Corso di aggiornamento

Gestione dei farmaci antiaggreganti e anticoagulanti in specifici contesti clinici

Rimini 15 Marzo 2011

Gestione di terapia antiaggregante e anticoagulante nelle manovre endoscopiche

L. Solmi

Gastroenterologia Rimini

GUIDELINE

Position statement on routine laboratory testing before endoscopic procedures

RECOMMENDATIONS FOR ROUTINE PRE-ENDOSCOPY LABORATORY TESTING

There are no data to support routine preprocedure testing in patients undergoing elective GI endoscopic procedures. Extrapolation from surgical data and from other nonsurgical interventions leads to the conclusion that routine pre-endoscopy testing will not alter the risk of the planned procedure and that the absence of such testing will not adversely affect outcome. Detection of unsuspected but clinically important abnormalities on routine screening is rare, and there is no clear relationship between detection of abnormalities and procedure-related morbidity. Even for higher-risk endoscopic procedures such as endoscopic sphincterotomy, there is no evidence to support routine preprocedure testing. Endoscopists should pursue preprocedure testing selectively on the basis of the patient's medical history and physical examination and associated risk factors.

Recommendations

Routine testing to include coagulation studies, chest x-ray films, ECG, blood cross-matching, hemoglobin level, urinalysis, and chemistry tests are not recommended before endoscopy.

Consider testing based on the perceived level of risk as determined by the medical history and physical examination as follows.

ASGE Standards of Practice Committee Gastrointest Endosc; 2008

	Azienda Ospedaliera di Bologna Policlinico S. Orsola - Malpighi	Servizio di Gastroenterologia Primario: Prof. E. Roda Tel. 051-6362265-6362264 FAX 051-300700	I03/PS12 Rev. 0 Pag. 1/2

NORME DA SEGUIRE PER LA PREPARAZIONE ALLA COLONSCOPIA TOTALE E PARZIALE

Acquistare in farmacia una confezione di SELG-ESSE (soluzione elettrolitica per il lavaggio gastrointestinale) oppure di ISOCOLAN (soluzione isosmotica a preparazione estemporanea per il lavaggio dell'intestino). Seguire scrupolosamente le seguenti modalità di impiego (rivolgendosi al proprio medico curante per eventuali chiarimenti, valutando anche quanto indicato nel foglietto illustrativo allegato alla confezione).

Per ottenere una buona pulizia intestinale si consiglia di assumere 4 litri di soluzione

DIETA

Evitare di ingerire cibi solidi ma prima (3-4 ore) ma durante l'assunzione della soluzione, sia nell'intervallo tra l'assunzione della soluzione e l'esecuzione dell'esame endoscopico. Si consiglia di iniziare la preparazione il giorno precedente l'esame assumendo due litri di preparazione al mattino (dalle ore 9.00) e due litri al pomeriggio (dalle ore 12.00 in poi). In ogni caso la cena sarà costituita solo da liquidi (brodo, tisa, camomilla). Se il paziente ha un problema di stitichezza è consentibile una dieta a basso contenuto di scorie nelle 72 ore che precedono l'esam
(uva, fichi, kiwi, ecc.)

MATERIALE

SELG-ESSE: una con
litro di acqua).
ISOCOLAN: una con
preparazione di 4 lit
L'accettabilità minim
Si consiglia di bere
evitando i piccoli sor

AZIONE

L'evacuazione inizia
E' necessario essere

DOCUMENTI

E' utile, ai fini di una accurata esecuzione dell'esame, che il paziente abbia con sé:

- referti di esami endoscopici precedenti
- referti di altri accertamenti pertinenti la patologia per cui eseguo la colonscopia;
- lista delle patologie note da cui è affetto;
- lista dei farmaci in terapia, con la posologia.

ESAMI EMATOCHIMICI DA ESEGUIRE SE SI PREVEDE L'ESECUZIONE DI POLIPECTOMIA

Dal momento che l'indagine richiede che non siano presenti tube coagulative, è necessario eseguire alcuni giorni prima dell'indagine i seguenti controlli ematochimici:
- Attività protrombinica, PTT, Emocromo completo con conta piastrine.

