

(Continues in the next page)

Table I (Cont.). Incidence, clinical characteristics and outcomes of patients with and without type 2 diabetes mellitus that underwent an endoscopic biliary sphincterotomy in Spain, 2003-2013

Biliary sphincterotomy	*2003*	*2004*	*2005*	*2006*	*2007*	*2008*	*2009*	*2010*	*2011*	*2012*	*2013*	*Total*
Type 2 diabetes mellitus												
CCI = 0, n (%); p < 0.001	771 (61.3)	892 (62.5)	928 (61.6)	946 (59.5)	1,056 (60.5)	1,260 (60.1)	1,297 (56.3)	1,369 (55.1)	1,454 (53.2)	1,513 (53.8)	1,638 (53.8)	13,124 (57.1)
CCI = 1, n (%)	370 (29.4)	385 (27.0)	448 (29.8)	461 (29.0)	497 (28.5)	614 (29.3)	725 (31.5)	797 (32.1)	913 (33.4)	918 (32.7)	1,006 (33.0)	7,134 (31.0)
CCI ≥ 2, n (%)	116 (9.2)	150 (10.5)	130 (8.7)	183 (11.5)	193 (11.1)	224 (10.7)	283 (12.3)	320 (12.9)	365 (13.4)	379 (13.5)	401 (13.2)	2,744 (11.9)
Obesity, yes (%); p < 0.001	88 (7)	79 (5.5)	83 (5.5)	82 (5.2)	108 (6.2)	140 (6.7)	161 (7.0)	192 (7.7)	219 (8.0)	249 (8.9)	296 (9.7)	1,697 (7.4)
Urgent admission procedure, yes (%); p < 0.001	966 (76.9)	1,091 (76.5)	1,122 (74.5)	1,202 (75.6)	1,287 (73.7)	1,538 (73.3)	1,684 (73.0)	1,773 (71.3)	1,893 (69.3)	1,970 (70.1)	2,121 (69.7)	16,647 (72.4)
Biliary stent insertion, n (%); p < 0.001	118 (9.4)	156 (10.9)	200 (13.3)	250 (15.7)	266 (15.2)	333 (15.9)	342 (14.8)	405 (16.3)	469 (17.2)	512 (18.2)	545 (17.9)	3,596 (15.6)
Biliary dilatation, n (%); p < 0.001	11 (0.9)	20 (1.4)	27 (1.8)	31 (2.0)	34 (2.0)	33 (1.6)	55 (2.4)	99 (4.0)	101 (3.7)	95 (3.4)	111 (3.7)	617 (2.7)
Biliary fistula or perforation, n (%); p = 0.451	13 (1.0)	26 (1.8)	25 (1.7)	21 (1.3)	33 (1.9)	39 (1.9)	37 (1.6)	37 (1.5)	37 (1.4)	41 (1.5)	60 (2.0)	369 (1.6)
Cholangitis, n (%); p = 0.708	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)	0 (0)	1 (0)
Pancreatitis, n (%); p = 0.071	237 (18.9)	255 (17.9)	246 (16.3)	259 (16.3)	273 (15.6)	336 (16.0)	352 (15.3)	401 (16.1)	425 (15.6)	423 (15.1)	457 (15.0)	3,664 (15.9)
Gastrointestinal bleeding, n (%); p = 0.361	63 (5.0)	70 (4.9)	70 (4.7)	85 (5.4)	74 (4.2)	109 (5.2)	126 (5.5)	116 (4.7)	126 (4.6)	166 (5.9)	164 (5.4)	1,169 (5.1)
LOHS, median (IQR); p < 0.001	11 (13)	10 (12)	10 (13)	10 (12)	10 (12)	10 (12)	10 (12)	9 (12)	8 (10)	9 (10)	8 (11)	9 (12)
IHM, n (%); p = 0.151	28 (2.2)	21 (1.5)	25 (1.7)	25 (1.6)	32 (1.8)	33 (1.6)	56 (2.4)	44 (1.8)	57 (2.1)	42 (1.5)	42 (1.4)	405 (1.8)

[a]Crude incidence per-estimated population; [b]SD: Standard deviation; [c]CCI: Modified Charlson Comorbidity Index excludes diabetes; [d]LOHS: Length of hospital stay.

