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ORIGINAL ARTICLE

Risk of thromboembolic events in relation to the management of anticoagulant and antiagregant therapy in patients subjected to endoscopic retrograde cholangiopancreatography

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KEYWORDS
Endoscopic retrograde cholangiopancreatography;
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Thromboembolic event;
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Abstract
Background and objectives: The main clinical practice guidelines recommend adequate periprocedural withdrawal and reintroduction of antithrombotic drugs in case of invasive techniques. The main objective of this study was to assess whether in patients receiving anticoagulant or antiplatelet therapy, the suppression or reduction of the pharmacological dose for the performance of endoscopic retrograde cholangiopancreatography (ERCP) implies a greater risk of thromboembolic events.
Patients and methods: A prospective observational study was carried out, which included 644 ERCP performed with therapeutic intention during 2019 at the Reina Sofía University Hospital with follow-up during the 30 days after the endoscopic intervention.
Results: 6 patients presented a thromboembolic event, finding no differences between the incorrect withdrawal/reintroduction of antithrombotic treatment and a higher proportion of thromboembolic or hemorrhagic events after the procedure ($p > 0.05$). The incidence of thrombotic events was significantly higher in patients treated with heparin or apixaban ($p = 0.001$), as well as with a history of atrial fibrillation ($p = 0.05$), rheumatic valve disease ($p = 0.037$) and recurrent pulmonary embolism ($p = 0.035$), this being also an independent risk factor. Likewise, the incidence of hemorrhage in the 30 days postphincterotomy was significantly lower in those with implantation of a biliary prosthesis ($p = 0.04$).

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Conclusions: Inadequate periprocedural management of antithrombotic therapy is not associated with a significant increase in the incidence of thromboembolic events in the 30 days after ERCP. However, close follow-up and surveillance during the days after this is essential in those patients with a condition that significantly increases the risk of thrombosis.

PALABRAS CLAVE
Colangiopancreatografía retrógrada endoscópica;
Esfinterotomía;
Evento tromboembólico;
Anticoagulante;
Antiagregante

Riesgo de eventos tromboembólicos en función del manejo de la terapia anticoagulante y antiagregante en pacientes sometidos a colangiopancreatografía retrógrada endoscópica

Resumen
Antecedentes y objetivos: Las principales guías de práctica clínica recomiendan un adecuado manejo periprocedimiento de los fármacos antitrombóticos en caso de realización de técnicas invasivas. El principal objetivo de este estudio fue evaluar si existe mayor riesgo de eventos tromboembólicos por la supresión o disminución de la dosis de anticoagulantes o antiagregantes en pacientes sometidos a una colangiopancreatografía retrógrada endoscópica (CPRE).
Pacientes y métodos: Se realizó un estudio observacional prospectivo que incluyó 644 CPRE realizadas con intención terapéutica durante el año 2019 en el Hospital Universitario Reina Sofía con un seguimiento de 30 días posprocedimiento.
Resultados: 6 pacientes presentaron un evento tromboembólico, no hallando diferencias entre la incorrecta retirada/reintroducción del tratamiento antitrombótico y una mayor proporción de eventos tromboembólicos o hemorrágicos tras el procedimiento (p > 0,05). La incidencia de eventos trombóticos fue significativamente mayor en pacientes en tratamiento con heparina o apixaban (p = 0,001), así como con antecedente de fibrilación auricular (p = 0,05), valvulopatía reumática (p = 0,037) y tromboembolismo pulmonar recurrente (p = 0,035) siendo éste además factor de riesgo independiente. Asimismo, la incidencia de hemorragia en los 30 días posesfinterotomía fue significativamente menor en aquellos con implantación de prótesis biliar (p = 0,04).
Conclusiones: El inadecuado manejo periprocedimiento de la terapia antitrombótica no se asocia a un aumento significativo de la incidencia de eventos tromboembólicos en los 30 días posCPRE. No obstante, se aconseja seguir las recomendaciones para una adecuada suspensión/reintroducción de fármacos antitrombóticos, realizando una vigilancia y seguimiento estrechos tras el procedimiento en pacientes con factores que aumenten el riesgo trombótico.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a mixed endoscopic and radiological procedure, for diagnostic and, mainly, therapeutic purposes, to treat biliopancreatic obstructive pathologies[1]. Although its main complication is pancreatitis (1.3–7.2%), other adverse events have been described, such as bleeding (0.76–2.3%)[2–4].