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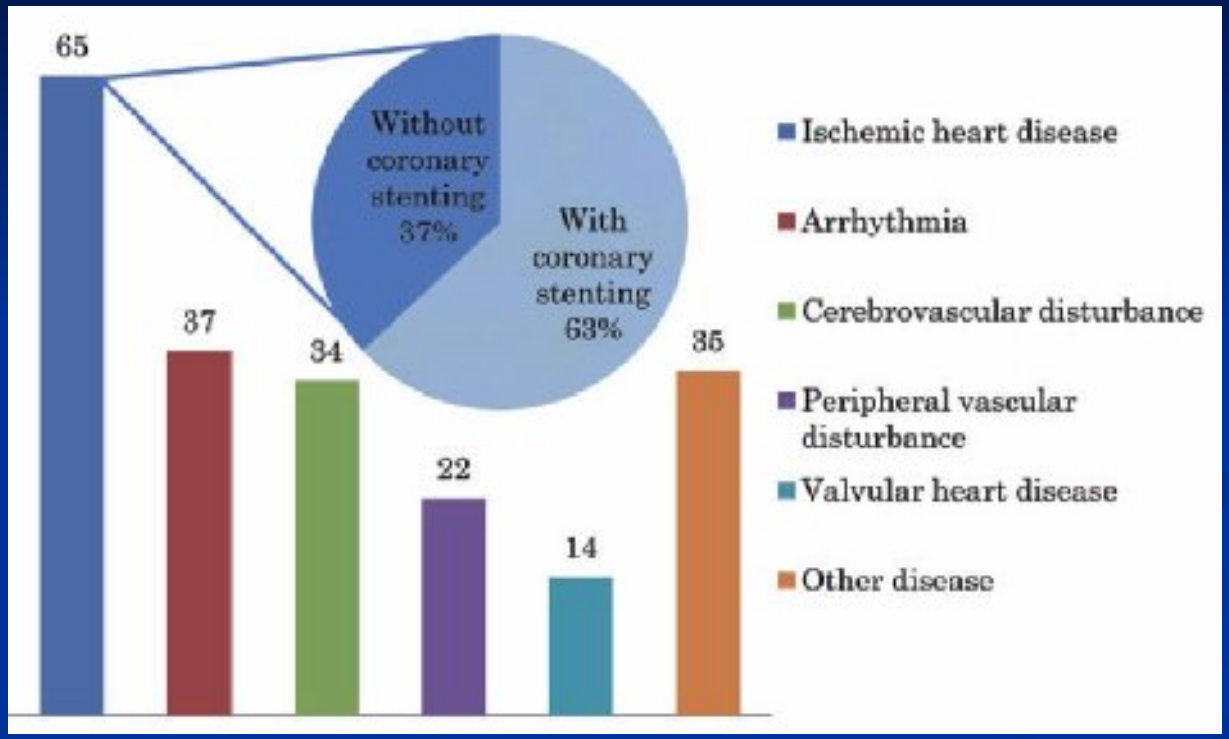
CONTROVERSY ON THE MANAGEMENT OF ANTICOAGULANTS AND ANTIPLATELET AGENTS FOR SCHEDULED ENDOSCOPY



Comorbidities of 208 patients taking anticoagulants or antiplatelet agents. Among 65 patients with ischemic heart disease, 41 patients (63%) had a mechanical stent in the coronary artery.

Ono et al Dig Endosc; 2011

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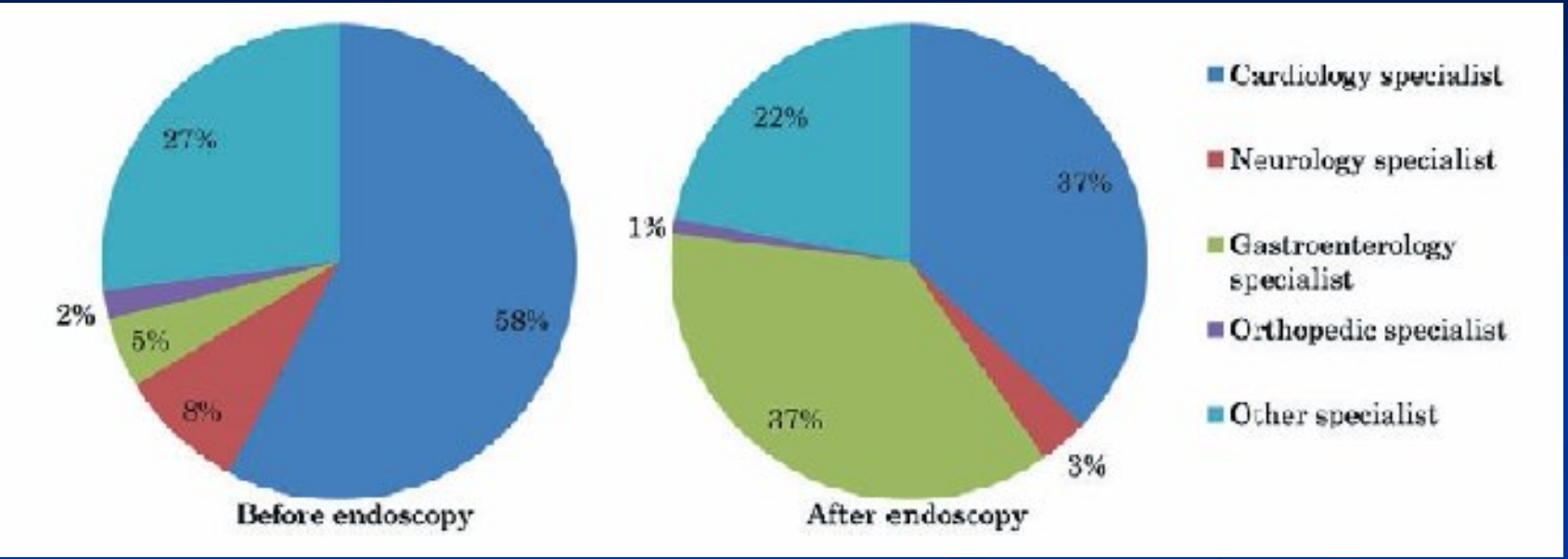


Specialties of doctors who determined cessation periods before and after endoscopy.

