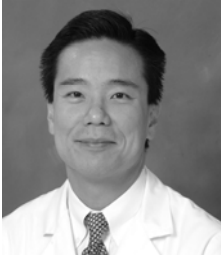


GI Bleeding

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Dr. Lee is involved in the research of outcomes of GI endoscopy. He has published extensively in journals such as the New England Journal of Medicine, American Journal of Medicine and Gastrointestinal Endoscopy.

Good morning. We're going to review 11 abstracts. There are an additional seven in your packet that are of some interest that you can look through on your own. Let's get started.

Abstract 218606: "Can aspirin be reintroduced with proton pump inhibitor infusion after endoscopic hemostatic? A double blinded randomized controlled trial"

This is from Dr. Sung and colleagues from the Prince of Wales Hospital in Hong Kong. This is a randomized, controlled study. It was conducted at three university hospitals in Hong Kong. They looked at 113 patients who required cardiovascular or cerebrovascular prophylaxis using aspirin at 80 mg a day. All of these patients presented with peptic ulcer bleeding which was defined as having active bleeding, a visible vessel, or a clot. These patients underwent endoscopic therapy consisting of injection and thermal therapy and were randomized to 80 mg ASA or placebo. All were treated with pantoprazole 80 mg bolus followed by 8 mg an hour for three days followed by oral pantoprazole 40 mg a day for eight weeks. The primary endpoint was 30-day rebleeding rate and secondary endpoints were transfusion, surgery, hospital stay, one- and two-month mortality, cardiovascular events, and CNS events. In the analysis of 113 patients, 58 patients received aspirin and 55 were randomized to identical placebo. There were no significant differences in demographics and ulcer distributions (duodenal or gastric) between the groups.

Their primary outcome revealed that the 30-day rebleeding rate was 18.9% for patients receiving aspirin versus 10.9% for those receiving placebo. There was no significant difference (P=0.25). Additionally, there were no significant differences in the secondary outcomes of transfusion, surgery, and hospital stay. The main difference noted was that one- and two-month mortalities were significantly different. Patients who received aspirin prophylaxis had a 1.7% mortality at one month versus 9.1% for patients who did not continue aspirin, P=0.08. At two months, patients who were on aspirin had 1.7% mortality versus 14.5% mortality in patients who did not get aspirin (P=0.012).

The conclusion of the authors was that the presence of IV and oral pantoprazole and immediate introduction of aspirin does not substantially increase their risk of recurrent bleeding from peptic ulcers. However, there is increased mortality with discontinuation of aspirin. That's the abstract.

One of the problems is that we do not know what the mortality was from and that the one- and two-month mortalities are very high. If you look at the ISIS-2 trial published in *Lancet* a number of years ago that validated the efficacy of using streptokinase over placebo in patients who were admitted with acute MI, the death rate of patients who got placebo after an acute MI at five weeks was only 13.2%. This is in someone who had an acute MI and got placebo (no aspirin) and had a 13.2% mortality. It seems a bit odd that patients who have a GI bleed and discontinued aspirin should have such a high mortality. We will have to wait to hear that in their presentation or read it in the manuscript. The assumption would be that these patients did not bleed to death, but again it doesn't make any sense why the mortality would be so high.

Another issue with this abstract is that the follow-up was relatively short. Obviously, this is preliminary data and the primary outcome, the rebleeding rate, had a trend towards increased rebleeding in patients who were on aspirin. It was 18.9% versus 10.9%. If they carried this out to six months, is there going to be a difference in rebleeding rate if they enrolled more patients? I don't know, but certainly there is a trend suggesting an increased rebleeding.

So, according to this abstract, it appears safe to restart ASA immediately and it's probably more harmful to stop the aspirin rather than to continue it, especially at the 80 mg dose.

Remember, these patients all had hemostasis, so if you're talking about somebody who didn't get hemostasis for whatever reason, that's a different question. If you can stop the bleeding, certainly the suggestion is you can continue aspirin at the 80 mg dose.

Another concern with this study is that there is a significant difference in mortality in the first two months. As they enroll more patients, is that going to remain significant? I'm not sure.

They don't address the *H. pylori* status, but this is a study done by a very experienced group so I am sure they either stratified it or treated it.

Another question is, why were these patients on aspirin? Was it primary prophylaxis or a secondary prophylaxis – somebody who is at high risk, had an MI, and needs to continue aspirin? It would make a big difference in terms of mortality and morbidity if we knew what complications we're dealing with.

Again, it seems like a very unusual group of patients.

In summary, in terms of recommendations in the U.S., if patients meet criteria for being on ASA prophylaxis, and you see these patients with GI bleeding from aspirin, I think there is support for you to continue aspirin for prevention of cardiovascular and CNS events.

