Cost of incorrect application of antithrombotic prophylaxis prior to invasive procedures

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Abstract

Background We analyze the cost of an incorrect application, by the hematologist, of bridging anticoagulation in patients with low-risk atrial fibrillation (AF) needing interruption of treatment prior to a scheduled invasive procedure. Although not recommended, bridging therapy is widely used, resulting in avoidable costs and increased workload. Methods Observational retrospective study. We recorded demographic and clinical data including age, sex, type of procedure, use of bridging therapy with low molecular weight heparin (LMWH), and hemorrhagic complications within 30 days of acenocoumarol withdrawal. Results Acenocoumarol was stopped in 161 patients, 97 (60%) were male and 64 (40%) female. Average age was 76,11 ± 8,45 years. Procedures included: minor surgical intervention 58 (36%), colonoscopy 61 (38%), gastroscopy 11 (7%), breast biopsy 4 (2.5%), prostate biopsy 4 (2.5%), infiltration 5 (3%), and other 18 (11%). All patients received bridging anticoagulation with LMWH (40mg enoxaparin per day) 3 days before and 3 days after the procedure (6 doses). We used a total of 966 doses, at €4.5 per unit, resulted in €4,347 of total cost. No complications occurred in 156 patients (97%). Hemorrhage was observed in 5 cases: 1 major hemorrhage needing 6 days of hospital stay and transfusion, and 4 minor hemorrhages (2 patients needed Emergency attendance and 2 required hospital admission for 3 and 2 days, respectively). The cost of Emergency care was €237.36, and the cost of hospital stay was €6860.81 (€623.71 per day, for 11 days). The total cost of the incorrect application of the protocol was €11445.17. Conclusion Guidelines about bridging anticoagulation in low risk AF patients undergoing scheduled invasive procedures were not followed. This practice increments the complications and supposes an increase in costs besides to an inadequate use of the human resources.

Background

Anticoagulation therapy with oral vitamin K antagonists (VKA) is indicated for the prevention of thromboembolic events in patients presenting with atrial fibrillation (AF) (1).

Given that embolic and hemorrhagic risks vary among patients, risk stratification scores aimed to identify candidates for anticoagulation therapy have been proposed (2). The $CHADS_2$ score (Congestive heart failure, Hypertension, Age, Diabetes mellitus, Stroke) is currently considered a simple and reliable tool (3,4).

In Spain, the oral VKA acenocoumarol is preferentially used (5) mainly because its pharmacokinetics seems to be more predictable and allows easier postoperative management compared to warfarin (6).

However, anticoagulation needs to be stopped prior to any invasive procedure, and about 10% of these patients require treatment discontinuation every year (7).

In the perioperative management of these patients we need to consider the balance between the risk of thromboembolic events and the risk of postoperative hemorrhage.

Douketis et al (7) report that AF patients with a $CHADS_2$ score 0 to 2 present low-risk (5% annual risk of thromboembolism after discontinuation of oral anticoagulation treatment) and bridging anticoagulation is thus not recommended.

Scientific societies have provided Guidelines for the interruption and re-initiation of oral anticoagulation within the perioperative period (8). Depending on the individual risk, anticoagulation needs to be stopped 3 to 5 days before the procedure, and low molecular weight heparin (LMWH) is generally used as bridging anticoagulation.

In recent years, the number of patients under anticoagulation therapy has increased with accompanying raised costs, partly attributable to a higher demand of healthcare workers attending these patients.

Healthcare managers should be aware of the challenges posed by anticoagulation therapy in terms of adherence to established guidelines, which may help to better adjust the workload to the personnel (9).

The objective of this study is to analyze the complications and costs derived from the use of bridging anticoagulation among low-risk AF patients treated with acenocoumarol undergoing invasive procedures.

Methods

It is a 1-year observational retrospective study that included all patients under oral anticoagulation therapy and followed by hematologists belonging to the Anticoagulation Unit of the Hematology Department of the University Hospital in Burgos, in collaboration with General Practitioners from several Primary Care Centers within the province of Burgos, Spain.

We included AF patients scoring 0 to 2 in $CHADS_2$ that were treated with acenocoumarol and needed interruption of therapy because of a scheduled invasive procedure. Currently, the Anticoagulation Unit of

our center shares responsibility with Primary Care physicians and nurses regarding the performance of INR (International Normalized Ratio) tests and registration of relevant treatment commentaries in the electronic medical records of these patients.

Our electronic resource TAONET® allows the inclusion of any relevant information inside the “Comments” section, like the need for anticoagulant therapy discontinuation prior to surgery or other invasive procedure. Additionally, the hematologist can prescribe and register the dose of acenocoumarol, when to withdraw the treatment, and how to substitute it by another anticoagulant agent.

We searched for hemorrhagic complications registered in the patients’ clinical records, occurring within 30 days following the interruption of oral anticoagulant therapy due to an invasive procedure.

Patient demographic and clinical data, reasons for therapy discontinuation, type of invasive procedure, use of bridging anticoagulation, and type of hemorrhagic complications were recorded and analyzed. Laboratory data including hemoglobin values and number of red-cell concentrate blood units transfused were also recorded.