Ono et al Dig Endosc; 2011

Differences in managing anticoagulants and antiplatelets for gastrointestinal endoscopy between east and west

Summary on major differences between the East and West

	East	West
Risk of embolism	Lower than the Westerners. Common form is cerebrovascular variety that may lead to death or disability.	Higher than the Easterners. Common form is cardiovascular variety including deep vein thrombosis.
Risk of bleeding	Higher than the Westeners due to different drug metabolism (greater body weight-normalized plasma unbound clearance of drug) and higher rate of *H. pylori* infection.	Lower than the Easterners. Tolerates well with low-risk endoscopic procedures during antiplatelet and/or anticoagulant medications.
Managing warfarin	Lower international normalized ratio value (1.6-2.6) than the Westerners are appropriate for prophylaxis of thromboembolism.	Tolerates well with low-risk procedures (endoscopic biopsy) without significant bleeding.
Managing aspirin	Lower dose is recommended than the Westerners due to higher risk of bleeding.	Tolerates well with few high-risk procedures (endoscopic sphincterotomy and colon polypectomy) without significant bleeding.

Lee SY Gastroenterol Res; 2009

Guidelines for the management of anticoagulant and antiplatelet therapy in patients undergoing endoscopic procedures

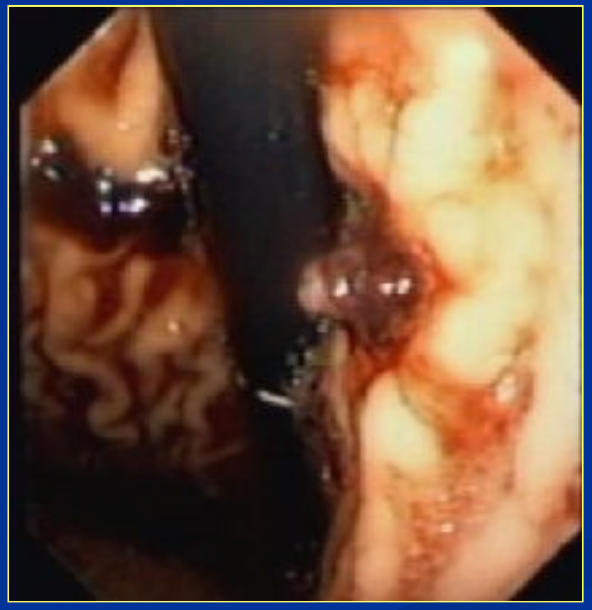
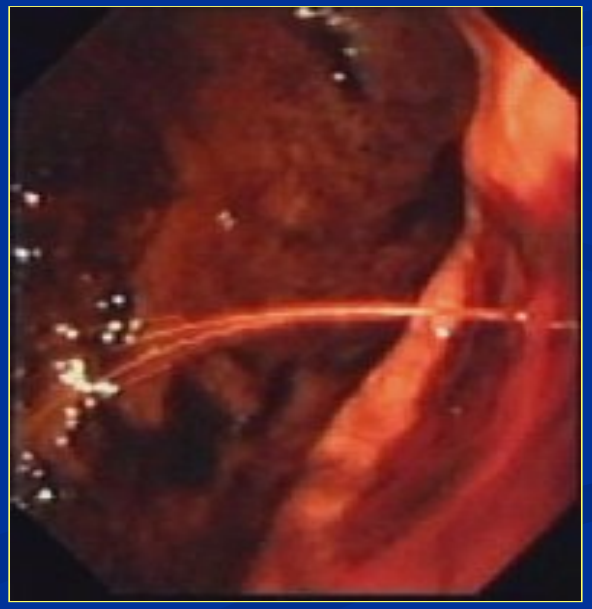
Acute gastro-intestinal haemorrhage

Acute gastro-intestinal haemorrhage in patients on anticoagulant or antiplatelet agents is a high-risk situation. The immediate risk to the patient from haemorrhage may outweigh the risk of thrombosis as a result of stopping anticoagulant or antiplatelet therapy.

There is a high risk of acute myocardial infarction or death if clopidogrel is discontinued in patients with coronary stents, particularly early after implantation, but extending up to 1 year after this. Endoscopy should be attempted as soon as safely possible after urgent liaison between the patient's cardiologist and the consultant specialist undertaking endoscopy. Clopidogrel should not be discontinued without discussion with a cardiologist. If clopidogrel therapy needs to be discontinued in this context, then this should be limited to a maximum of 5 days as the risk of stent thrombosis increases after this interval. (Evidence grade III. Recommendation grade B.) Early therapeutic endoscopic intervention may achieve haemostasis with minimal or no cessation of anticoagulant or antiplatelet therapy, and should be the first aim. (Evidence grade IV. Recommendation grade C.)