Abstract 219718: “Proton pump inhibitor plus a COX-2 inhibitor for the prevention of recurrent ulcer bleeding in patients with arthritis: A double-blinded, randomized trial”

The first author is Francis Chan from the same group. Francis Chan has published a number of articles relating to the use of aspirin and NSAIDs. A number of these publications have been in very prestigious journals including the *New England Journal of Medicine*, etc. and I think he has probably done the most work in this area and, at least in my opinion, the highest quality work. This was another double-blinded, randomized study from a single university hospital in Hong Kong. The trial consisted of 273 patients presenting with NSAID-induced ulcer bleeding. All had healed ulcers by endoscopy before they were enrolled. If they had *H. pylori* they were eradicated or they were confirmed to have a negative *H. pylori*

status. All required ongoing NSAID treatment; they don't exactly say why. They excluded patients who had renal failure defined as creatinine greater than 2.2, concomitant use of low-dose aspirin, steroids or anticoagulants, and terminal illness such as cancer. They also defined the use of prohibited drugs such as low-dose aspirin as a protocol violation. Their primary measurement endpoint was recurrent bleeding defined by an adjudication committee using pre-specified criteria during a 12-month period. That actually brings up a good point. Many studies that are published don't really define rebleeding. If you think about it, it ends up being a very complex problem because when someone is throwing up blood, you endoscope them, they have a pumping ulcer, it's a no-brainer- it's rebleeding. For somebody who drops their hematocrit a couple points and gets a little bit of a transfusion a day or two after your endoscopic hemostasis, it's unclear if that's a rebleeding. Most of the higher quality studies either document rebleeding based on specific criteria and/or all of the suspected rebleeders are sent to a blinded adjudication committee who rules it as rebleeding or not rebleeding. I think that is the cleanest way to do it and that may explain some of the differences in rebleeding incidences. Again, studies that have less robust criteria where it is very subjective, where the endoscopists are assessing rebleeding, have a potential for bias and I don't think those studies are as relevant.

This particular study consisted of 137 patients who received celecoxib at 200 BID plus esomeprazole 20 BID. The second group of 136 patients received celecoxib plus placebo. These are all patients who had non-steroidal anti-inflammatory drug-related bleeding. After the ulcers healed, they were switched to a COX-2 plus PPI or a COX-2 plus placebo. This is sort of a belt and suspenders approach of using a COX-2 and a PPI to minimize the risk of bleeding.

Demographics were similar between groups. The primary outcome of recurrent bleeding showed a significant difference. Patients who were on a COX-2 plus esomeprazole had 0% rebleed versus patients who were on COX-2 only with rebleed rate of 8.9%. The 95% confidence interval is highly significant at 4.1 to 13.7% and p-value is highly significant at P=0.004. Patients who used concomitant low-dose aspirin were considered to be in protocol violation.

The conclusion of this group was that among patients with a history of NSAID-induced bleeding, esomeprazole plus celecoxib was superior to celecoxib alone for prevention of ulcer bleeding. This makes intuitive sense, but now we actually have data to back that up.

Let me review some of the background regarding this abstract. In the past, one of the strategies for decreasing NSAID-related bleed was to give a PPI. In fact, the only two drugs that have been shown to clinically significantly improve outcome in patients who are on chronic NSAIDs are misoprostol or PPI. In one study, the six-month rebleed rate for patients who took Naprosyn 500 mg bid plus omeprazole 20 mg bid was 4.4%. Whether that 4.4% is significantly higher than what was quoted in this study (0%) is not able to be determined, but you can get pretty good bleeding control using a regular NSAID and PPI. It intuitively makes sense that you would get the best control using a COX-2 and a PPI, and now it has been confirmed. Remember though if you use aspirin and celecoxib, the outcomes are no different from patients taking regular NSAIDs. So if you take a COX-2 and an aspirin, you're losing your additional protection. So it doesn't make sense to use a COX-2 if the patient has to continue on low dose aspirin for cardiovascular or CNS prophylaxis.

In this country only lansoprazole and esomeprazole are FDA approved for NSAID indication. However, I think most of us, including myself, will use any of the other PPIs interchangeably for prophylaxis.

Abstract 222910: “Effects of antisecretory drugs and nitrates on the risk of ulcer bleeding associated with NSAIDs and anti-platelet agents”

This is a study from Spain by Dr. Lanás and colleagues; another group of very experienced investigators with lots of publications on GI bleeding. Let me give you a little bit of background on this particular abstract because not everyone may be familiar with the effect of nitrates on GI bleeding. It has been known experimentally that nitric oxide increases blood flow in the gastric mucosa. At least in rats, administration of drugs that release nitric oxide, such as transdermal nitroglycerin, accelerates the healing of ulcers. In fact, there are drugs that are under development including NSAIDs and aspirin and other drugs that release nitric oxide with the thinking that they may be less damaging to the gastric mucosa. Preliminary studies have shown that aspirin derivatives that release nitric oxide may induce less damage in the GI mucosa. On the other hand, nitrovasodilators inhibit platelet aggregation which may contribute to GI bleeding. Because of this information, known in the basic science literature, this group from Spain did a preliminary study followed by a larger study that was published in the *New England Journal of Medicine* in September, 2000 entitled “Nitrovasodilators, low dose aspirin or other non-steroidal anti-inflammatory drugs and the risk of upper GI bleeding.” The authors are the same group. They found that use of non-steroidal anti-inflammatory drugs other than low-dose aspirin were associated with an increased risk of bleeding from peptic ulcers. The important conclusion, however, was that use of nitrovasodilators was associated with a decreased risk of bleeding (odds ratio was 0.6, 95% CI of 0.4-0.9, similar to antisecretory therapy). Their thought was that nitrates might be protective. Building on that particular study, they did another study which is being presented at this meeting.