It is common for many patients undergoing ERCP to take anticoagulant and antiplatelet drugs. The administration of these should be modified prior to the procedure, being resumed later, following the recommendations of the guidelines for action in the management of antithrombotic therapy.

This modification of the antithrombotic regimen is determined by the prothrombotic risk of the patient and by the bleeding risk of the technique performed. Inappropriate modification could lead to an increased risk of venous thromboembolic events (VTEs), increasing morbidity and mortality up to 30 days after ERCP.

High prothrombotic risk factors are considered to be the presence of a mechanical heart valve, atrial fibrillation (AF) and/or CHA_2DS_2-VASc score >7, cerebrovascular accident (CVA), transient ischaemic attack (TIA), recent venous thromboembolism (<3 months) or severe thrombophilia.

Regarding the bleeding risk in ERCP, it is considered high when sphincterotomy is performed, but not when sphincteroplasty or biliary or pancreatic stent placement is performed without sphincterotomy[5,6].

In summary, the recommendations for periprocedural modification of anticoagulant therapy are (Fig. 1):

- Regarding the *suspension* of treatment:
  - In patients treated with oral dicoumarin anticoagulants (acenocoumarol), it is recommended to maintain anticoagulation if the technique is considered to have low bleeding risk[7,8]. If the ERCP is of high bleeding risk, acenocoumarol should be discontinued 3–5 days before the procedure, performing bridging therapy