Veitch AM et al Gut; 2008



Guidelines for the management of anticoagulant and antiplatelet therapy in patients undergoing endoscopic procedures

Risk stratification for discontinuation of anticoagulant therapy

High risk	Low risk
Prosthetic metal heart valve in mitral position	Prosthetic metal heart valve in aortic position
Prosthetic heart valve and atrial fibrillation	Xenograft heart valve
Atrial fibrillation and mitral stenosis	Atrial fibrillation without valvular disease
<3 months after venous thromboembolism Thrombophilia syndromes	>3 months after venous thromboembolism

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Risk stratification for discontinuation of clopidogrel

High risk	Low risk
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Bare metal coronary artery stents within 1 month of placement	Cerebrovascular disease
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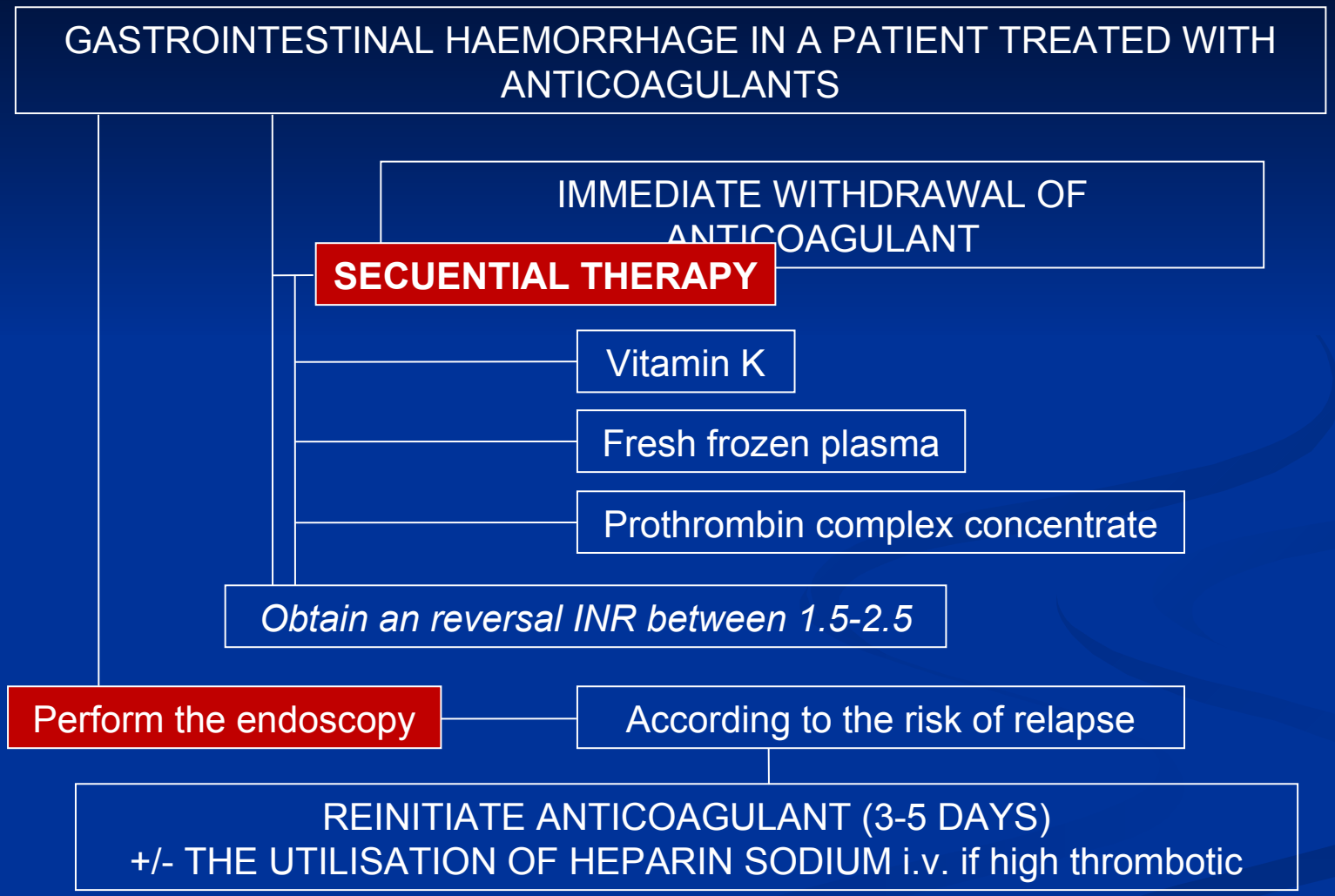
Veitch AM et al Gut; 2008

Clinical practice guidelines for managing coagulation in patients undergoing endoscopic procedures



Alberca de las Parras F. Rev Esp Enferm Dig; 2010

Management of anticoagulation before and after gastrointestinal endoscopy

Reversal of anticoagulant therapy

Drug(s)	Reversing agent
Warfarin	Vitamin K, fresh frozen plasma, prothrombin complex concentrates, activated factor VII
Aspirin / NSAIDs	Platelet infusion, DDAVP
Clopidogrel	Platelet infusion, DDAVP
Heparin / LMWH	Protamine sulfate
Fondaparinux	Activated factor VII
Glycoprotein IIa / IIIb	Platelet infusion, DDAVP

DDAVP, desmopressin;
LMWH, low-molecular-weight heparin;
NSAID, nonsteroidal anti-infl ammatory drug.