Table II. Multivariate analysis of the factors potentially associated with in-hospital mortality for all the subjects hospitalized in Spain having an endoscopic biliary sphincterotomy (2003-2013), by type 2 diabetes mellitus status

		In-hospital mortality		
		Endoscopic biliary sphincterotomy		
		No diabetes, [a]OR (95% CI)	*Type 2 diabetes, OR (95% CI)*	*All, OR (95% CI)*
Age group (years)	< 60	[b]1	1	1
	60-69	1.73 (1.41-2.14)	1.02 (0.59-1.77)	1.65 (1.35-2.00)
	70-79	1.99 (1.66-2.38)	1.20 (0.73-1.95)	1.89 (1.60-2.24)
	≥ 80	2.77 (2.33-3.30)	1.86 (1.15-3.00)	2.71 (2.30-3.18)
Gender	Male	1	1	1
	Female	1.01 (0.91-1.11)	1.48 (1.20-1.82)	1.08 (0.99-1.18)
[c]Charlson Index	0	1	1	1
	1	3.33 (2.98-3.74)	2.75 (2.15-3.53)	3.23 (2.91-3.59)
	≥ 2	6.18 (5.40-7.06)	6.67 (5.13-8.67)	6.32 (5.61-7.12)
Obesity	No	1	1	1
	Yes	0.87 (0.67-1.13)	0.71 (0.47-1.09)	0.83 (0.66-1.04)
Urgent admission procedure	No	1	1	1
	Yes	2.19 (1.91-2.52)	3.16 (2.26-4.44)	2.33 (2.05-2.64)
Biliary dilatation	No	1	1	1
	Yes	1.03 (0.75-1.41)	1.24 (0.71-2.20)	1.07 (0.82-1.41)
Type 2 diabetes	No	[d]NA	NA	1
	Yes	NA	NA	0.82 (0.74-0.92)
Year		1.00 (0.98-1.02)	0.97 (0.94-1.00)	0.99 (0.98-1.01)

[a]OR (95% CI): Odds ratio (95% confidence interval). ORs were calculated with logistic regression models built using "death (yes/no)" as the dependent variable and the remaining variables as the independent ones. In the last model, T2DM status was included. [b]Odds ratio = 1 denotes reference group. [c]Modified Charlson Comorbidity Index excludes diabetes. [d]NA: Not applicable because the variable has been excluded from the model during the regression steps for this particular subgroup.

nificant reductions in IHM over time only in people with T2DM, yet slight reductions in IHM or procedural complications combined in the population overall. We have to be cautious about the finding of a lower mortality risk for people with T2DM, as the data was collected retrospectively and from a registry database. However, in order to avoid getting biased results, we tested the hypotheses in inclusive regression models to account for potential confounding factors, although we are aware that residual confounding due to allocation bias could be playing some role. The behavior of patients with T2DM undergoing these procedures could actually be different in case late infectious complications occurred, in terms of tolerance to oxidant stress, the probability of developing acute lung injury or antibody responses or other immunologic functions (23,24). We admit that it is merely speculative, but an interaction effect between obesity and T2DM could not be fully discarded: obesity was more frequently coded in the T2DM population. The better outcomes associated with obesity have been described as the "obesity paradox" by others (25). Finally, we had no information about the exact time when sphincterotomies were done for the urgently admitted patients, which might have confounded results as well.

As a limitation, for some variables we had to rely exclusively on the information the physician included in the discharge report. Under or over-report of different conditions is possible for some subgroups of patients. However, as opposed to diagnoses issues, we believe that infra-coding for procedures like endoscopic biliary sphincterotomy is unlikely, especially because in almost one third of the cases the procedure was performed during a non-urgent admission, probably specifically programmed with that aim.

