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Vitamine K Antagonist and Colonoscopy: Proposal to Get out of a Dilemma

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Abstract: The management of anticoagulants in patients requiring digestive endoscopy, and particularly VKA, is not always easy. There is indeed often a discrepancy between the recommendations of leaned societies and practice in the conduct of VKA treatment before a screening colonoscopy. The recommendations take into account the haemorrhagic risk of the endoscopic procedure and the nature and importance of the thrombotic risk for which the patient is under treatment. A colonoscopy with or without a biopsy is considered a low bleeding risk procedure for which it is recommended not to stop VKA treatment. If the examination reveals a lesion, the resection gesture will be programmed in a second time after stopping the AVK which will possibly be substituted by a Low molecular weight heparin according to a very precise schedule. In practice, this recommendation is poorly followed, because the continuation of VKA does not allow to carry out simultaneously a diagnostic and therapeutic gesture and sometimes imposes an overload of work. Its systematic stopping is also not the right solution, because it often consists of unnecessary thromboembolic risk taking. To resolve this dilemma, we propose to decide whether to discontinue VKA treatment based on the level of risk of adenoma and colorectal cancer.

Keywords: Colonoscopy, VKA, Risk of Adenoma, Kaminski Score

1. Introduction

The management of patients on vitamine K antagonist (VKA) to benefit from digestive endoscopy has been the subject of recommendations in 2016 from the European Society of Gastroenterology (ESGE) that were updated in 2021 [1]. They fall within the overall framework of the management of drugs affecting hemostasis, antiplatelet drug, direct oral anticoagulants (DOA) and VKA.

By establishing a balance between the hemorragic risk linked to the endoscopic procedure and the thromboembolic risk linked to the patient, they draw guidelines for each class and subclass of antithrombotic. Unlike the relatively simple management of antiplatelet drug and DOA, the management of VKA is often faced with practical difficulties that we highlight in this paper.

2. ESGE Recommendations

The ESGE recommendations for management of patients on VKA in endoscopy, which are significantly close to the US recommendations, are summarized in table 1.

2.1. Risk of Bleeding from Endoscopic Procedures

Depending on the risk of bleeding, endoscopic procedures are divided into two groups: low risk and high risk. Acts with a low risk of bleeding are diagnostic procedures with or without biopsy sampling; biliary or pancreatic stenting; device-assisted enteroscopy without polypectomy; oesophageal, enteral or colonic stenting; and endoscopic ultrasound without sampling or interventional therapy. These procedures can be performed without interrupting the VKA provided that the absence of overdose is checked by an INR located in the therapeutic zone during the week preceding the examination. However, taking other drugs that interfere with haemostasis and the presence of increased haemorrhagic risk factors may lead to opting for prior discontinuation of treatment.

Endoscopic procedures that require resection, section, puncture or dilation are acts with a high risk of bleeding [2].

Above all, it is the colorectal endoscopic polypectomy, but also sphincterotomy; ampullectomy; mucosal resection or submucosal dissection; dilatation of strictures; therapy of varices; gastrostomy; ultrasound-guided sampling or with interventional therapy; and oesophageal or gastric radiofrequency ablation.

Stopping of VKA and normalization of the coagulation balance sheet are necessary before they are carried out. A last dose of the drug fixed at D-5 aims to obtain an INR of less than 1.5 the day before the procedure. If the INR remains above this value, 5 mg of vitamin K is administered orally and a second check is performed on the morning of the endoscopy.

The VKA is resumed the evening of the endoscopic procedure at the usual dose. A check of the INR level is carried out one week later.

Table 1. *Recommendations for management of patients on VKA in endoscopy.*

		Haemorrhagic Risk of the act	
		low risk of bleeding	***high risk of bleeding***
		Diagnostic procedures with or without biopsy sampling; biliary or pancreatic stenting; device-assisted enteroscopy without polypectomy; oesophageal, enteral or colonic stenting; endoscopic ultrasound without sampling or interventional therapy.	**polypectomy; sphincterotomy; ampullectomy; mucosal resection or submucosal dissection; dilatation of strictures; therapy of varices; gastrostomy; ultrasound-guided sampling or with interventional therapy; oesophageal or gastric radiofrequency ablation.**
The thromboembolic risk of patients on VKA	*Low thromboembolic risk* Xenograft heart valve, Atrial fibrillation without high-risk factors, thromboembolic episode more than three months old	*Continuation VKA* Verification of absence of overdose	*Stop VKA without relay* last dose at D-5 INR control < 1.5 at D0 Resume VKA on the evening D0
	High thromboembolic risk Metallic mitral or aortic prosthetic; prosthetic heart valve and AF; AF and mitral stenosis; AF with previous stroke or transient ischemic attack and 3 or more of congestive cardiac failure, hypertension, age >75 years or Diabetes mellitus	*Continuation VKA* Verification of absence of overdose	*Stop VKA with relay* last dose at D-5; relay LMWH (48h after last dose VKA to H-24 before acte); INR control < 1.5 at D0; Resume VKA and LMWH on the evening D0