This abstract is a case-controlled study with prospective data collection. Patients were seen at 40 general hospitals in Spain which included 2,077 consecutive patients admitted with upper GI bleeding confirmed by endoscopy. They had a control group in a 2:1 ratio so the control patients were 5,532 patients who were matched by age, hospital, and month of interview. The controls were not hospitalized for ulcer bleeding, NSAID, or aspirin-related diagnosis. Their primary endpoint was risk of being admitted with upper GI bleeding according to PPI, H₂ receptor antagonist and nitrate use. They did not do any intervention.

Of the 2,077 overall patients, they found that PPI, H₂ blockers and nitrates all reduced risk of being admitted with GI bleeding. The risk reduction ranges from 0.33 to 0.65 to 0.52 for nitrates. When they looked at the group of patients who took aspirin and NSAIDs only, patients who had PPI and H₂ blockers were less likely to be admitted with bleeding. If they looked at patients who took low dose aspirin, PPIs and H₂'s were protective but nitrates were not. They also state that there was no significant difference among the three most common NSAIDs used in Spain (diclofenac, ibuprofen, and Naprosyn). All had the same bleed risk. In terms of clopidogrel (Plavix), only PPI was effective with a relative reduction of 0.19. In patients on anticoagulants, none of these drugs were protective.

Their conclusion was people with nitrates, H₂ blockers, or PPIs are associated with reduction of risk of developing upper GI bleeding when taking NSAIDs or aspirin or a subset taking aspirin only at regular doses. Only PPI was associated with a marked and consistent risk reduction among patients receiving all types of agents including non-aspirin antiplatelet agents, which if reproduced is relatively new. In other words, PPIs are the best. Again, something I think all of us knew in this room. Lastly, they concluded that nothing was effective for patients who are on anticoagulation.

I had a few comments about the abstract. We're looking at only the abstract, so it is hard to know what was actually done since they only have a small amount of room to describe the study. Because this was a large study collected from a number of hospitals, the definition of medication use was not exactly specified. Is that all of the time, some of the time, were they on it chronically, etc. Patients were not

stratified by the type of bleeding. Naturally, you would think that H2 wouldn't work all that well for ulcer prophylaxis for NSAIDs. It might work for something else, I don't know. PPIs should work for mucosal disease such as ulcers but if these patients came in with a Mallory-Weiss tear, I would think it would have no effect on them. Again, it would be interesting to see what the results would be if the patients were stratified according to the type of lesion. Nitrates were effective in the entire group of 2,077 patients that came in with bleeding. When they looked at the subset, it was only effective in patients who took regular dose aspirin and not against low-dose aspirin or aspirin plus NSAIDs, which is kind of odd. It doesn't make complete sense. If you go back and look at the figures, however, the 95% confidence interval for protective effect of nitrates on patients who took regular dose aspirin is 0.44 to 0.98 and if the 95% CI reaches one, that means it is basically not significant, so 0.98 seems pretty close to 1. That may suggest that nitrates may not be all that protective, but we need to see some better studies that look specifically at using nitrates to see if there is any benefit. There are a number of drugs that are under development, as far as I understand, that may clarify this issue.

Abstract 221680: "Major GI events among elderly chronic users of COXIBs and non-selective NSAIDs, with/without aspirin"

This is a retrospective cohort review of an electronic medical record database from 5,000 physicians in 27 states and approximately three million patients. They picked out 12,729 patients who used NSAIDs or COX-2s chronically. Chronic use was defined as two or more medication mentions of the same drug class within 60 days. It's not entirely clear to me what that means. I think it means that it was documented in the chart that the patient was on some sort of a COX-2, two times a day for a 60-day period. All of these patients were greater than 65 years old and they were not allowed to switch between NSAID and COX-2. If they switched back and forth, they were excluded. In those 12,729 patients, their primary endpoint was GI bleeding occurring within one year. GI hemorrhage was defined based on ICD-9 codes of 578, 578.0, 578.1, and 578.9 which are a little restricted. They controlled for a number of other variables – age, gender, prior GI protective drug use, major and minor GI events, and pre- and post-index harmful GI drug use.

When they compared NSAIDs versus a COX-2, the odds ratio was 1.35 favoring COX-2. The 90% CI was 1.01 to 1.8. When they compared NSAID plus aspirin to a COX-2, the results were a little bit more impressive with an odds ratio of 1.68, and when they compared COX-2 plus aspirin versus a COX-2, the odds ratio went the other way and was 0.96.

Their conclusion was that risk of major GI events was highest among chronic users of NSAIDs plus aspirin, followed by those on NSAIDs alone. Again, makes sense. Chronic users of NSAIDs alone have statistically significant higher risk of bleeding than users of COX-2 alone. Additionally, aspirin did not significantly increase the risk of GI events among COX-2 users; this is not consistent with other studies that suggest that the reverse was actually true.

I had a couple of comments with regard to the design of the study. This study included a very large number of patients. One of the downsides to doing that is you can't get a lot of details because you have so many records. Perhaps because of that it is not clear to me what major and minor GI events were or how they were defined. Even though the differences were statistically significant, the odds ratios of 1.35 (NSAIDs v. COX-2) and 1.68 (NSAIDs + ASA v. COX-2) have confidence intervals very close to 1. I don't know what this means clinically.

Lastly, the results do not agree with the CLASS study that looked at celecoxib plus aspirin. As I mentioned earlier, in patients on celecoxib and aspirin, the protective effect of COX-2 is negated by the use of aspirin. In this particular study that was not really the case, but the odds ratio was 0.96 on that

particular comparison and again, that is very close to 1. So, intriguing but I think there are some problems with this study.