Kwok A, Faigel D.O. Am J Gastroenterol; 2009

GUIDELINE

ASGE guideline: the management of low-molecular-weight heparin and nonaspirin antiplatelet agents for endoscopic procedures

Recommendations

Acute GI hemorrhage in the patient taking LMWH. The decision to reverse or to stop this therapy, risking an adverse ischemic event or a thromboembolic complication, must be weighed against the risk of continued bleeding by maintaining continued systemic anticoagulation. Because of the short half-life of the LMWHs, the anticoagulant effect may be reversed within 8 hours of the last dose. If quick reversal is required, intravenous protamine sulfate can be used. Note that the administration of protamine sulfate can cause severe hypotension and anaphylactoid reactions.

Standard of Practice Committee Gastrointest Endosc; 2005

Management of low-molecular-weight heparin and nonaspirin antiplatelet agents for endoscopic procedures

Management of LMWH in patients undergoing endoscopic procedures

Procedure risk	Recommendation
High	Consider discontinuation at least 8 h before procedure
Low	No change in therapy

Management of antiplatelet medication (clopidogrel or ticlopidine) in patients undergoing endoscopic procedures

Procedure risk	Recommendation
High	Consider discontinuation 7-10 d before procedure
Low	No change in therapy

Standard of Practice Committee Gastrointest Endosc; 2005

Management of low-molecular-weight heparin and nonaspirin antiplatelet agents for endoscopic procedures

Procedure risk

High-risk procedures	Low-risk procedures
Polypectomy	Diagnostic
Biliary sphinterotomy	EGD ± biopsy
Pneumatic or bougie dilation	Flexible sigmoidoscopy ± biopsy
PEG placement	Colonoscopy G biopsy
EUS-guided FNA	ERCP without endoscopic sphincterotomy
Laser ablation and coagulation	Biliary/pancreatic stent without endoscopic sphincterotomy
Treatment of varices	EUS without FNA Enteroscopy

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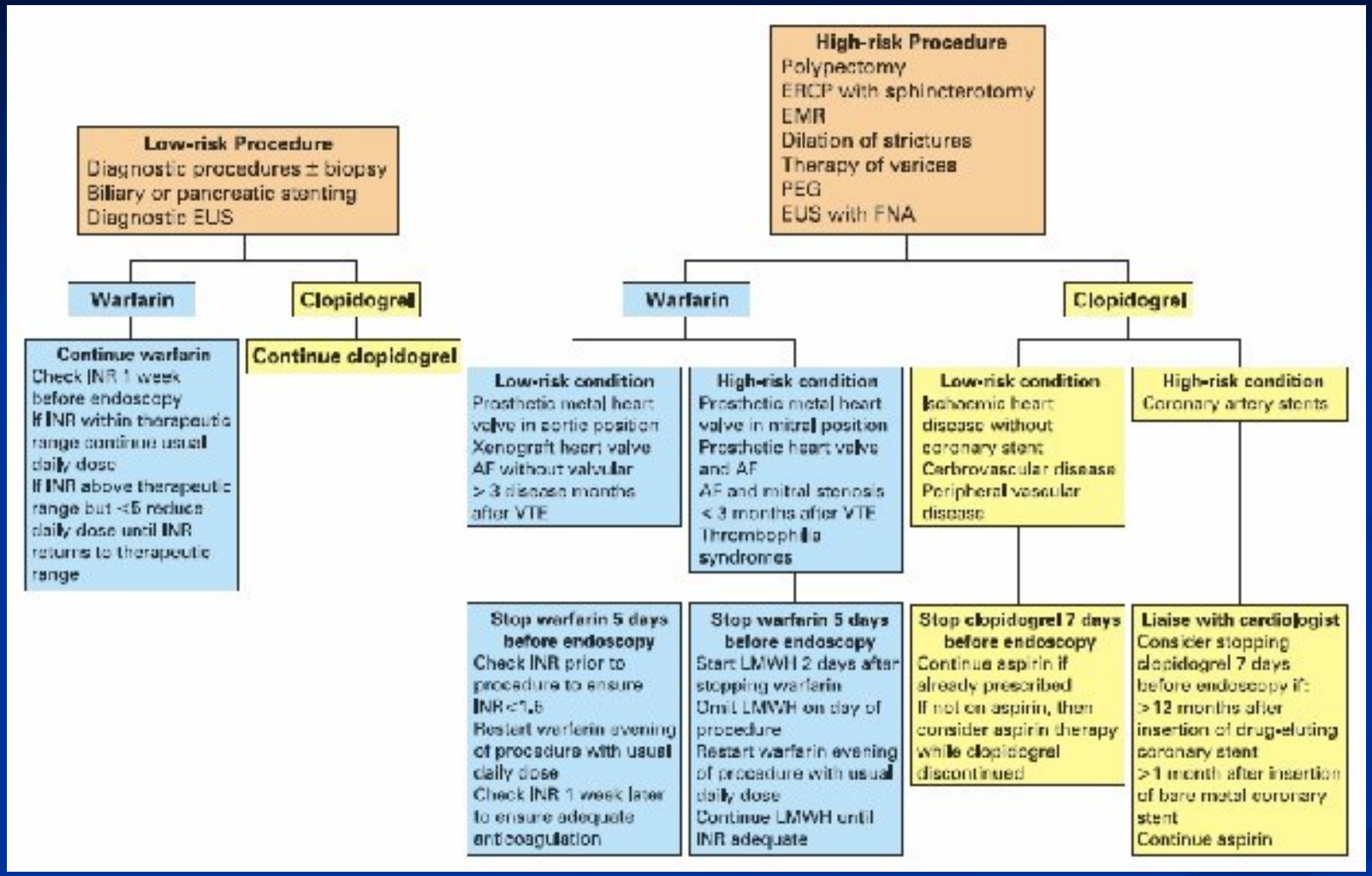