2.2. The Thromboembolic Risk of Patients

The Thromboembolic Risk of Patients on VKA is Classified into Two Levels: Low and High. When thromboembolic risk is low (Xenograft heart valve, Atrial fibrillation without high-risk factors, thromboembolic episode more than three months old) interruption of VKA does not require therapeutic relay either before or after the procedure.

When thromboembolic risk is high (prosthetic metal heart valve in mitral or aortic position; prosthetic heart valve and atrial fibrillation; atrial fibrillation and mitral stenosis; atrial fibrillation with previous stroke or transient ischemic attackand 3 or more of congestive cardiac failure, hypertension, age >75 years or Diabetes mellitus) VKA must be substituted by a low molecular weight heparin (LMWH) according to a very specific schedule.

LMWH is started 48 hours after the last dose of fluindione. A final injection is prescribed 24h before the act. VKA at the usual dosage and LMWH are resumed within 24 hours of the endoscopic procedure. LMWH is continued until an INR is obtained in the therapeutic zone.

An adjustment of the treatment regimen is recommended for large polyp excision, because too early resumption of VKA is associated with a higher risk of late bleeding [3].

Given this risk of delayed bleeding when treatment is resumed, it is recommended to use all preventive measures that have proven their effectiveness (clips, releasable loop…) as much as possible and to immediately treat any bleeding, even minor, during the examination.

2.3. Recommendations That Are Poorly Followed

The various recommendations for perioperative management of antiplatelet drug and anticoagulant, which sometimes differ from one learned society to another, and the multitude of therapeutic regimens, confuse the decision-making process and weaken adherence to guidelines.

A prospective multicenter study collecting data from 1602 patients treated with anticoagulants (1004 on VKA and 598 on DOA) undergoing a total of 1874 digestive endoscopies, the majority of which were colonoscopies, showed that a heparin relay was prescribed in 85% of patients while 70.9% of them were classified at low thromboembolic risk. This prescription, which did not comply with the recommendations of the learned societies, was associated with an increased risk of bleeding during the procedure [4].

In addition, out of a series of 220 successive patients treated with antiplatelet or anticoagulant and programmed for digestive endoscopy, the drug management was not in accordance with the recommendations in more than half of the cases. Deviations were more frequent in low than high endoscopy, they particularly concerned the management of VKA and mainly consisted of an unmotivated discontinuation of treatment for a procedure with a low risk of bleeding [5].

Clinical practice guidelines exist to assist with VKA management decisions before an endoscopy. However, for many procedures, assumptions about the dangers of

periprocedural bleeding often lead to a recommendation for anticoagulation interruption, despite limited evidence of the incremental risks of bleeding while continuing anticoagulation therapy [6].

The discrepancies observed in the conduct of VKA treatment for a digestive endoscopy act particularly concern screening colonoscopies for which there is an unjustified tendency to stop anticoagulant treatment. This attitude reflects the concern to avoid the risk of bleeding above all.

However, if bleeding after a polypectomy is three to five times more frequent in patients on anticoagulants, it is in the vast majority of cases easily controllable without the need to resort to surgery [7]. Estimates of immediate and delayed postpolypectomy bleeding associated with VKA agents vary widely in the literature. With temporary interruption and prompt resumption of the drug, overall postpolypectomy bleeding is 1.8% to 7.0% [8]. The use a hemostatic clip after polypectomy in patients who require reinitiation of antithrombotic drugs within 24 hours is particulary effective in preventing a secondary bleeding [9].

The haemorrhagic risk cannot be placed at the same level of severity as the risk of thromboembolic accident. The latter, while rare, is more serious. Its mortality reaches 9.1% [4].

With regard to small polyps of less than 1 cm, bleeding is insignificant. Their cold loop resection could be performed without interrupting the VKA [10]. This approach is supported by the Japanese society of gastroenterological endoscopy which recommends the continuation of VKA for small polypectomies provided that the INR is less than 3 [11].

