A Canadian clinical practice algorithm for the management of patients with nonvariceal upper gastrointestinal bleeding

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A Barkun, CA Fallone, N Chiba, et al. A Canadian clinical practice algorithm for the management of patients with nonvariceal upper gastrointestinal bleeding. Can J Gastroenterol 2004;18(10):605-609.

AIM: To use current evidence-based recommendations to provide a user-friendly clinical algorithm for the management of upper gastrointestinal bleeding, adapted to the Canadian environment.

METHODS: A multidisciplinary consensus group of 25 participants representing 11 national societies used a seven-step approach to develop recommendations according to accepted standards. Sources of data included narrative and systematic reviews as well as published and new meta-analyses. A small writing subgroup subsequently created the algorithm.

RESULTS: Recommendations emphasize appropriate initial resuscitation of the patient and a multidisciplinary approach to clinical risk stratification that determines the need for early endoscopy. Early endoscopy allows safe and prompt discharge of selected patients classified as low risk. Endoscopic hemostasis is reserved for patients with high-risk endoscopic lesions. Although monotherapy with injection or thermal coagulation is effective, the combination is superior to either treatment alone. High-dose intravenous proton-pump inhibition is recommended in patients who have undergone successful endoscopic therapy. Routine second-look endoscopy is not recommended. Patients with upper gastrointestinal bleeding secondary to ulcer disease should be tested and treated for *Helicobacter pylori* infection.

CONCLUSIONS: This algorithm should facilitate appropriate risk stratification, use of endoscopic therapy and the appropriate utilization of proton-pump inhibition to optimize the care of patients with upper gastrointestinal bleeding. The algorithm should be customized to the resources of individual medical centres. Its application should be studied with appropriate outcomes recorded and validation performed.

Key Words: *Algorithm; Bleeding; Gastrointestinal; Nonvariceal*

Un algorithme de pratique clinique canadien pour la prise en charge de patients souffrant de saignements non variqueux des voies gastro-intestinales supérieures

OBJECTIF : Utiliser les recommandations courantes fondées sur des faits probants pour fournir un algorithme facile à utiliser et adapté au milieu canadien dans la prise en charge des saignements des voies gastro-intestinales supérieures.

MÉTHODOLOGIE : Un groupe multidisciplinaire consensuel de 25 participants représentant 11 sociétés nationales a recouru à une démarche en sept étapes pour élaborer des recommandations fondées sur des normes acceptées. Les sources de données incluaient des analyses narratives et systématiques et des méta-analyses publiées ou nouvelles. Un petit sous-groupe de rédaction a ensuite créé l'algorithme.

RÉSULTATS : Les recommandations font ressortir l'importance d'une réanimation initiale convenable des patients et d'une approche multidisciplinaire de la stratification des risques cliniques qui détermine le besoin d'une endoscopie précoce. Cette endoscopie permet d'accorder un congé hospitalier sécuritaire et rapide à des patients sélectionnés classés comme à faible risque. L'hémostase endoscopique est réservée aux patients présentant des lésions endoscopiques à haut risque. Bien qu'une monothérapie par injection ou une coagulation thermique soit efficace, l'association est supérieure à l'un ou l'autre des traitements employé seul. De fortes doses d'inhibiteurs de la pompe à protons par voie intraveineuse sont recommandées pour les patients qui ont subi un traitement endoscopique réussi. Les patients souffrant de saignements des voies gastro-intestinales supérieures secondaires à une maladie ulcéreuse devraient subir des examens et un traitement contre l'infection à l'*Helicobacter pylori*.

CONCLUSIONS : Cet algorithme devrait faciliter une stratification pertinente des risques, l'usage du traitement endoscopique et l'utilisation pertinente des inhibiteurs de la pompe à protons pour optimiser les soins des patients souffrant de saignements de voies gastro-intestinales supérieures. L'algorithme devrait être personnalisé selon les ressources de chaque centre médical. Son application devrait être évaluée, les issues devraient être prises en note et une validation devrait être exécutée.