Abstract 225143: “The effect of scheduled second endoscopy against intravenous high dose omeprazole infusion as an adjunct to therapeutic endoscopy in prevention of peptic ulcer rebleeding – A prospective randomized study”

This is from Hong Kong. I'd like to present a little bit of background because in the United States, second look endoscopy after therapeutic endoscopy is not routinely done. It is more commonly done in Europe and in Asia, and there are a number of studies that looked at second look endoscopy. There was a meta-analysis of second look endoscopy that was published in *Gastrointestinal Endoscopy* in 2004. They found that the five studies that looked at second look endoscopy in a randomized, controlled fashion did, in fact, decrease the rebleeding rate from 18.2% to 12%. The number needed to treat was 16, meaning you need to scope 16 patients twice to get a benefit. At least that particular study seemed to suggest that there was some benefit to doing a second look on a routine basis on patients who've had endoscopic hemostasis. The same group of authors looked at this in a randomized controlled fashion, and in their publication in *Gut*, revealed a decrease in rebleeding from 14% to 5% at the end of 30 days. Relative risk reduction was 0.33 and this was significant with a p-value of 0.031. In their study, the rate of surgery was also significantly lower for patients undergoing second look endoscopy; 1 versus 6% with a p-value of 0.05. In the meta-analysis, there was no significant difference for things like surgery, mortality, transfusion, etc. I think we are all also aware that proton pump inhibitor therapy is effective for decreasing rebleeding after endoscopic hemostasis. In my opinion, the best study comes from Hong Kong which was published in the *New England Journal of Medicine* and really got the ball rolling. There was a nice review published in the Cochrane database in 2004 that looked at 24 randomized controlled trials that addressed the issue of PPI after GI bleeding and the Cochrane review conclusion was that rebleeding was significantly decreased with PPI therapy. It went from 17.3% to 10.6% with PPI therapy. PPI therapy also significantly decreased surgery from 9.3 to 6.1%. At least looking at the background, it would suggest both PPI and second look endoscopy might be good ways to decrease the risk of rebleeding.

Because of that, these authors randomized patients to either PPI or second look endoscopy. This was a randomized controlled trial done in two university hospitals in Hong Kong. There were 164 patients with active bleeding who underwent endoscopic hemostasis. Their primary endpoint was not exactly stated but assumed to be a 30-day rebleeding rate. The secondary endpoints were ICU stay, hospital stay, transfusion, and mortality. Their intervention consisted of 80 patients who had second look endoscopy in 16-24 hours. If they still had persistent stigmata, they got more therapy. Eighty-four patients did not get a second look but they received high-dose omeprazole, which I assume meant high-dose continuous infusion. Their results revealed a rebleed rate of 9.4% versus 6.3%. For patients with second look endoscopy, it was not significantly different. If you look at the surgery rate, again not significantly different.

Their conclusion was second look endoscopy and adjunctive high dose omeprazole infusion are effective strategies in prevention of peptic ulcer rebleeding after therapeutic endoscopy and there were no significant differences.

Abstract 222326: “Meta-analysis of bleeding with low-dose aspirin and clopidogrel in randomized controlled trials”

This is a meta-analysis from McQuaid and Laine. Patients were from 25 randomized controlled trials of aspirin or clopidogrel (Plavix®) for cardiovascular prophylaxis. The reason they did this study is to address problems and shortcomings of previous meta-analyses. The primary endpoint in this meta-

analysis was major bleeding (author-defined, or what led to hospitalization), transfusion, or death. The second primary endpoint was intracranial bleeding. There was no intervention. They assessed the Jadad score. Jadad score is a numerical score between 0-5 that looks at the quality of the study. It uses seven items, five of which are positives and two of which are negatives. For example, if you have a study described as randomized, you get a point. You deduct a point if the study was described as double blinded but the method of blinding was inappropriate. The highest is 5, the lowest is 0. Five means you have a very high-quality study. In this study, 19 out of 25 studies were of very high quality and 23 were reasonably high-quality studies.

They found when comparing aspirin versus placebo that there was an absolute increase in bleeding of 0.12% per year (1.2/1000 patients). Number needed to harm was 833. In other words, you needed to give aspirin to 833 patients to cause one bleed. No study compared clopidogrel to placebo. The studies that compared aspirin to clopidogrel showed a relative risk of 1.45 for major GI bleeding rate for aspirin. But, the 95% CI crossed to 1 so it was not significant. If they looked at all GI bleeding, again aspirin was worse with a relative risk of 1.34. Absolute increase incident was 0.12% per year. The number needed to harm was exactly the same at 833. They performed a cost analysis showing that the cost to prevent one major GI bleed by switching someone from aspirin to clopidogrel was \$1,216,080. Yes, you can decrease the bleeding by switching to clopidogrel but it's going to cost a lot of money. When they compared aspirin to aspirin versus clopidogrel, as you can imagine, giving aspirin alone was better with the relative risk reduction of 0.56. Finally when they compared clopidogrel versus aspirin plus clopidogrel again, single therapy was better with a relative reduction of 0.34.