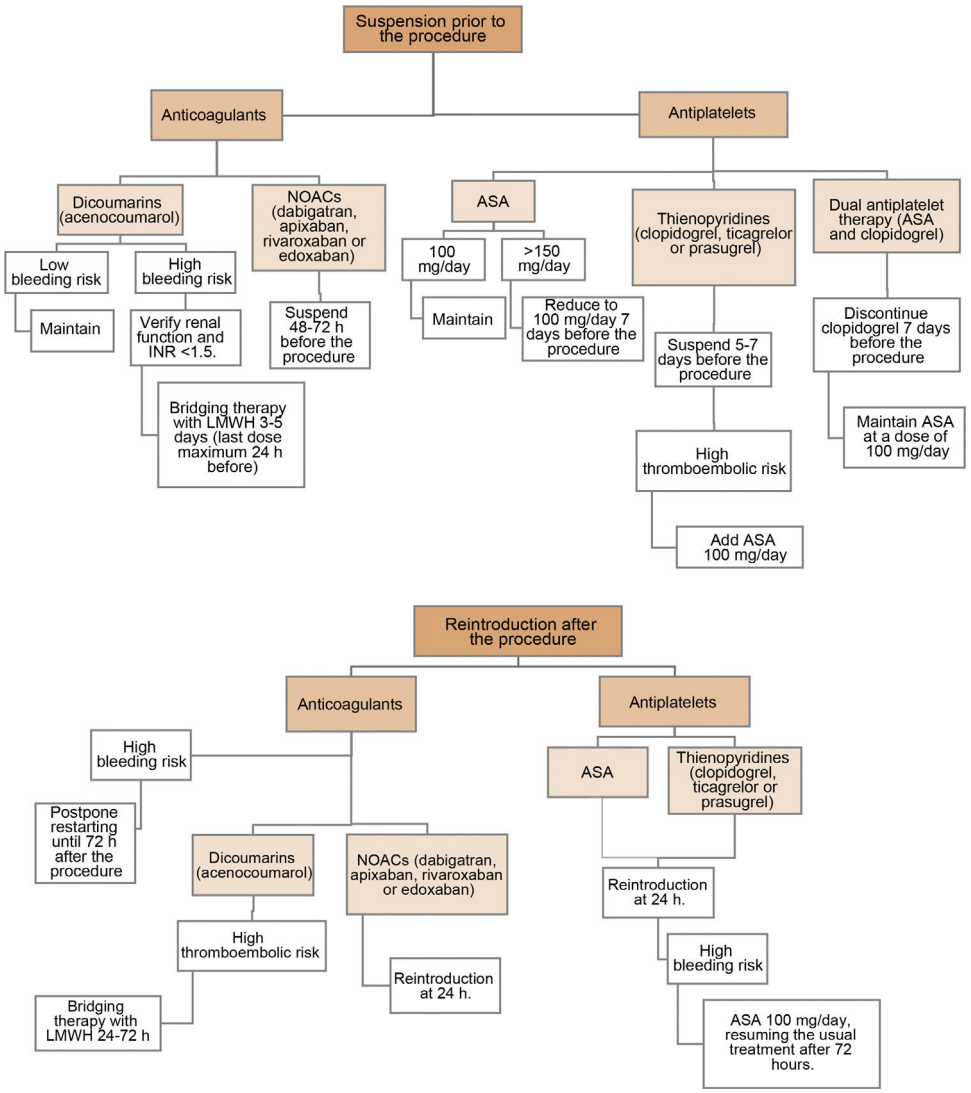

Figure 1 Therapeutic algorithms for periprocedural modification of antithrombotic therapy in ERCP.

with low molecular weight heparin (LMWH) at therapeutic doses, administering the last dose a maximum of 24 h before the ERCP, assessing the patient's renal function and previously verifying that the INR is less than 1.5[9].

- In relation to novel oral anticoagulants (NOACs) — dabigatran, apixaban, rivaroxaban or edoxaban, it is recommended to suspend them 48—72 h prior to the procedure depending on the bleeding risk and renal function[10,11]. The regimen of bridging therapy with LMWH could be considered only in cases of high thrombotic risk.

- The *reintroduction* of anticoagulant treatment should generally be performed 24 h after the procedure. If treatment is with dicoumarin, bridging therapy with LMWH is recommended for 24—72 h if the thromboembolic risk is high. Likewise, only when there is a high risk of bleeding should the reintroduction of treatment be postponed until 72 h after the procedure[12].
- Regarding *antiplatelet* therapy, the recommended suspension schedule is:
  - Acetylsalicylic acid (ASA) at a dose of 100 mg/day should not be changed. In the case of a dose greater than 150 mg/day, it should be reduced to 100 mg/day seven days before ERCP.
  - Treatment with thienopyridines should be discontinued for 5–7 days prior to the procedure, depending on previous treatment with clopidogrel/ticagrelor or prasugrel. In cases with a high risk of thrombosis, it is advisable to add ASA 100 mg/day. In a context of dual antiplatelet therapy, it is preferable to suspend treatment with thienopyridines during the seven days prior to the examination, maintaining ASA 100 mg/day[13–15].
- *Antiplatelet therapy should be restarted* after 24 h with ASA 100 mg/day in the case of high bleeding risk, resuming the usual treatment after 72 h[16].

The main objective of this study was to assess whether, in patients receiving anticoagulant or antiplatelet therapy, the suppression or reduction of the pharmacological dose in order to perform ERCP entails an increased risk of VTE in the first 30 days after the procedure.

The secondary objectives established were the following:

- Carry out a descriptive analysis of the patients who undergo ERCP in our centre: epidemiological variables, personal history, antithrombotic drugs and ERCP characteristics.
- Analyse the variables associated with the appearance of thromboembolic events in the 30 days after ERCP.
- Identify the variables associated with the occurrence of post-procedure bleeding events.
- Compare the mortality 30 days after ERCP in the different groups.

Patients and methods

Patients

A prospective and open observational study was carried out in the Department of Digestive Disorders of the Hospital Universitario Reina Sofía (HURS) [Reina Sofía University Hospital] in Córdoba, Spain. A total of 644 ERCP procedures, in 544 patients, with therapeutic intent performed in the period between 1 January and 31 December 2019 were included.