We analyzed each occurrence of hemorrhagic complication in terms of Emergency Unit assessment, need for hospital admission, need for transfusion, hospital stay attributable to the hemorrhagic complication, and final outcome.

A major hemorrhagic event was defined as: lethal hemorrhage, symptomatic hemorrhage in a critical organ (intracranial, intra-spinal, intra-ocular, retroperitoneal, intra-articular, pericardial, and intramuscular provoking a compartment syndrome), hemoglobin value decrease of more than 20 g/L or need for transfusion of 2 or more erythrocyte concentrates (10). Non-life-threatening hemorrhages (epistaxis, ecchymosis or hematuria) not needing transfusion were considered minor hemorrhagic events.

All clinical data was included in a Microsoft Office Excel 2010 data sheet and later exported and analyzed with the IBM SPSS v.19 software. A descriptive statistical analysis was performed which included costs of bridging therapy and hemorrhagic complications attributed to LMWH treatment.

Results

Within the study period, oral acenocoumarol was interrupted prior to a scheduled invasive procedure in 161 AF patients scoring 0 to 2 in $CHADS_2$. The average age was 76.1 years (standard deviation, 8.5 years); 64 (40%) were female (average age 77.0 ± 8, 09) and 97 were male (average age 75.5 ± 8,66). Table 1 shows the types of procedures performed.

No complications occurred in 156 patients (97%). Five patients (3%) presented hemorrhagic complications: 1 major hemorrhage and 4 minor (Table 2).

All patients recovered from the hemorrhagic complication without sequels. All patients received 40 mg per day subcutaneous enoxaparin for 6 days, acenocoumarol was stopped 3 days before the scheduled procedure, and re-initiated the same day of the procedure.

Bridging anticoagulation was begun 3 days prior to the procedure and kept 3 days afterwards, thus overlapping with acenocoumarol.

We used 966 doses of enoxaparin for the entire cohort, with a cost of €4.50 per dose, yielding a total cost of €4,347.

The cost of attendance at the Emergency Unit was €237.36 (€118.68 per patient) and the cost related to hospital admissions was €6860.81 (€623.71 per day, 11 days). Thus, we estimate the total cost of an incorrect application of antithrombotic prophylaxis in €11445.17 (Table 3).

Discussion

According to the recommendations provided by the American College of Chest Physicians (ACCP 2012), the thrombotic risk of patients previously under treatment with oral anticoagulants, needing treatment interruption because of an invasive procedure, is classified in three groups (7). Patients presenting with AF and a $CHADS_2$ score 0 to 2 (without a history of stroke or transient ischemic event) and patients with a history of venous thromboembolism at least 12 months before but no other risk factors, are considered as low-risk. However, evidence about the perioperative management of oral VKA is limited and stems from observational studies and recommendations provided by scientific societies (11). In fact, there seems to be a great discrepancy between hematologists and primary care physicians regarding the timing and appropriateness of bridging anticoagulation prior to invasive procedures.

Aiming to clarify this controversy, Douketis et al conducted the BRIDGE study, a double-blind, placebo-controlled randomized trial in which, following interruption of warfarin therapy prior to an invasive procedure, patients were randomized to receive either bridging anticoagulation with LMWH or placebo. The objective was to identify the need for bridging anticoagulation in AF patients undergoing invasive procedures. The primary endpoints of the study included the occurrence of arterial thromboembolism and major bleeding episodes within 30 days after the procedure.

The study included 1,884 patients, 950 received placebo and 934 received bridging anticoagulation. The incidence of thromboembolism was 0.4% and 0.3% in the placebo and treatment groups, respectively risk difference, 0.1 percentage points; 95% confidence interval [CI], -0.6 to 0.8; P=0.01 for noninferiority). However, the occurrence of a major hemorrhagic episode was 1.3% and 3.2% in the placebo and treatment groups, respectively (relative risk, 0.41; 95% CI, 0.20 to 0.78; P=0.005 for superiority). The authors concluded that patients not receiving bridging therapy had not only similar thromboembolic complications but fewer major bleeding episodes (12).

In our study, in which bridging anticoagulation was used in all patients, we observed an incidence rate of 0.62% and 2.4% of major and minor bleeding events, respectively.

Misuse of bridging anticoagulation by hematologists and primary care physicians is a matter of concern among scientific societies that have questioned its applicability. Moreover, the Canadian Hematology Society has suggested that bridging anticoagulation should not be offered to patients unless the risk of thrombosis clearly outweighs the risk of hemorrhage, given that the majority of patients will likely not benefit and might result in unwanted complications, increasing cost and avoidable work overload (14).

The study by Rios et al has shown that, in AF patients under VKA treatment, bridging anticoagulation prior to an invasive procedure was independently associated to a higher risk of all peri-procedure complications (15).

In Spain, the use of warfarin is marginal (5.2%) and we lack specific data regarding bridging anticoagulation. However, the management of non-valvular AF patients under acenocoumarol does not seem to be different from that of warfarin and data is generally extrapolated (16).