Aspirin therapy should be continued.

Veitch AM et al Gut; 2008

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When to withdraw medication before an endoscopic procedure

	Diagnostic endoscopy, %		Endoscopic biopsy, %		Polypectomy, %	
	Eastern endoscopist (n = 105)	Western endoscopist (n = 106)	Eastern endoscopist (n = 105)	Western endoscopist (n = 106)	Eastern endoscopist (n = 105)	Western endoscopist (n = 106)
Warfarin	Do not stop, 50.9	Do not stop, 90.5	> 7 d, 44.8	4-6 d, 45.3	> 7 d, 70.5	4-6 d, 66.0
Aspirin	Do not stop, 79.2	Do not stop, 93.3	Do not stop, 54.3	Do not stop, 93.3	> 7 d, 73.6	Do not stop, 69.6
NSAIDs	Do not stop, 73.5	Do not stop, 96.2	Do not stop, 67.5	Do not stop, 96.2	Do not stop, 58.1	Do not stop, 85.8
Ticlopidine, clopidogrel, dipyridamole	Do not stop, 59.5	Do not stop, 93.8	Do not stop, 38.7	Do not stop, 93.8	> 7 d, 71.4	> 7 d, 55.7
Abciximab, tirofiban	Do not stop, 44.3	Do not stop, 84.8	Do not stop, 37.2	Do not stop, 84.8	> 7 d, 60.0	> 7 d, 27.4

Lee SY et al Gastroint Endosc; 2008

Managing anticoagulation and antiplatelet medications in GI endoscopy: a survey comparing the East and the West

When to restart medication after an endoscopic procedure

	Diagnostic endoscopy, %		Endoscopic biopsy, %		Polypectomy, %	
	Eastern endoscopist (n = 105)	Western endoscopist (n = 106)	Eastern endoscopist (n = 105)	Western endoscopist (n = 106)	Eastern endoscopist (n = 105)	Western endoscopist (n = 106)
Warfarin	Same day, 94.3	Same day, 94.4	1-3 d, 56.2	Same day, 73.6	1-3 d, 46.7	1-3 d, 48.1
Aspirin	Same day, 95.3	Same day, 94.4	1-3 d, 44.8	Same day, 75.5	1-3 d, 44.8	Same day, 35.9
NSAIDs	Same day, 95.3	Same day, 93.4	Same day, 65.8	Same day, 76.5	Same day, 49.6	Same day, 37.7
Ticlopidine, clopidogrel, dipyridamole	Same day, 95.3	Same day, 92.5	1-3 d, 46.7	Same day, 67.0	1-3 d, 44.8	1-3 d, 35.8
Abciximab, tirofiban	Same day, 84.8	Same day, 73.6	1-3 d, 40.0	Same day, 47.2	1.3 d, 44.8	1-3 d, 33.0

Lee SY et al Gastroint Endosc; 2008

Management of anticoagulation before and after gastrointestinal endoscopy

Timing of reinstitution of anticoagulant / antiplatelet therapy after gastrointestinal endoscopy

Drug	Timing of reinstitution	Grade of recommendation	Special considerations
Warfarin	Same night	Grade 1C	Consider recommencing ≥ 3 days in the case of sphincterotomy, gastric/duodenal polypectomy, large colonic polypectomy, EMR
Heparin	2–6 h after procedure	N / A	
LMWH	24 h after procedure	Grade 1C	
Individualize			
Clopidogrel	Next day	Grade 2C	

Guidelines for the management of anticoagulant and antiplatelet therapy in patients undergoing endoscopic procedures

The key messages are:

- All patients should carry a warning card.
- Discuss the case with the interventional cardiologist who performed the procedure so that the risks of stent thrombosis (with its 50% risk of AMI/death) can be weighed against the bleeding risk associated with the noncardiac surgical procedure.
- If possible, procedures should be undertaken without complete lack of antiplatelet cover, such that if clopidogrel does need to be stopped because of excess bleeding risk, then aspirin should be continued if possible.
- For patients with known high risk of needing a future noncardiac surgical procedure (eg, planned future surgery for cancer) bare metal stenting will be undertaken since dual antiplatelet therapy will only be required for 1 month.