Variables

The impact of adequate management or not of antithrombotic therapy in the periprocedural period was assessed by means of the *main study variable*: the appearance of VTE in the first 30 days after ERCP in the group of patients taking antithrombotic treatment previously and in the group of patients not receiving this therapy. For the purpose of the study, pathologies such as deep vein thrombosis (DVT), pulmonary thromboembolism (PTE) or thrombosis of the splanchnic region, diagnosed by ultrasound or computed tomography (CT), were grouped within the concept V̈TE.̈

The following were collected as *secondary variables*:

- *Quantitative*. Demographic data, analytical data: blood count and coagulation.
- *Qualitative*. Ischaemic heart disease, revascularisation, cerebrovascular event, antiplatelet therapy, anticoagulant therapy, arterial hypertension, diabetes mellitus, AF, DVT, PTE, valve disease, chronic kidney disease, heart failure, neoplasia, thrombophilia, appropriate therapy modification, death in the 30 days after ERCP, indication for ERCP, CHA_2DS_2-VASc, type of admission, and data related to the endoscopic technique.

Inclusion and exclusion criteria

This study included patients older than 18 years who underwent urgent or scheduled ERCP at HURS who adequately completed the ERCP informed consent process.

Patients who died within 30 days after ERCP due to non-thromboembolic causes, who were unable to undergo ERCP due to particular conditions (previous surgery or advanced dementia), those with unsuccessful ERCP (cannulation not possible, poor tolerance, inability to finish), and pregnant women, were excluded.

Sample size

For the sample size, the sample size calculator software GRANMO v.7.12.April 2012 was used.

Accepting an alpha risk of 0.05 and a beta risk of 0.2 in a bilateral contrast, 3973 patients on antithrombotic drugs and 3973 patients without antithrombotic treatment were needed to detect a minimum relative risk of 3.5817, if the rate of patients in the group without treatment was 0.00151[18]. A loss to follow-up rate of 10% was estimated. The Poisson approximation was used.

Given the large sample size required and with the application of the inclusion criteria, a cohort of 644 procedures was formed.

Statistical study

A descriptive analysis of the variables was performed, calculating absolute and relative frequencies for the qualitative variables, as well as the arithmetic mean and standard deviation for the quantitative variables. The 95% confidence interval (95% CI) of security was estimated.

For the bivariate analysis of the quantitative variables, the Student's *t*-test for independent data and the analysis of variance of repeated measures were used. For qualitative variables, the chi-square (χ^2) test or Fisher's test, depending on the expected frequencies, was used.

Univariate logistic and multivariate regression analyses were performed to relate the VTE variable with certain clinical covariates.

All the contrasts were bilateral, considering those where p was <0.05 to be significant.

The data was collected in Microsoft Access and processed and analysed in the statistical program SPSS v.17.

Results

Patient characteristics

The study was an observational study with prospective follow-up of 644 ERCP procedures performed on a total of 544 patients, of whom 51.6% were male, with a mean age of 72 (±15.1) years. The main patient characteristics are listed in Table 1.

According to the aetiology of biliary obstruction that justified ERCP, in 472 patients (73.3%) the cause was identified as being lithiasic; in 98 (15.2%), malignant stricture, and in 74 (11.5%), benign stricture. It was observed that 281 (43.6%) of the patients required urgent hospital admission.

Regarding mortality, 31 patients (4.8%) died within 30 days after ERCP. In only one patient was the main cause the appearance of a VTE. In the other cases, death was a consequence of the pathology responsible for the biliary obstruction, generally neoplastic or severe cholangitis with multiple organ dysfunction. We did not identify any case of death due to a complication directly derived from the endoscopic procedure.

Table 1 Baseline patient characteristics ($n = 644$).