Abstract 216388: "Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in unselected upper gastrointestinal bleeding: A Cochrane systematic review and meta-analysis"

This is a highly relevant question because when we see patients in the ER with bleeding, they often are started on a PPI before we even get to them. If they are not started on a PPI, we usually ask them to start a PPI. This meta-analysis selected five randomized controlled trials that addressed this issue. Patients with unselected GI bleeding of unknown source were given either oral or IV PPI versus placebo or an H2 blocker. The primary endpoint was 30-day mortality. Secondary endpoints were 30-day rebleeding, surgery, stigmata, recent hemorrhage, hospital stay and transfusion. They were able to perform full meta-analysis on dichotomous outcomes. So if the outcome was recorded as yes or no – a patient died or lived – they were able to do the meta-analysis; however, they could not get adequate data to do meta-analysis on continuous variables.

Their results were that early PPI, either oral or IV, reduced the chance of finding a stigmata of recent hemorrhage. In patients who did not get PPIs, there was a 46.5% chance of finding a stigmata of recent hemorrhage versus 37.2% chance of finding stigmata of hemorrhage (OR = 0.67 and this was highly significant). If they looked at clinically significant variables of mortality, rebleeding, surgeries, clotting, upper GI tract, active bleeding, transfusion, there was no significant difference.

Their conclusions were that PPI treatment initiated prior to endoscopy in unselected upper GI bleeding significantly reduced the proportion of patients with stigmata of recent hemorrhage at index endoscopy. However, there was no evidence that PPI treatment could improve clinically important outcomes such as mortality, rebleeding, or need for surgery. This is intriguing and something that I did not expect.

Abstract 219251: “Use of GI prophylaxis in patients discharged from hospital on ulcerogenic medicines”

This is a retrospective chart review from a single university hospital in the U.S. The study looked at 338 patients discharged on aspirin, NSAIDs, warfarin, or corticosteroids over a three-month period. Primary endpoint was discharge medication of PPI or misoprostol. The question they asked for patients being discharged on ulcerogenic medication was how many patients are on appropriate prophylaxis? This addresses an important question.

Results showed that 35% of patients received PPI prescription, 1% misoprostol, 4% H2 receptor antagonists, and 12% bid PPI. They risk stratified patients using age, Charlson index and type of medication, and found that the chance of being prescribed prophylaxis went up as the risk went up. It was 24% in low risk versus 60% at high. They also stratified it according to Charlson index and again, it went from 40% at low risk to 51% at high risk.

Their conclusion was although there was a trend toward higher use of prophylaxis in the highest risk patients, only 60% were discharged on appropriate therapy. Twenty-four percent of low risk patients were prescribed prophylaxis without a clear indication. Adherence to current guidelines was suboptimal.

One comment I have is about their stratifying patients according to risk. Interestingly enough, there are no specific guidelines on how to risk stratify patients who are at high risk or low risk. There have been several attempts. The American College of Gastroenterology published a risk stratification scheme in 1998. According to these guidelines, high risk was defined as patients who have prior history of adverse GI event such as bleeding (increased risk was 4-5 fold), age greater than 60 (increased risk 5-6 fold), high dose of NSAIDs (increased risk 10 fold), concurrent steroids (increased risk 4-5 fold), and concurrent anticoagulation (increased risk 10-15 fold.) This particular study did not use that. If we look at the literature, how do we risk stratify patients into high or low risk? One of the studies we can use is the MUCOSA trial (misoprostol for prophylaxis of NSAID induced ulcer) published in the *Annals of Internal Medicine* in 1995. In that particular study, risk factors were increasing age, history of peptic ulcer, bleeding, and cardiovascular disease. Patients who have all four risk factors had a 9% risk of major complication in six months. Again, this study did not use that risk stratification regimen and I could not find anything in the literature that validates using the Charlson index, the Charlson index and age, and type of medication as risk stratification. They also did not talk about *H. pylori*. This is a chart review. There is a meta-analysis that looked at worldwide *H. pylori* infection on NSAIDs and peptic ulcer disease. This was published in *Lancet*, 2002 and they found that NSAIDs with *H. pylori* infection were 61 times more likely to have peptic ulcer than non-infected NSAID ulcers. Again, a huge difference if you have *H. pylori*. Either factor alone increases the risk of ulcer disease by 20-fold. *H. pylori* infection and NSAID use increase risk of ulcer bleeding by 1.8 and 4.9 fold respectively. When present together, they increase the risk of ulcer bleeding by 6 fold. So, again, not knowing what the *H. pylori* status is introduces a huge bias into this particular paper. They also talk about H2 receptor antagonists which I believe is inappropriate because there are no studies to suggest that H2 receptor antagonists are an effective prophylaxis. In fact, all the studies show that it is not effective against NSAIDs.

Finally, there is the question of who do you prophylax? Again, I could not find any official society guidelines recommending who to prophylax. I looked at a number of expert opinions and what I culled out of the literature was patients who have history of complicated ulcer it is definitely worthwhile to test and treat *H. pylori*. I think that is a no-brainer even if you are not on NSAIDs. If someone comes in and says I had ulcer bleeding, of course, we are going to test and treat for *H. pylori*. If they have a history of complicated ulcers, most of the expert consensus appears to be that they need to be on prophylaxis which consists of either misoprostol or PPI. Again, they don't really talk about that here. If they don't have a

history of complicated ulcer, consider testing for *H. pylori*. Most of the experts feel that is worthwhile, again, because there is such an increased risk of complication with *H. pylori* and NSAIDs. Consider giving misoprostol or PPI if they have other risk factors. If somebody has no history of ulcer and no risk factor, you cannot really find any clear-cut recommendation that these patients need to be on prophylaxis. I don't think anybody recommends putting a young patient who needs 6 weeks of naproxen for knee pain on prophylaxis. Again, this study does not address that.