Veitch AM et al Gut; 2008

CONTROVERSY ON THE MANAGEMENT OF ANTICOAGULANTS AND ANTIPLATELET AGENTS FOR SCHEDULED ENDOSCOPY

Western guidelines recommend biopsy without cessation, Japanese physicians principally secure cessation before biopsy and the JGES guidelines also recommend this. We speculate that the most important reason is racial differences, as mentioned in the JGES guidelines. However, after invasive procedures, thromboembolic events during cessation are reported to result in lethal outcomes rather than bleeding events. Additionally, there are not enough data on racial differences to conclude that bleeding events are more lifethreatening than thromboembolic events for Japanese compared to Western people. Although we need further accumulation of data concerning this problem, minimally invasive biopsy without cessation might be acceptable for Japanese.

Ono et al Dig Endosc; 2011

Adverse events associated with anticoagulation therapy in the periendoscopic period

Take-home Message

- Chronic anticoagulation is a risk factor for GI hemorrhage in the periprocedural period. A large cohort study was performed by using patients enrolled in the Clinical Outcomes Research Initiative database to determine the incidence of postprocedural hemorrhage and stroke. ASGE guidelines recommend management of warfarin therapy according to the risk of hemorrhage associated with the endoscopic procedure and the underlying risk of thrombosis.
- Anticoagulated patients managed according to current society guidelines did not appear to have a higher incidence of postprocedural hemorrhage. Polypectomy, but not usage of periprocedural heparin, was a factor for postprocedural bleeding.

Gerson LB et al Gastrointest Endosc; 2010

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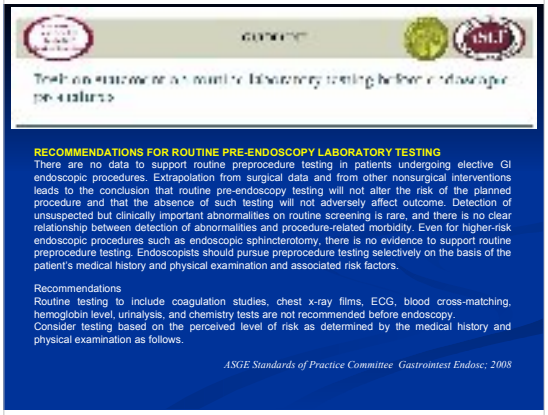
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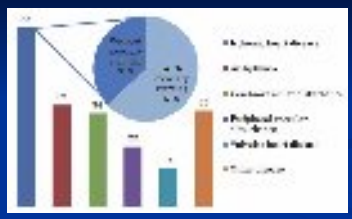

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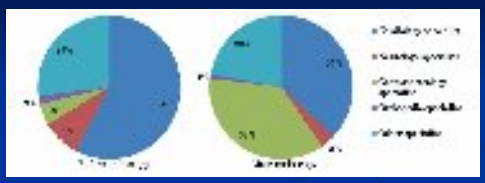

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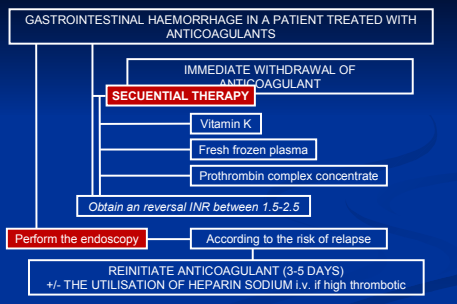

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DDAVP, desmopressin;
LMWH, low-molecular-weight heparin;
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Recommendations

Acute GI hemorrhage in the patient taking LMWH. The decision to reverse or to stop this therapy, risking an adverse ischemic event or a thromboembolic complication, must be weighed against the risk of continued bleeding by maintaining continued systemic anticoagulation. Because of the short half-life of the LMWHs, the anticoagulant effect may be reversed within 8 hours of the last dose. If quick reversal is required, intravenous protamine sulfate can be used. Note that the administration of protamine sulfate can cause severe hypotension and anaphylactoid reactions.