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Received for publication March 15, 2004. Accepted July 13, 2004

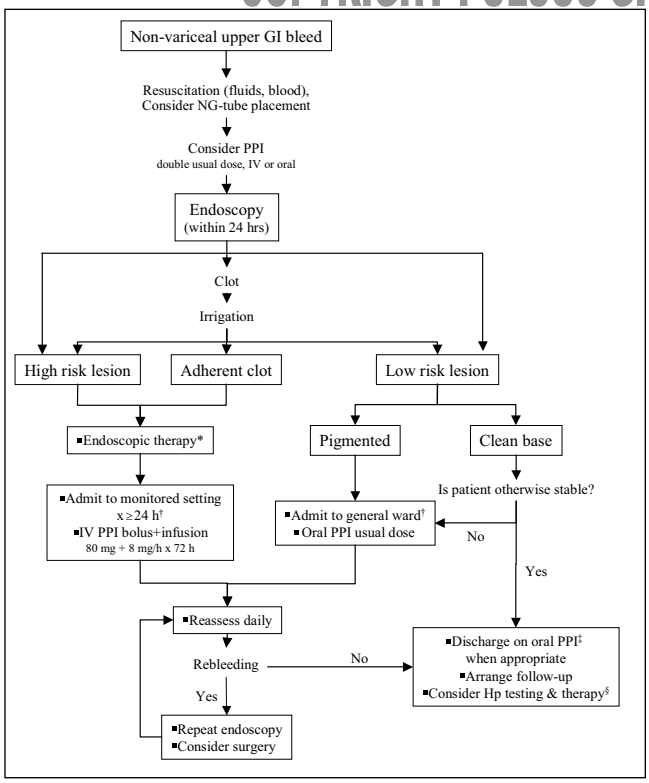

Figure 1) *A Canadian clinical practice algorithm for the management of patients with nonvariceal upper gastrointestinal (GI) bleeding. Refer to the text for relevant references. *Combination therapy with injection plus thermocoagulation is preferred; †High-risk patients can be moved to a general ward after 24 h if appropriate. The duration of admission should take into consideration the rebleeding period (72 h), local practice and availability of resources; ‡There are no data favouring proton-pump inhibitors (PPIs) over histamine$_2$-receptor antagonists as oral follow-up therapy, but this is a reasonable approach, because this was the strategy in the high-dose intravenous (IV) PPI studies; §Acute testing for* Helicobacter pylori *(Hp) should be followed, if negative, by a confirmatory test once bleeding has resolved. There is no rationale for urgent IV eradication therapy; oral therapy can be initiated either immediately or during follow-up of patients who are* H pylori*-positive. Early discharge is appropriate in the absence of risk factors such as age over 65 years, shock, comorbid illnesses and fresh red blood on rectal examination, in the emesis or in the nasogastric (NG) aspirate*

Upper gastrointestinal (GI) bleeding represents a substantial clinical and economic burden, with a prevalence of approximately 170 cases per 100,000 adults per year (1). Approximately 50% to 70% of cases are due to peptic ulcer disease (2,3), and despite recent advances in therapy, an estimated 6% to 8% of these patients die (1,4,5). Causes can broadly be divided into variceal and nonvariceal with limited accurate prediction based on clinical criteria alone.

With the exception of the recent British Society of Gastroenterology guidelines (2002) (6), the last widely disseminated consensus conference and publication of practice guidelines occurred more than 10 years ago (7,8). For this reason, a multidisciplinary consensus conference was held in Canada in June 2002. The group included Canadian and international gastroenterologists, endoscopists, surgeons, family physicians, emergency room physicians, pharmacologists, epidemiologists (with methodological and health economic expertise) and a hospital pharmacist, representing 11 national societies. Using stringent, accepted criteria for guideline development, new data and a series of evidence-based systematic reviews and meta-analyses (9,10), recommendations for the management of nonvariceal upper GI bleeding were developed (11). The complete review and consensus processes details are published in full elsewhere (11). These consensus recommendations have now been used to develop an algorithm for the management of patients with nonvariceal upper GI bleeding specifically tailored to the Canadian environment.

RECOMMENDATIONS

The present article will present highlights of the recommendations (published in full in the *Annals of Internal Medicine* 2003 [11]) as they relate, in a Canadian setting, to decision points in the algorithm shown in Figure 1.

Stabilization

When a patient presents with a nonvariceal upper GI bleed, appropriate initial resuscitation, including stabilization of blood pressure and restoration of intravascular volume, is paramount and should precede any further diagnostic and therapeutic measures (11). Placement of a nasogastric tube should be considered in selected patients because the findings may have prognostic value (11,12). Empiric therapy with a high dose, oral or intravenous, proton-pump inhibitor (PPI) should be considered for patients awaiting endoscopy (11), but is not a replacement for urgent endoscopy and hemostasis, where appropriate (3,13-16). Although there are no controlled data directly assessing this approach, its possible usefulness is suggested by the conclusions of randomized trials of post-endoscopy high dose oral (13-16) and intravenous PPI (17-20), coupled with results from preliminary observational and cost-effectiveness studies (3,21,22).