Cohort characteristics	*n* (%)
Parentage details	
Gender (male)	332 (51.6%)
Age (years)	72 ± 15.12
Personal history	
Arterial hypertension	418 (64.9%)
Diabetes mellitus	170 (26.4%)
Heart failure	46 (7.1%)
LVEF ≥30%	628 (97.5%)
Stroke/TIA	57 (8.9%)
Peripheral arterial embolism	5 (0.8%)
Ischaemic heart disease	58 (9%)
Atrial fibrillation	100 (15.5%)
CHA_2DS_2-VASc score	2.58 ± 1.73
Chronic kidney failure	46 (7.1%)
Deep vein thrombosis	18 (2.8%)
Pulmonary thromboembolism	18 (2.8%)
Neoplasm	5 (0.8%)
Thrombophilia	5 (0.8%)
Rheumatic valve disease	13 (2%)
Metallic valve	5 (0.8%)
Aortic valve disease	5 (0.8%)
Mitral valve disease	3 (0.5%)
ERCP data	
Emergency admission	281 (43.6%)
Coagulation correction	52 (8.1%)
Platelet correction	8 (1.2%)
Haemoglobin correction	4 (0.6%)
Sphincterotomy	462 (71.7%)
Sphincteroplasty	95 (14.8%)
Lithiasic aetiology	472 (73.3%)
ERCP repeated during same admission	39 (6.1%)
Post-ERCP bleeding	63 (9.8%)
Post-ERCP pancreatitis	22 (3.4%)
Perforation	6 (0.9%)
Fogarty balloon	563 (87.4%)
Dormia basket	329 (51.1%)
Plastic biliary prosthesis	177 (27.5%)
Metallic biliary prosthesis	20 (3.1%)
Anticoagulation - Antiplatelet	
Pre-ERCP anticoagulation	112 (17.4%)
Acenocoumarol	59 (52.7%)
Rivaroxaban	24 (21.4%)
Heparin	11 (9.8%)
Dabigatran	9 (8.1%)
Apixaban	6 (5.3%)
Edoxaban	3 (2.7%)
Pre-ERCP antiplatelet therapy	156 (24.2%)
ASA	142 (91%)
100 mg dose	102 (71.8%)
P2Y12 inhibitor	26 (16.7%)
Clopidogrel	25 (16%)
Prasugrel	1 (0.7%)
Dual antiplatelet therapy	13 (8.3%)

Thrombotic events

Of the total of 644 ERCPs performed, in six of them there was a VTE in the 30-day period after the procedure (Table 2). The 15 days immediately after ERCP were shown to be the period with the highest incidence of VTE, with a total of five cases (83.3%) (Fig. 2). In four of these patients, the absence of early ambulation and prolonged bed rest in the seven days after ERCP were identified as a common factor, either due to baseline limited mobility or in the context of a hospital admission longer than 24 h after ERCP. However, when analysing the association between the start of walking or physical activity from 24 h after ERCP and the appearance of VTE, no relationship was identified between the two ($p > 0.05$).

AF was related to a greater presence of VTE (50% vs 15.2%; χ^2: 10.91; $p = 0.05$), independently of thrombotic risk, quantified using the CHA_2DS_2-VASc score. Values of this score less than or greater than 1 were not associated with a lower or higher incidence of VTE ($p > 0.05$). However, an increased probability of VTE occurrence was observed in patients with higher thrombotic risk according to this score, although this relationship did not reach statistical significance.

Recurrent PTE was associated with a higher proportion of thrombotic events (16.7% vs 0.15%; χ^2: 52.34; $p < 0.001$), as was the presence of rheumatic valve disease (16.7% vs 0. 2%, χ^2: 6.58, $p = 0.037$) (Table 3). After applying a multivariate analysis, it was verified that the presence of recurrent PTE maintained statistical significance in the sense of independently increased thrombotic risk after ERCP ($p = 0.035$). In contrast, the use of metallic prostheses was not statistically associated with the appearance of VTE ($p > 0.05$).

The incidence of thrombosis was not related to the existence of biliary neoplasia ($p > 0.05$) or to other indications for the procedure, nor to the type of admission, whether urgent or scheduled.

Of the total of 22 cases (3.4%) of acute pancreatitis after ERCP, nine cases (1.4%) were mild, five cases (0.8%) were moderate, and eight cases (1.2%) were severe. The appearance of acute pancreatitis was not related to the subsequent development of VTE ($p > 0.05$).

Overall, the patients were on anticoagulant or antiplatelet therapy in a total of 264 procedures (41%). Based on the management of periprocedural antithrombotic therapy, recommended by the 2018 *Consensus Document of the Sociedad Española de Cardiología (SEC)* [Spanish Society of Cardiology][9], taken as a reference by our group, appropriate suspension of treatment was performed in 136 (51.5%) of these interventions. In 15 (5.7%) of the ERCP procedures, it is unknown if it was done appropriately since the suspension regimen was not recorded in the digital medical record. Regarding treatment reintroduction, in at least 171 cases (64.7%) it was resumed correctly. In 127 (48.1%) of the ERCPs, patients underwent bridging therapy before and after the procedure.