An increasing number of patients under VKA necessarily means more personnel working in Anticoagulation Units. In our area, management and control of oral anticoagulation therapy has been decentralized and shared with general practitioners using a telemedicine system.

This system enhances communication between hematologists and primary care physicians, reduces costs attributed to specialized consultations, and improves patient satisfaction (17,18). This decentralization process granted new competences to primary care physicians, who have demonstrated good quality management of this therapy (19,20). In our center, the electronic clinical record application allows to issue recommendation forms about withdrawal of anticoagulation, so the patient can undergo bridging anticoagulation as outpatient treatment, thus avoiding hospital stay, as also reported by Pappas et al (21). However, costs do increase whenever anticoagulation withdrawal and bridging therapy are unnecessarily offered to patients. Given that the cost of controlling oral anticoagulation therapy is lower in primary care than in specialized consultation (22), it seems reasonable that forms about anticoagulation withdrawal prior to invasive procedures should ideally be issued by primary care physicians, thus reducing specialist workload. We believe that primary care physicians should be involved in the implementation of oral anticoagulation guidelines. A close observation of such guidelines should result not only in fewer adverse effects and complications but also in reduced costs (23).

In our center, we have been using unnecessary bridging therapy with LMWH which resulted in cases of post-procedure hemorrhage. It increased costs because of Emergency attendance and hospital stay due to the management of hemorrhagic complications. In Europe, such discrepancy between Guidelines' recommendations and clinical practice has led to the design of electronic resources aimed to help in the correct application of protocols and to enhance adherence to guidelines (24).

Conclusions

An incorrect application of guidelines may increase the risk of hemorrhage, so efforts should be made to update local procedures according to international recommendations. Subsequently, the implementation of protocols based on such recommendations needs periodic analysis and follow up in order to ensure correct adherence and better control and rationalization of costs and personnel workload.

Abbreviations

VKA: Vitamin K antagonists

AF: Atrial fibrillation

LMWH: Low molecular weight heparin

CHADS2: Congestive heart failure, Hypertension, Age, Diabetes mellitus, Stroke

INR: International Normalized Ratio

CEIm: Drug Research Ethics Committee

Declarations

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The conduction of this study was approved by the local Ethics Committee (Ref. 1550 CEIm (Drug Research Ethics Committee of Burgos and Soria) being asked for informed consent to patients.

CONSENT FOR PUBLICATION

Not applicable

AVAILABILITY OF DATA AND MATERIAL

All data generated or analysed during this study are included in this published article [and its supplementary information files].

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHORS' CONTRIBUTIONS

M.V.C., I.M-S., J.A., C. G-D and B.C. have participated in the desing, data collection and analysis of the results. All authors read and approved the final manuscript

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Tables

Table 1: Invasive procedures

Procedure	Patients (n)	Patients (%)
	161	100 %
Minor surgical intervention	58	36
Colonoscopy	61	38
Gastroscopy	11	7
Prostate biopsy	4	2,5
Breast biopsy	4	2,5
Infiltration*	5	3
Other procedure**	18	11

*Knee, left saphenous neuropathy, internal anal sphincter, ankle and left femorocutaneous nerve.

**salivary gland biopsy, implant of intraocular corticoid-deliver device, cystoscopy (5 patients), biopsy of cavum, lung biopsy, thyroid nodule biopsy (3 patients), bronchoscopy, lumbar puncture, endometrial biopsy, pancreatic

mass biopsy, renal mass biopsy and sentinel node biopsy.

Table 2. Patients clinical features.

Variable	Female (n/%)	Male (n/%)	Global (n/%)
Sex	64 (40)	97 (60)	161 (100)
Age (years)	77. 03 (± 8, 09)	75.51 (± 8,66)	76,11 (± 8,45)
Invasive procedure			
Minor surgical intervention	23 (39.6)	35 (60.4)	58 (36)
Colonoscopy	24 (39.3)	37 (60.7)	61(38)
Gastroscopy	6 (54.5)	5 (45.5)	11(7)
Prostate biopsy		4 (2.5)	4 (2.5)
Breast biopsy	4 (2.5)		4 (2.5)
Infiltration	0	5 (3)	5 (3)
Other procedures	7 (38.8)	11 (61.2)	18 (11)
No complications	62 (38.5)	93 (58.5)	156 (96.9)
Complications:	2	3	5 (3.1)
Major hemorrhage	1 (0.6)	0	1 (0.6)
Minor hemorrhage	1 (0.6)	3 (1.8)	4 (2.4)

Table 3. Cost of incorrect application of antithrombotic prophylaxis.

	Use of LMWH and healthcare resources	Euro	Total (€)
Bridging anticoagulation (LMWH)	966 (6 doses/161 patients)	4.5 €/unit	4.347
Emergency Unit	2 patients	118.68 €/ patient	237.36
Hospital Admission	3 patients (11 days)	623.71 €/day	6860.81
Total cost			11445.17