Clinical risk stratification

Approximately 80% of patients will stop bleeding spontaneously without recurrence, but the main goal of management is to identify the remaining 20% of patients who are at greatest risk of morbidity and mortality from continued or recurrent bleeding (23).

Once patients are clinically stabilized, they should be stratified into low- and high-risk categories for rebleeding and mortality, based on clinical criteria initially, with endoscopic criteria also considered when available (11). The most important clinical predictors of increased risk of rebleeding or mortality are age over 65 years, shock, comorbid illnesses and fresh red blood on rectal examination, in the emesis or in the nasogastric aspirate (3,11,24-30). Endoscopic stigmata defined as low- and high-risk are discussed below.

The need for urgent endoscopy, or conversely, suitability for early discharge, can be determined using risk stratification tools, such as those reported by Blatchford et al (31) or Cameron et al (32), which include older age, significant comorbid illnesses, presence of hematemesis, shock or syncope.

Endoscopic risk stratification and therapy

Endoscopy should be performed within the first 24 h, the patient stratified according to the endoscopic stigmata and endoscopic therapy performed if needed. Clinical risk stratification

according to the criteria mentioned above, can assist in differentiating between those who require urgent endoscopy (based on clinical criteria) and those who can safely wait for a finite period of time, depending on available resources. Evidence indicates that the risk of further bleeding is strongly associated with the hemorrhagic stigmata seen at endoscopy. The risk is reportedly less than 5% in patients with a clean ulcer base, and increases progressively with a flat spot (10%), adherent clot (22%), nonbleeding visible vessel (43%) or active bleeding (oozing and spurting, 55%) (11,23).

Recently it has been demonstrated in randomized controlled trials that a single dose of intravenous erythromycin (3 mg/kg infusion over 30 min or 250 mg bolus) administered 20 min to 90 min before endoscopy improves the visibility and quality of the examination, and decreases the need for repeat examinations (33,34). Erythromycin acts as a potent gastrokinetic to empty the stomach of blood; a clear stomach was found significantly more often with erythromycin than with placebo (82% versus 33%) (34). Erythromycin may be useful in patients undergoing emergency endoscopy for upper GI bleeding when blood obscures visibility.

A finding of active bleeding or a visible vessel in an ulcer bed (high-risk lesion) requires immediate endoscopic hemostatic therapy, while a finding of a clean-based ulcer or a nonprotuberant pigmented dot (low-risk lesion) does not (11,23). The optimal management of adherent clots remains more controversial (11). Adherent clots obscure underlying stigmata that may be at high or low risk of rebleeding. Recent evidence supports that a clot in an ulcer bed should undergo targeted irrigation in an attempt to dislodge it and the underlying lesion treated appropriately (35,36).

High-risk lesions should be treated with endoscopic therapy. Monotherapy, with injection or thermal coagulation (9,10), is an effective endoscopic hemostatic technique for high-risk stigmata, but the combination is superior to either treatment alone (11,35-37).

Clinical and endoscopic classification of risk allows for safe and prompt discharge of patients classified as low-risk; improves patient outcomes for patients classified as high-risk; and reduces resource utilization for patients in all classifications (11,38-44). Clinical criteria for early discharge generally include age less than 60 years, stable vital signs, no endoscopic stigmata or flat spot, and no concomitant serious medical illness (39,45).

Acid suppressive therapy

Recent meta-analyses have found PPIs to be more effective than histamine$_2$-receptor antagonists (H_2-RAs) in preventing persistent or recurrent bleeding (9,10,46,47). H_2-RAs have demonstrated inconsistent and only marginal benefits, and, as such, are not recommended for the management of acute upper GI bleeding (11). High-dose PPI therapy administered by intravenous bolus followed by continuous infusion is effective in decreasing rebleeding in patients who have undergone successful endoscopic therapy and should be used to treat patients with high-risk endoscopic stigmata, including adherent clots (9-11). Evidence suggests a class effect for PPI treatment and that improvement in rebleeding rates can be achieved using either intravenous omeprazole or pantoprazole at a dose of 80 mg bolus followed by 8 mg/h for the 72 h following endoscopic therapy (11). Patients can be safely switched to oral PPI therapy following the 72 h, or when oral intake has been reestablished in those at lower risk. As mentioned above in the section on stabilization, empiric therapy with an oral PPI can be considered for patients awaiting endoscopy, particularly in institutions where intravenous PPI or endoscopy is not available (11).