Table 2 Type of thromboembolic event that appeared in each of the 6 patients during the 30 days after ERCP was performed, as well as their comorbidities.

Patient	Gender	Age	Notable comorbidities/PH	Anticoagulation/ Antiplatelet	Indication for ERCP	Thromboembolic event <30 days post-ERCP
1	♂	82	AHT, AF, pacemaker, exertional angina, cholangitis, portal thrombosis	Apixaban. Appropriate suspension. Inappropriate reintroduction	Suspected malignant biliary stricture	AMI with sudden death. Death
2	♀	78	AHT, AF, biological aortic prosthesis	Heparin. Appropriate suspension and reintroduction	Inoperable distal cholangiocarcinoma	Acute ischaemic stroke
3	♀	84	AHT, DM2	No	Choledocholithiasis	Acute ischaemic stroke (TIA)
4	♂	66	AHT	No	Cholangitis due to choledocholithiasis	Thrombosis of an intrahepatic branch of the right portal vein
5	♂	84	AHT, DLP, CRF, AF, CH, SAH, several episodes of DVT/PTE	Rivaroxaban. Appropriate suspension and reintroduction	Pancreatic neoplasm (stage IV: liver metastasis)	DVT in left lower limb (left femoral vein)
6	♀	39	No PH of interest	No	Multiple choledocholithiasis (post-ERCP subcapsular haematoma)	DVT in left lower limb (left femoral vein)

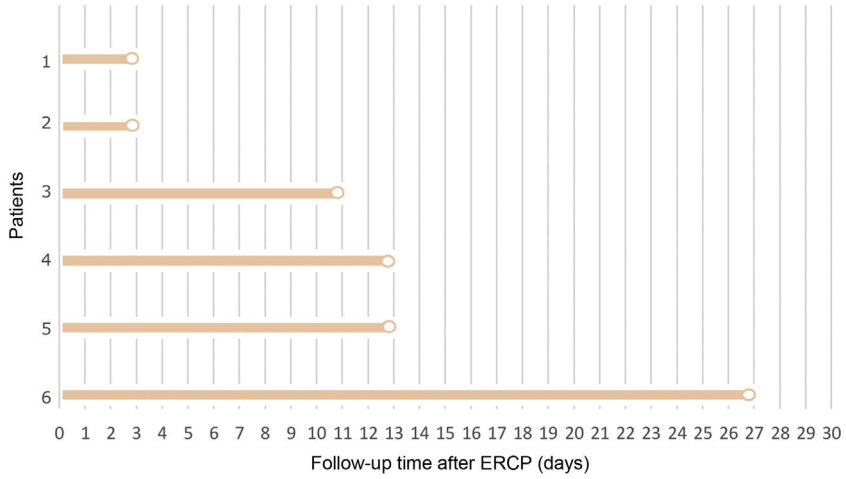

Figure 2 Representation of the follow-up time until the appearance of a thromboembolic event in the six cases detected in the total of the series studied. Most of the patients presented this event during the first 15 days of follow-up, while only one patient suffered it at a later time, on day +27.

No relationship was observed between inappropriate therapeutic management of periprocedural antiplatelet and/or anticoagulation therapy and the appearance of VTE after ERCP ($p > 0.05$).

Of the sample studied, in 112 interventions (17.4%) the patients were anticoagulated with different drugs before the ERCP was performed. The main cause of anticoagulation, present in 85 cases (13.7%), was AF. The type of anticoag-

ulant was associated with the presence of VTE in the first 30 days (χ^2: 81.19; $p < 0.001$), finding that the incidence of thrombosis cases was higher in patients taking apixaban and heparin compared to those being treated with other anticoagulants ($R > 1.96$). However, these results were not confirmed after performing a multivariate analysis.

In 156 procedures (24.2%), the patients were on antiplatelet drugs before the procedure. The most frequent indications for antiplatelet therapy were cerebrovascular disease in 31 cases (19.87%), acute coronary syndrome in 27 cases (17.3%), and stable coronary disease in 15 cases (9.61%).

The type of antiplatelet agent was not associated with the appearance of VTE ($p > 0.05$).

Table 3 Recognised risk factors for the occurrence of thromboembolic events in the 30-day follow-up after ERCP.