Unfortunately, in Spain a validation study to assess the rate of unreported diagnosis of diabetes in administrative databases has not been conducted so far. However, Leong A et al. recently concluded that a commonly-used administrative database definition for diabetes had a pooled sensitivity of 82.3% (95% CI 75.8, 87.4) and specificity of 97.9% (95% CI 96.5, 98.8%), based on the findings of six studies with complete data available (26). While this definition appears to miss approximately one fifth of cases with diabetes and wrongly classifies 2.1% of non-cases in the population as diabetes cases, it

Table III. Multivariate analysis of the factors potentially associated with the composite of in-hospital mortality and procedural complications for all the subjects hospitalized in Spain having an endoscopic biliary sphincterotomy (2003-2013), by type 2 diabetes mellitus status

		In-hospital mortality, biliary perforation, biliary fistula, acute cholangitis, acute pancreatitis or gastrointestinal bleeding		
		Endoscopic biliary sphincterotomy		
		No diabetes, [a]OR (95% CI)	*Type 2 diabetes, OR (95% CI)*	*All, OR (95% CI)*
Age group (years)	< 60	[b]1	1	1
	60-69	0.98 (0.94-1.04)	1.02 (0.89-1.16)	0.99 (0.95-1.03)
	70-79	0.87 (0.84-0.91)	0.95 (0.85-1.07)	0.89 (0.86-0.92)
	≥ 80	0.78 (0.76-0.82)	0.81 (0.71-0.91)	0.79 (0.76-0.82)
Gender	Male	1	1	1
	Female	1.17 (1.13-1.20)	1.21 (1.14-1.29)	1.17 (1.14-1.21)
[c]Charlson Index	0	1	1	1
	1	1.14 (1.10-1.18)	1.08 (1.00-1.15)	1.13 (1.09-1.16)
	≥ 2	1.29 (1.22-1.37)	1.19 (1.07-1.31)	1.27 (1.21-1.33)
Obesity	No	1	1	1
	Yes	1.12 (1.04-1.20)	1.20 (1.07-1.35)	1.14 (1.07-1.21)
Urgent admission procedure	No	1	1	1
	Yes	2.49 (2.40-2.58)	2.60 (2.39-2.82)	2.51 (2.43-2.59)
Biliary dilatation	No	1	1	1
	Yes	0.82 (0.75-0.91)	0.78 (0.64-0.97)	0.82 (0.75-0.89)
Type 2 diabetes	No	[d]NA	NA	1
	Yes	NA	NA	0.85 (0.82-0.88)
Year		0.99 (0.98-1.00)	0.99 (0.98-1.00)	0.99 (0.98-1.00)

[a]OR (95% CI): Odds ratio (95% confidence interval). ORs were calculated with logistic regression models built using "death or complications (yes/no)" as the dependent variable and the remaining variables as the independent ones. In the last model, T2DM status was included. [b]Odds ratio = 1 denotes reference group. [c]Modified Charlson Comorbidity Index excludes diabetes. [d]NA: Not applicable because the variable has been excluded from the model during the regression steps for this particular subgroup.

is likely sufficiently sensitive for monitoring prevalence trends in the general population if its accuracy remains reasonably stable over time. We have no data about the duration of the disease or the specific antidiabetic treatments followed by the patients. Nevertheless, the quality and validity of our dataset has been assessed and shown to be useful for health research (27), even though some concerns have been raised about the accuracy of routinely collected datasets.

CONCLUSIONS

People with T2DM more frequently undergo endoscopic biliary sphincterotomies during hospital admissions than non-T2DM people. T2DM was associated with an 18% lower IHM after an endoscopic biliary sphincterotomy when accounting for additional potentially confounding factors. More studies are needed to confirm whether endoscopic biliary sphincterotomies are associated with a lower IHM in the population with T2DM and provide insight into the possible reasons for this finding.

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