Admission and follow-up

Patients identified as being at high risk of rebleeding, such as those with active bleeding or visible vessels, and those with adherent clots, should be admitted to a monitored setting for at least the first 24 h and receive high-dose PPI therapy (6,11). If intensive care beds are unavailable, wards with more intensive monitoring than standard units can be considered. The greatest risk of rebleeding is in the first 72 h after endoscopy. Routine second-look endoscopy is not recommended (11,48); a second look is indicated in cases of rebleeding, and perhaps in selected patients at high risk of rebleeding (11,49). Patients who have failed endoscopic therapy or who are at high risk of failing endoscopic therapy should receive a surgical consultation (11), or alternatively, angiography with possible embolization could be considered (50).

Patients with a low-risk lesion who are not yet stable or those with pigmented lesions should be admitted for at least the first 24 h and treated with an oral PPI (11). Those with endoscopic findings of a Mallory-Weiss tear or an ulcer with a clean base or flat spot, who are otherwise stable, may be discharged home on an oral PPI (11). Studies show that patients with these endoscopic findings are at low risk and no major complications have been reported in those triaged to outpatient care (38-41,51-54).

All hospitalized patients, high or low risk, should be monitored and assessed daily, and when stable, discharged with appropriate follow-up arranged (11). If not performed during the hospitalization, *Helicobacter pylori* testing should be done as part of follow-up in patients with peptic ulcers (11). Eradication of *H pylori* can reduce the rate of ulcer recurrence and rebleeding (55-58). Negative tests in the setting of acute bleeding or after initiation of PPI therapy should be interpreted with caution (11,59).

This treatment approach also applies to patients with nonsteroidal anti-inflammatory drug-associated ulcers; however, the roles of cyclooxygenase-2 selective inhibitors, and coprescription with a PPI or misoprostol, were beyond the scope of the published recommendations (11).

SUMMARY

It is hoped that this algorithm will be used to direct clinical and endoscopic risk stratification, the application of endoscopic therapy and the appropriate use of PPIs, and thus help optimize the care of patients with upper GI bleeding. The algorithm should be customized to the resources of individual medical centres. The impact of the recommendations should be studied with appropriate outcomes recorded and validation performed. The efficacy of newer endoscopic therapeutic technologies, the optimal regimen of PPIs and the roles of other pharmacological agents all require further research and as such, it is anticipated that the guidelines and this algorithm will need to be updated as new data become available.

APPENDIX 1: LIST OF ATTENDEES

***Nonvariceal Upper GI Bleeding Consensus Conference Group**

Canadian participants: John K Marshall (nonvoting chair), David Armstrong, Marc Bardou, Alan Barkun, J Decker Butzner, Naoki Chiba, Alan Cockeram, Brian Craig, Robert Enns, Carlo A Fallone, Marty Fishman, Nigel Flook, Jamie Gregor, Jonathan Love, Norm Marcon, Janet Martin, Joseph Romagnuolo, Alaa Rostom, Sandrine Sabbah, Anthony Taylor, Alan Thomson, Sander Veldhuyzen van Zanten, Robin McLeod (reviewed manuscript only).

International participants: Livio Cipolletta, Martin Freeman, James Lau, Joseph Sung.

ACKNOWLEDGEMENTS: The authors wish to thank Pauline Lavigne for the preparation of the manuscript.

ENDORSEMENT: The consensus conference was endorsed and organized by the Canadian Association of Gastroenterology and was held in Banff, Alberta, from June 8 to 9, 2002.

FINANCIAL SUPPORT: This work was supported, in part, by "arms length" grants to the Canadian Association of Gastroenterology from Abbott Laboratories Ltd, Altana Pharma Canada Inc, AstraZeneca Canada, Carsen Group Inc (distributors for Olympus in Canada), Janssen-Ortho Inc, Pentax Precision Instrument Corp, a peer-reviewed grant from the Canadian Institutes for Health Research and an institutional award from the McGill University Health Centre Research Institute.

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