Variables	Logistic regression OR (95% CI)	Statistical significance (p)
AF	5.57 (1.14—27.23)	0.037
Recurrent PTE	64.10 (12.45—329.78)	0.001
Rheumatic valve disease	9.71 (1.21—77.36)	0.039

The results are obtained in univariate analysis of logistic regression. After applying a multivariate analysis, recurrent PTE maintained statistical significance ($p = 0.035$).

Bleeding events

Of the total of 63 procedures (9.8%) in which the patients presented bleeding after ERCP, 49 (8%) were mild cases that did not resolve spontaneously, requiring the performance of an intraprocedural endoscopic therapeutic technique, generally injection of adrenaline, without subsequent recurrence. Three cases (0.4%) were considered serious, due to the appearance of any of the following characteristics: heart rate greater than 100 beats per minute; systolic blood pressure less than 80 mmHg; decrease in haematocrit equal to or greater than 10% with respect to the baseline figure; requirement of more than two units of packed red blood cells in the interval of 24 h, or prolongation of hospitalisation due to bleeding for more than seven days. Bleeding was classified as moderate in 11 patients (1.8%), in the context of the appearance of gastrointestinal bleeding manifestations after ERCP with analytical repercussions less than that referred to as the severity criterion, need to increase hospitalisation time by less than seven days and without alteration of haemodynamic stability. After discharge, six patients (0.9%) had bleeding that, in all cases, was controlled after readmission to hospital and endoscopic intervention for therapeutic purposes.

Performing a biliary or pancreatic sphincterotomy was associated with a higher proportion of bleeding after ERCP during admission (92.1% vs 7.9%; χ^2: 14.11; $p < 0.001$), and was also considered a risk factor for bleeding. This association was maintained after the application of multivariate analysis ($p = 0.002$). The use of plastic biliary stents was associated with a lower proportion of biliary post-sphincterotomy bleeding during admission, both in univariate and multivariate analysis (14.37% vs 6.14%; χ^2: 5.37; $p = 0.02$), and also considered a protective factor (Table 4). Regarding the metallic biliary stent, its use was not associated with a lower incidence of bleeding after ERCP ($p > 0.05$). However, no cases of bleeding after the placement of a metallic prosthesis have been reported, and in only one case was it placed as an endoscopic treatment for bleeding associated with sphincterotomy.

Periprocedural therapeutic management of the antithrombotic therapy, in accordance or not with the modification recommendations used as a reference, was not associated with the proportion of patients who suffered bleeding during admission. Nor was it related to bridging therapy before and after the process, or to the appropriate reintroduction of treatment ($p > 0.05$). Similarly, it was not related to an INR greater than 1 prior to ERCP or to the requirement for coagulation correction ($p > 0.05$).

Discussion

This study evaluated the association of the management of antithrombotic therapy on the occurrence of thrombotic and bleeding events in patients undergoing ERCP in 2019. There are few studies on this topic in the international arena. The clinical management guidelines establish recommendations and decision algorithms in this context, based mainly on observational studies due to the virtual non-existence of randomised controlled clinical trials. In 2010, a first Spanish version of these guidelines was published[19], with new updates subsequently released, the most recent one being in 2019[20] which was the one used by our group as a reference.

Regarding the available studies[21,22], Venkatachalapathy et al.[17] conducted a case-control study on thromboembolic risk in patients undergoing endoscopic exploration within 90 days after ERCP. Each case was matched by sex and age with three controls who attended an outpatient appointment on the same date that they were diagnosed with VTE. Forty-five of 436 patients (10.3%) had undergone endoscopy in the VTE group, compared with 14 of 436 controls (3.2%) ($p < 0.001$). The odds ratio of developing a VTE after the endoscopic procedure was 3.58 (95% CI: 1.86–7.46) for cases compared to controls. When those with known VTE risk factors were excluded, no significant increased risk of VTE was found.

These results are consistent with our study, in which no relationship was observed between inappropriate periprocedural therapeutic management of antithrombotic drugs and a higher proportion of VTE. However, an association between certain pathologies and a higher incidence of VTE, such as recurrent PTE, has been identified. In this context, given the indication for anticoagulation, one must be particularly careful in follow-up, since stricter control is crucial in order to anticipate the appearance of thrombosis or make an early diagnosis of these cases.

