Cost-Effectiveness of Proton-Pump Inhibition Before Endoscopy in Upper Gastrointestinal Bleeding

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Background & Aims: **Randomized trials suggest high-dose proton-pump inhibitors (PPIs) administered before gastroscopy in suspected upper gastrointestinal bleeding downstage bleeding ulcer stigmata. We assessed the cost-effectiveness of this approach.** ***Methods:*** **A decision model compared high-dose IVPPI initiated while awaiting endoscopy with IVPPI administration on the basis of endoscopic findings. IVPPIs were given to all patients undergoing endoscopic hemostasis for 72 hours thereafter. Once the IV regimen was completed or for patients with low-risk endoscopic lesions, an oral daily PPI was given for the remainder of the time horizon (30 days after endoscopy). The unit of effectiveness was the proportion of patients without rebleeding, representing the denominator of the cost-effectiveness ratio (cost per no rebleeding). Probabilities and costs were derived from the literature and national databases.** ***Results:*** **IVPPIs before endoscopy were both slightly more costly and effective than after gastroscopy in the U.S. and Canadian settings, with cost-effectiveness ratios of US$5048 versus $4933 and CAN$6064 versus $6025 and incremental costs of US$45,673 and CAN$19,832 to prevent one additional rebleeding episode, respectively. Sensitivity analyses showed robust results in the US In Canada, intravenous proton-pump inhibitors (IVPPIs) before endoscopy became more effective and less costly (dominant strategy) when the uncomplicated stay for high-risk patients increased above 6 days or that of low-risk patients decreased below 3 days.** ***Conclusions:*** **With conservative estimates and high-quality data, IVPPIs given before endoscopy are slightly more effective and costly than no administration. In Canada, this approach becomes dominant as the duration of hospitalization for high-risk ulcer patients increases or that of low-risk ulcer patients decreases.**

Upper gastrointestinal bleeding (UGIB) is a common condition with an estimated cost of US$750 million.[1,2] High-dose IV proton-pump inhibition (PPI) in patients having initially undergone endoscopic hemostasis results in improvements in outcomes,[3,4] while being cost-saving.[5,6] In contrast, the administration of high-dose intravenous proton-pump inhibitors (IVPPI) before endoscopy has remained controversial,[7] and exploratory cost-effectiveness analyses[8,9] did not benefit from recent individual[10] and summary clinical data.[11] The present cost-effective analysis studied the role of high-dose IVPPI administration before endoscopy in patients with suspected UGIB on the basis of contemporary clinical trial data. Any benefit of the IVPPI is assumed to be a class effect,[10–12] and we have thus not intended to support the use of one IVPPI over another. Because of existing variability in health care resource utilization and costs, we assessed both American and Canadian health care settings separately.

Methods

Model Structure and Patient Population

We constructed a decision tree model with the TreeAge Pro Suite Healthcare module 2005 (TreeAge Software Inc, Williamstown, MA) for patients with a suspected episode of acute UGIB, comparing 2 managements: In one, high-dose IVPPI (pantoprazole 80-mg bolus followed by 8 mg hourly) was started while awaiting an initial endoscopy for bleeding; the wait time until endoscopy was modeled to be 24 hours on the basis of existing data.[10,11,13–15] In the second, the same IVPPI regimen was started only after endoscopy. For both, the infusion was continued for 72 hours after the gastroscopy only in patients receiving endoscopic hemostasis for a lesion at high risk for rebleeding[16] followed by a daily oral dose of pantoprazole 40 mg until the end of the time horizon (30 days after endoscopy). All other patients received the daily oral dose after endoscopy. Patients who failed initial endoscopic hemostasis were referred for surgery. The model structure (Figure 1) was based on published trials and validated by expert clinicians (A.B., C.F.). The first strategy was referred to as the pre-endoscopy IVPPI and the second as the post-endoscopy IVPPI.

Patients were stratified into those bleeding from gastroduodenal ulcers, esophageal varices, or other causes (Table 1). Patients with ulcer bleeding were further categorized into high, low, and very low risk groups. The possibility of rebleeding with its consequences was modeled. Patients who died were excluded from the analysis. Our 30-day time horizon is a commonly reported length of follow-up in UGIB trials.[7]

Abbreviations used in this paper: CER, cost-effectiveness ratio; DRG, diagnosis-related group; ICER, incremental cost-effectiveness ratio; LOS, length of stay; PPI, proton pump inhibitor; RIW, resource intensity weight; UGIB, upper gastrointestinal bleeding.