Abstract 217224: “Early is good; is very early better? Does endoscopy within 6 hours of presentation improve outcomes in high-risk patients presenting with acute non-variceal upper gastrointestinal bleeding (ANVUGIB)”

This was a retrospective chart review of a five-year period from a single tertiary care university hospital in Canada. They looked at 221 patients with non-variceal upper GI bleed and a Rockall score of greater than or equal to three. Their primary endpoint was rebleeding, surgery, mortality, or readmission within 30 days (any adverse outcome). Their secondary endpoint was length of hospital stay and transfusion 24 hours after endoscopy. There was no intervention.

Results showed that when they compared the patients who had endoscopy within six hours versus patients who had endoscopy between six hours and one minute and 24 hours, there was no significant difference in any adverse outcome. However, patients who had very early endoscopy were more likely to undergo hemostasis (50% versus 36%) and they were more likely to have a length of stay greater than five days (64% versus 49%). Their conclusion was that there is no difference in the rate of adverse outcomes in high-risk acute non-variceal upper GI bleed patients who undergo very early endoscopy and early endoscopy. Patients who received very early endoscopy are more likely to require both endoscopic hemostasis and longer stays in the hospital. Because it is a retrospective, non-randomized study, it is really hard to know what to say about this.

Abstract 222841: “Serum markers of prognosis following emergency department presentation for GI bleed”

This is a retrospective chart review from a single university hospital in the U.S. designed to determine risk factors for death after presentation with GI bleed. There were 231 patients with GI bleeding over a 30-month period. The primary endpoint was death at any time. Fifty (22%) patients died (upper and lower GI bleed). The chance of being alive six months after a GI bleed was 89%, after one year 85.4%, after 18 months 79%, and after two years, 69% of patients were alive. What factors predicted death after a GI bleed? Multivariate analysis revealed significant factors to be older age, high creatinine, high troponin, low sodium, and high partial thromboplastin time (PTT). Relative risk ranged from 1.4 for age to 4.2 for high creatinine.

I think it makes intuitive sense, the sicker you are, the more markers you have, the higher the mortality. Interesting, but we need some validation to see if this is true elsewhere.

Abstract 225089: “The predictive value of admission hematocrit in patients hospitalized with acute upper and lower GI bleeding (GIB)”

This is a retrospective cohort study from a single university hospital in the U.S. They looked at 7,909 patients admitted with GI bleeding to their institution and measured the primary endpoint on inpatient mortality. For all GI bleeders, in hospital mortality was 3.3%. For upper GI bleeders it was 3.7% and for lower GI bleeders it was 1.8%. Multivariate logistic regression was performed to determine if admission hematocrit (HCT) was an independent predictor of mortality adjusting for age, sex, race, pulse, blood

pressure, platelet count, prothrombin time (PT), history of GI bleed, diabetes, cirrhosis, and renal failure. Serum hematocrit less than 25% was an independent predictor ranging from 19% higher mortality to 69% if your hematocrit was less than 10%. The odds ratio were all less than 2.5 but were statistically significant.

Thank you for your attention.

Abstracts Discussed

218606: Can aspirin Be Reintroduced With Proton Pump Inhibitor Infusion After Endoscopic Hemostasis? A Double Blinded Randomized Controlled Trial. *Joseph Sung, James Lau, Jessica Ching, Wai-Keung Leung, Yuk-Tong Lee, Justin Wu, Vincent Leung, Francis Chan*

Background: Among patients with aspirin-induced bleeding ulcers who received pantoprazole infusion after endoscopic hemostasis, it is uncertain whether aspirin can be reintroduced immediately. Aim: This study aims to investigate whether early reintroduction of aspirin is safe in patients who received intravenous pantoprazole for peptic ulcer bleeding. Method: This double-blind, placebo-controlled, randomized trial included patients who required aspirin for cerebrovascular (CNS) or cardiovascular (CVS) diseases but developed ulcer bleeding. After confirmation of peptic ulcer bleeding (active bleeding, visible vessel or adherent clot), endoscopic hemostasis was applied using epinephrine injection and thermal coagulation. Patients were randomized to receive aspirin 80mg daily or placebo aspirin daily. All patients received intravenous pantoprazole (80mg bolus injection followed by 8mg/hour) for 72 hours and then oral pantoprazole 40 mg daily until end of follow up at 8 weeks. The primary endpoint was recurrent upper gastrointestinal bleeding within 30 days. Secondary endpoints included blood transfusion, requirement for surgery, hospital stay, 1-month and 2-month mortality, and cardiovascular/cerebrovascular event. Results: In this interim analysis, 113 patients were randomized (58 to aspirin and 55 to placebo). The aspirin and placebo groups were comparable in age (74.2yr vs 73yr), gender (men: 62% vs 69%), indications for aspirin (CVS:CNS:both 33:19:6 vs 30:19:6), previous history of ulcer (6.9% vs 3.7%) and concomitant use of NSAID (12% vs 11%). Patients randomized to aspirin and placebo also have comparable ulcer location (GU:DU 28:30 vs 33:22), size (1.13cm vs 1.20cm) and ulcer appearance (bleeding: visible vessel: adherent clot 16:24:18 vs 17:21:17). Recurrent bleeding within 30 days was documented in 11 (18.9%) who received aspirin and 6 (10.9%) who received placebo (Log rank test P=0.25). There was no difference in requirement for blood transfusion, surgery and hospital stay. The aspirin-treated patients have lower 1-month (1.7% vs 9.1%, P=0.08) and 2-month (1.7% vs 14.5%, P=0.012) mortality compared to those who received placebo. Conclusion: In the presence of intravenous and oral pantoprazole, immediate reintroduction of aspirin has not substantially increased the risk of recurrent bleeding from peptic ulcers. There is, however, an associated increased mortality with discontinuation of aspirin.