In order to avoid deviations from the recommendations, a specific application has been developed to assist in the decision in the management of anthithrombotics in digestive endoscopy [12]. This tool is freely accessible on the website www.endoaid.net.

However, the poor observance of the recommendations can also be explained by organizational reasons because, for a patient on VKA, they formulate the impossibility of performing a diagnostic and therapeutic endoscopic procedure at the same time.

To carry out a diagnostic colonoscopy in a patient under VKA, one is faced with a dilemma: either do the examination without stopping the anticoagulant then, if necessary, perform a resection after stopping treatment, or systematically stop the VKA in order to be able to carry out concurrently a diagnosis and possibly a therapeutic gesture [13].

Each of these two options has drawbacks. For the first, an overload of work and a repetition of general anesthesia in a fragile patient. For the second, a particularly demanding therapeutic protocol when it comes to performing heparin coverage and sometimes useless thromboembolic risk-taking for a colonoscopy which may turn out to be "white".

3. For Targeted Management of VKA

To solve this dilemma and limit these disadvantages, we propose that the management of VKA takes into account the level of risk of adenoma and colorectal cancer (CRC). The greater the likelihood of the presence of a lesion, the more the discontinuation of anticoagulant treatment is recommended. Table 2 summarizes this proposed support table 2.

Table 2. *Colonoscopy and management of VKA according to the level of risk of adenoma and CRC.*

		Risk level of adenoma and CRC		
		Medium	***High***	***Very high***
		Kaminski score < 5	**personal history of adenoma or CRC or chronic inflammatory bowel disease; Kaminski score ≥ 5**	**genetic predisposition; suggestive clinical signs**
Thromboembolic risk of patients on VKA	*Low*	*Continuation VKA*	*Stop VKA without relay*	*Stop VKA without relay*
	Higt	*Continuation VKA*	*Continuation VKA*	*Stop VKA with relay*

The risk level of adenoma and CRC is classified as medium, high and very high.

The risk is very high when the patient has a genetic predisposition such as familial adenomatous polyposis and Lynch syndrome or when he presents suggestive clinical signs (bleeding, change in intestinal transit, rectal syndrome and/or unexplained abdominal pain). In this category, we stop VKA treatment before a colonoscopy regardless of the level of thromboembolic risk.

The risk is high in patients with a personal history of adenoma or CRC, in patients with chronic inflammatory bowel disease evolving for more than 20 years, and in people whose Kaminski score is higher or equal to 5.

The Kaminski score makes it possible to quantify the level of risk of adenoma and CRC according to age, sex, BMI, smoking, number of family history, degree of kinship and index subject age [14].

With a score ≥ 5 the risk of adenoma and CRC is 10 to 20%. Among the many validated scores, the Kaminski score was retained by the French society of digestive endoscopy because it is easier to use and validated on a Caucasian population [15].

In this category of people at high risk of adenoma and CRC, we temporarily discontinue VKA treatment only for patients at low thromboembolic risk, therefore without the need for LMWH relay. On the other hand, anticoagulant treatment is continued when the thromboembolic risk is high, even if it means rescheduling a colonoscopy for excision in the isocoagulable zone according to the heparin relay protocol.

The risk of adenoma and CRC is medium if Kaminski's score is less than 5. In these cases, in accordance with the recommendations of the ESGE, we do not stop the VKA to perform a colonoscopy.

For a screening colonoscopy, the management of patients under VKA based on the basis of an assessment of the risk of

adenoma and CRC makes it possible to reconcile the two opposing attitudes: stopping or continuing treatment. This approach needs to be evaluated on a large scale.

4. Conclusion

The recommendations of the ESGE are clear: no stopping of VKA before a colonoscopy, with or without biopsies, because it is a gesture that is considered non-haemorrhagic, and stopping the anticoagulant before polypectomy because it is a potentially haemorrhagic act. The impossibility of being able to carry out a diagnostic and therapeutic act in one time leads to poor compliance with these recommendations, often with a systematic interruption of the anticoagulant, which is not without risk. In order to avoid as much as possible the rescheduling of examinations and unnecessary discontinuation of the VKA, we recommend a management approach targeted on groups of patients according to a stratification of the risk of adenoma and CRC. This approach needs to be evaluated on a large number of patients.

Conflict of Interest

All the authors do not have any possible conflicts of interest.

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