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Management of low-molecular-weight heparin and nonaspirin antiplatelet agents for endoscopic procedures

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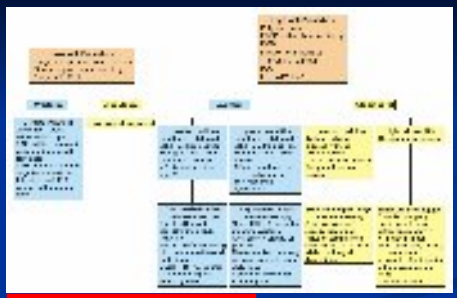

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NSAIDs	Do not stop, 73.5	Do not stop, 96.2	Do not stop, 67.5	Do not stop, 96.2	Do not stop, 58.1	Do not stop, 85.8
Ticlopidine, clopidogrel, dipyridamole	Do not stop, 59.5	Do not stop, 93.8	Do not stop, 38.7	Do not stop, 93.8	> 7 d, 71.4	> 7 d, 55.7
Abciximab, tirofiban	Do not stop, 44.3	Do not stop, 84.8	Do not stop, 37.2	Do not stop, 84.8	> 7 d, 60.0	> 7 d, 27.4

Lee SY et al Gastroint Endosc; 2008

Managing anticoagulation and antiplatelet medications in GI endoscopy: a survey comparing the East and the West

When to restart medication after an endoscopic procedure

	Diagnostic endoscopy, %		Endoscopic biopsy, %		Polypectomy, %	
	Eastern endoscopist (n = 105)	Western endoscopist (n = 106)	Eastern endoscopist (n = 105)	Western endoscopist (n = 106)	Eastern endoscopist (n = 105)	Western endoscopist (n = 106)
Warfarin	Same day, 94.3	Same day, 94.4	1-3 d, 56.2	Same day, 73.6	1-3 d, 46.7	1-3 d, 48.1
Aspirin	Same day, 95.3	Same day, 94.4	1-3 d, 44.8	Same day, 75.5	1-3 d, 44.8	Same day, 35.9
NSAIDs	Same day, 95.3	Same day, 93.4	Same day, 65.8	Same day, 76.5	Same day, 49.6	Same day, 37.7
Ticlopidine, clopidogrel, dipyridamole	Same day, 95.3	Same day, 92.5	1-3 d, 46.7	Same day, 67.0	1-3 d, 44.8	1-3 d, 35.8
Abciximab, tirofiban	Same day, 84.8	Same day, 73.6	1-3 d, 40.0	Same day, 47.2	1.3 d, 44.8	1-3 d, 33.0

Lee SY et al Gastroint Endosc; 2008

Management of anticoagulation before and after gastrointestinal endoscopy

Timing of reinstitution of anticoagulant / antiplatelet therapy after gastrointestinal endoscopy

Drug	Timing of reinstitution	Grade of recommendation	Special considerations
Warfarin	Same night	Grade 1C	Consider recommencing ≥ 3 days in the case of sphincterotomy, gastric/duodenal polypectomy, large colonic polypectomy, EMR
Heparin	2–6 h after procedure	N / A	
LMWH	24 h after procedure	Grade 1C	
Individualize			
Clopidogrel	Next day	Grade 2C	

Guidelines for the management of anticoagulant and antiplatelet therapy in patients undergoing endoscopic procedures

The key messages are:

- All patients should carry a warning card.
- Discuss the case with the interventional cardiologist who performed the procedure so that the risks of stent thrombosis (with its 50% risk of AMI/death) can be weighed against the bleeding risk associated with the noncardiac surgical procedure.
- If possible, procedures should be undertaken without complete lack of antiplatelet cover, such that if clopidogrel does need to be stopped because of excess bleeding risk, then aspirin should be continued if possible.
- For patients with known high risk of needing a future noncardiac surgical procedure (eg, planned future surgery for cancer) bare metal stenting will be undertaken since dual antiplatelet therapy will only be required for 1 month.

Veitch AM et al Gut; 2008

CONTROVERSY ON THE MANAGEMENT OF ANTICOAGULANTS AND ANTIPLATELET AGENTS FOR SCHEDULED ENDOSCOPY

Western guidelines recommend biopsy without cessation, Japanese physicians principally secure cessation before biopsy and the JGES guidelines also recommend this. We speculate that the most important reason is racial differences, as mentioned in the JGES guidelines. However, after invasive procedures, thromboembolic events during cessation are reported to result in lethal outcomes rather than bleeding events. Additionally, there are not enough data on racial differences to conclude that bleeding events are more lifethreatening than thromboembolic events for Japanese compared to Western people. Although we need further accumulation of data concerning this problem, minimally invasive biopsy without cessation might be acceptable for Japanese.

Ono et al Dig Endosc; 2011

Adverse events associated with anticoagulation therapy in the periendoscopic period

Take-home Message

❖Chronic anticoagulation is a risk factor for GI hemorrhage in the periprocedural period. A large cohort study was performed by using patients enrolled in the Clinical Outcomes Research Initiative database to determine the incidence of postprocedural hemorrhage and stroke. ASGE guidelines recommend management of warfarin therapy according to the risk of hemorrhage associated with the endoscopic procedure and the underlying risk of thrombosis.

❖Anticoagulated patients managed according to current society guidelines did not appear to have a higher incidence of postprocedural hemorrhage. Polypectomy, but not usage of periprocedural heparin, was a factor for postprocedural bleeding.

Gerson LB et al Gastrointest Endosc; 2010