219718: Proton Pump Inhibitor Plus a COX-2 Inhibitor for the Prevention of Recurrent Ulcer Bleeding in Patients With Arthritis: A Double Blinded, Randomized Trial. *Francis Chan, Vincent W Wong, Bing Y Suen, Justin C Wu, Wai K Leung, Yuk T Lee, James Y Lau, Joseph J Sung*

BACKGROUND Among patients with a history of NSAID-induced ulcer bleeding, neither NSAIDs plus a proton pump inhibitor (PPI) nor a COX-2 inhibitor is adequate to prevent recurrent ulcer bleeding. AIM To investigate whether PPI plus a COX-2 inhibitor is superior to COX-2 inhibitor alone for the prevention of recurrent ulcer bleeding in patients with previous ulcer bleeding. METHODS Patients with arthritis who presented with NSAID-induced ulcer bleeding confirmed by endoscopy were eligible if they: 1. had healed ulcers on follow-up endoscopy, 2. were H. pylori negative or eradicated, and 3. required regular NSAIDs. The exclusion criteria were renal failure (creatinine >2.2 mg/dl), concomitant use of low-dose aspirin, steroids or anticoagulants, malignancy and terminal illnesses. The use of prohibited drugs (low-dose aspirin, NSAIDs, steroids, anticoagulants, or other anti-ulcer drugs) during the study period was a protocol violation. RANDOMIZATION After the ulcers had healed, all patients received celecoxib 200 mg b.i.d. They were randomly assigned to esomeprazole 20 mg b.i.d. or its placebo for 12 months. PRIMARY ENDPOINT Recurrent ulcer bleeding determined by an adjudication committee using pre-specified criteria. RESULTS In the intention-to-treat analysis, which included 273 patients (137 receiving celecoxib plus esomeprazole and 136 receiving celecoxib plus placebo). The probability of recurrent ulcer bleeding during the 12-month period was 0% in the esomeprazole group and 8.9% (95% CI, 4.1 to 13.7) in the placebo group (log rank test, P=0.0004). During the study period, 16.1% of patients in the esomeprazole group and 15.4% in the placebo group used low-dose aspirin. Among patients who did not use concomitant aspirin, the probability of recurrent ulcer bleeding was 0% in the esomeprazole group and 7.1% (95% CI, 2.4 to 11.8) in the placebo group (P=0.004). CONCLUSION Among patients with a history of NSAID-induced ulcer bleeding, esomeprazole plus celecoxib was superior to celecoxib alone for the prevention of recurrent ulcer bleeding. This study was not sponsored by pharmaceutical companies.

Baseline characteristics

	Esomeprazole n=137	Placebo n=136
Men %	47	49
Mean age (SD)	70 (12)	72 (11)
OA/RA/Others %	83/3/14	90/2/8
Smoking %	10	10
Drinking %	10	9

Co-morbid illnesses %	34	35
>1 episode of prior ulcer bleed %	18	19
Previous H. pylori infection %	44	51
Location of bleeding ulcers prior to enrolment GU/DU/both %	58/34/8	57/36/7

222910: Effects of Antisecretory Drugs and Nitrates on the Risk of Ulcer Bleeding Associated With NSAIDs And Anti-Platelet Agents. Angel Lanas, Luis A Garcia-Rodriguez, Maria T Arroyo, Fernando Gomollon, Faust Feu, Montse Forne, Sofia Aleman, Enrique Garcia, Luis Bujanda, David Nicolas