The type of anticoagulant drug administered and the appearance of VTE do seem to be related, as can be deduced from the results obtained. In this regard, a higher incidence of thrombotic events was identified in the group of patients receiving anticoagulant treatment with apixaban and heparin in relation to the other anticoagulants. This finding is somewhat controversial, being in contrast to var-

Table 4 Recognised risk/protective factors for bleeding within 30 days of follow-up after ERCP.

Variables	Logistic regression OR (95% CI)	Statistical significance (p)
Sphincterotomy	4.56 (1.86—11.2)	0.002
Plastic biliary prosthesis	0.39 (0.17—0.88)	0.02

Sphincterotomy is considered to be a recognised risk factor for bleeding within 30 days of ERCP. Conversely, placement of a plastic biliary stent is associated with a lower risk of bleeding after endoscopic sphincterotomy in this series.

ious studies[9,23–25] that identify apixaban as being the NOAC with the most favourable safety profile.

Regarding the relationship between antiplatelet therapy and the occurrence of bleeding after ERCP, two retrospective studies[26,27] have examined this effect with inconclusive results. In our study, the association of antiplatelet management before and after ERCP and the proportion of patients who suffered bleeding after the procedure was not statistically conclusive, although, according to Nelson and Freeman[26], the bleeding risk was higher in patients in whom the ASA dose was not modified compared to the control group (6.5% vs 2.7%; $p = 0.04$), demonstrating that an adequate therapeutic management is preferable.

In relation to self-expanding metal stents, a meta-analysis[28] that included 338 patients from three different studies identified a lower risk of bleeding associated with their placement (OR = 9.70; 95% CI: 1.21–77.75; $p = 0.03$), based on the haemostatic effect of mechanical compression in persistent bleeding despite endoscopic sclerosing treatment[1,29,30]. In our series, this association cannot be demonstrated, probably due to the low number of metallic prostheses used (20) compared to the total sample. However, the association between the placement of a plastic biliary stent and the subsequent lower risk of post-sphincterotomy bleeding is striking. One of the hypotheses put forward by our group attributes this fact to the probable shorter length of the biliary sphincterotomy performed in those cases with an indication to ensure drainage of the bile duct by placing a plastic biliary stent, especially in biliary stricture of malignant (39.2%) or benign (18.2%) origin.

Detecting the different comorbidities of the patient, prior to performing ERCP, would make it possible to individualise each case and identify those, based on the findings of this study, that would increase the thrombotic risk in the 30 days post-intervention. Most of the VTEs identified were reported in the first 15 days of follow-up, so in this period efforts should be intensified to carry out active surveillance of the subgroup of patients with a higher risk of thrombotic complications. This attitude could allow its prevention or its early diagnosis, in order to carry out an earlier effective treatment that improves the prognosis.

Conclusions

- Incorrect therapeutic management of antithrombotic drugs is not associated in a statistically significant way with a higher rate of VTE or bleeding after ERCP in the series analysed. However, it seems prudent to carry out adequate management of these drugs based on clinical guidelines and follow their recommendations to prevent the potential appearance of VTE.
- The anticoagulant drug used is related to the presence of VTE, observing a higher thrombotic incidence in patients receiving treatment with apixaban and heparin, compared to other anticoagulants.
- Some patient comorbidities, such as AF, recurrent PTE and rheumatic valve disease, are associated with an increased risk of VTE. A history of recurrent PTE is also recognised as an independent risk factor.
- Performing a sphincterotomy during the procedure is associated with being an independent risk factor for bleeding after ERCP. The placement of a plastic biliary stent is associated with a lower incidence of post-sphincterotomy bleeding.

Ethical considerations

This study was governed by the Organic Law on Protection of Personal Data (LOPD 15/1999), the Declaration of Helsinki, Law 14/2007, of 3 July, on Biomedical Research and by good clinical practice guidelines.

The study was approved by the Ethics Committee of the Reina Sofía University Hospital in Cordoba (Spain).

Patient data was coded to maintain the anonymity of patients in the study and before third parties. Written informed consent was obtained for inclusion in the study.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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