1542-3565/08/$34.00
doi:10.1016/j.cgh.2007.12.037

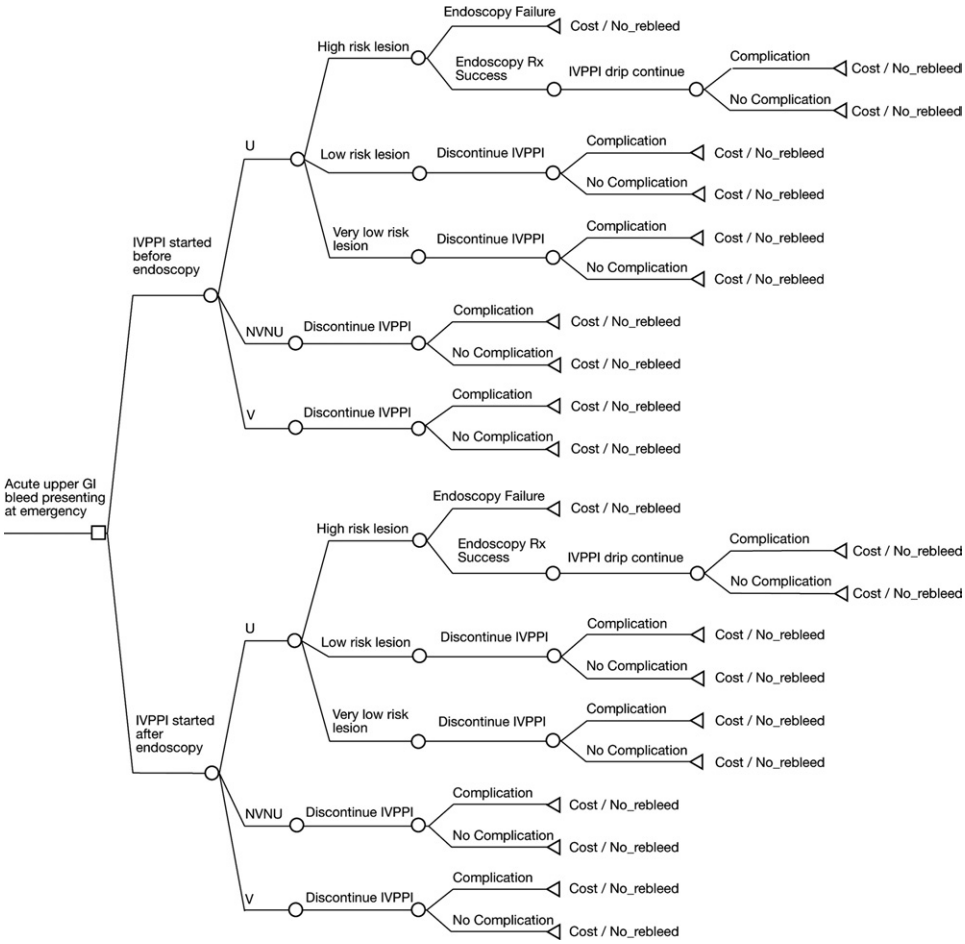

Figure 1. Decision tree of the model. NVNU, nonvariceal nonulcer etiology of bleeding; U, bleeding due to an ulcer; V, variceal cause of bleeding.

Base-Case Scenarios

The unit of effectiveness was the probability of no rebleeding during the 30 days after the gastroscopy. The same model structure and probabilities estimates were used for the Canadian and American settings, but assumptions differed for each with regard to pharmacologic and hospitalization costs, as well as length of stay (LOS).[17]

Probability Assumptions

Literature review. Model probabilities were obtained from a literature search, up to April 2007, of relevant articles in CENTRAL, EMBASE, and MEDLINE, including all randomized trials, meta-analyses, or reviews assessing PPI, greater than a single daily dose, before endoscopy for patients with suspected UGIB. Key words were "ulcer bleeding or hemorrhage, peptic ulcer, nonvariceal and gastric or duodenal erosions, rebleeding, surgery or mortality, intravenous, acid suppression, proton pump, omeprazole, lansoprazole, pantoprazole, rabeprazole, and esomeprazole." We also used the similar articles function and performed handsearches of articles with cross-referencing. We included all fully published human studies in French or English from which rebleeding rates could be estimated.

Probability estimates. The prevalence of bleeding lesions and the proportional repartition according to the level of risk among patients with bleeding ulcers were estimated, because individual trials and meta-analyses have shown that IVPPI given pre-endoscopy lowers the proportion of high-risk and raises that of low-risk ulcer lesions.[10,11,13] No effect of PPI administration pre-endoscopy on variceal or nonulcer nonvariceal lesions was modeled because of inadequate pertinent high-quality evidence. High-risk patients were defined as those with endoscopic high-risk lesions, ie, ulcers exhibiting active bleeding (spurting or oozing), a visible vessel, or an adherent clot.[16,18] Low-risk patients included patients with pigmented dots or clean base ulcers.[7,19] Among the latter, a subgroup of very low-risk patients were identified when they also met a set of published clinical criteria[1,20–23] that allowed discharge after endoscopy (with an empirical attribution of LOS of 1 day). The base-case scenario used estimated proportions from a Cochrane review[11] (which included preliminary data from Lau et al presented in abstract form), whereas an alternate scenario adopted assumptions on the basis of the recent full publication by Lau et al[10] with regard to the proportions of patients with different endoscopic appearances in both pre- and post-endoscopy PPI patient groups.

Costs

Costs (in 2005 US or Canadian dollars) included 2 components, hospital costs (to treat a patient with an UGIB) and additional pharmacologic costs (specific to acid suppression); this conservative approach allowed us the subsequent