Background and Aims: After the withdrawal of rofecoxib, an increased prescription rate of some non-selective NSAIDs has been observed, but, according to recent reports, additional prevention strategies are not being followed. In this study we report the effect of antisecretory drugs (proton pump inhibitors-PPI; H2-receptors antagonists- H2-RA) and nitrates on the risk of upper gastrointestinal ulcer bleeding (UGIB) associated with NSAID use in clinical practice Methods: Type of Study: hospital-based case-control study with prospective data collection. Setting: A network of 40 general hospitals integrated within the Spanish Association of Gastroenterology. Cases were consecutive patients with UGIB confirmed by endoscopy. Controls matched 2:1 to cases by age (5 years range), hospital and month of interview were individuals with an outpatient visit or hospitalised with a primary diagnosis that was neither an indication nor a known contraindication of NSAID or low dose aspirin treatment. The same structured questionnaire was used in all sites. Relative risk (RR) of UGIB was estimated using logistic regression analysis. Results: 2,777 cases and 5,532 controls have been included. Overall, current use of PPI (RR:0.33; 95%CI:0.27-0.39), H2-RA (RR:0.65; 0.50-0.85) and nitrates (RR:0.52; 0.38-0.70) reduced the risk of developing an UGIB event. The risk reduction was stronger with PPI use among both non-aspirin NSAID (RR: 0.13; 0.09-0.19; vs 0.30; 0.17-0.53 with H2-RA and 0.48; 0.19-1.24 with nitrates) and aspirin users (RR: 0.30; 0.20-0.40 vs. 0.40; 0.24-0.68 with H2-RA and 0.66; 0.44-0.98 with nitrates). Among individual NSAIDs, a similar risk reduction effect with PPI was observed for the 3 most widely used (diclofenac, ibuprofen and naproxen). Among low-dose aspirin users, PPI (RR:0.32; 0.22-0.51) and H2-RA (RR: 0.40; 0.19-0.73)use were associated with risk reduction, while nitrates had a weaker effect (RR: 0.69; 0.36-1.04). In patients taking clopidogrel, only PPI use was associated with a significant risk reduction (RR: 0.19; 0.07-0.49). However, among patients taking anticoagulants neither nitrates (0.67; 0.33-1.34), nor H2-RA (0.88; 0.32-2.45) or PPI use (0.67; 0.37-1.21) were associated with a significant effect on the risk of UGIB event. Conclusion: Treatment with nitrates, H2-RA or PPI is associated with a reduction of the risk of developing UGIB events in patients taking NSAID or aspirin. However, only PPI therapy was associated with a marked and consistent risk reduction among patients receiving all types of agents including non-aspirin anti-platelet agents. Protection was much less apparent in patients on anticoagulant therapy.

221680: Major GI Events among Elderly Chronic Users of COXIBs and Non-selective NSAIDs, with/without Aspirin. Jingshu Wang, C. Daniel Mullins, John Naradzay, Kimberly B Howard

Objective: The gastrointestinal (GI) risks associated with the use of COX-2s versus traditional non-steroidal anti-inflammatory drugs (NSAIDs) were documented in clinical trials. The objective of this study was to estimate the rates of major GI events among elderly chronic users of COX-2s versus traditional NSAIDs, with and without aspirin (ASA), in routine clinical practice. Methods: This analysis utilized a retrospective cohort from the GE logician database (Centricity EMR), which contained the medical records of 3 million patients seen by 5,000 physicians across 27 states. Inclusion/exclusion criteria: chronic use (defined as 2 or more medication mentions of the same drug class within 60 days) of NSAIDs or COX-2s between January 1, 1999 and June 30, 2003, age 65 or older on index date, no switch between COX-2s and NSAIDs during the follow-up period, which continued until the earlier of the end of one year or when a major GI event occurred. Major GI events were defined as GI hemorrhage including melena (ICD-9 codes: 578, 578.0, 578.1, and 578.9). Descriptive and multivariate logistic analyses were conducted to determine how the rate of major GI events differed across chronic users of COX-2s (reference group), NSAIDs, COX-2s+ASA, and NSAIDs+ASA. In order to account for channeling bias, we controlled for major and minor GI events in the year prior to the index date, and prior GI protective drug use. Other control variables included: gender, age, and pre or post-index GI harmful drug use. Results: Of the 12,729 patients in the study, 7,338 were on COX-2s alone (105 major GI events in the year prior to the index date and 127 in the year after), 3,826 were on NSAIDs alone (40 and 79), 963 were on COX-2s+ASA (13 and 17), and 602 were on NSAIDs+ASA (4 and 16). Compared to chronic COX-2s-alone users, NSAIDs-alone users had a statistically significantly higher rate of GI events (OR=1.35, 95% CI: 1.01-1.80). Chronic users of NSAIDs+ASA also had a higher rate of GI events, and the effects approached statistical significance (OR=1.68, 95% CI: 0.99-2.86). COX-2s+ASA users had similar rates of GI events as COX-2s-alone users (OR=0.96, 95% CI: 0.57-1.61). Conclusions: The risk of major GI events was highest among chronic users of NSAIDs+ASA, followed by those on NSAIDs alone. Only the chronic users of NSAIDs alone had a statistically significant higher risk than users of COX-2s alone. The addition of ASA did not significantly increase the risk of GI events among COX-2 users.

225143: The Effect of Scheduled Second Endoscopy Against Intravenous High Dose Omeprazole Infusion As an Adjunct to Therapeutic Endoscopy in Prevention of Peptic Ulcer Rebleeding - A Prospective Randomized Study. Philip W Chiu, Henry Joeng, Catherine Choi, Kwok Hung Kwong, Siu Ho Lam

Background From our randomized study, scheduled second endoscopy reduces rebleeding in bleeding peptic ulcers [GUT 2003.52: 1403-7]. Intravenous high dose omeprazole infusion is another strategy established to reduce rebleeding. This study aimed to compare second endoscopy against intravenous omeprazole infusion in prevention of ulcer rebleeding. Patients and Method We recruited patients who had bleeding peptic ulcer with endoscopic stigmata of acute bleeding, visible vessel or adherent clot and hemostasis achieved on primary endoscopy. One group (2nd OGD) received scheduled second endoscopy 16-24 hours after initial haemostasis, and further therapy applied if endoscopic stigmata persisted as above. Another group (PPI) received high dose adjunctive omeprazole infusion. Those patients that developed rebleeding would receive operation if further endoscopic therapy failed. The outcome measures included rebleeding, transfusion, length of stay, and mortality. Results From 2003 to 2005, 335 patients presented with bleeding peptic ulcers. After endoscopic haemostasis, 164 eligible patients were randomized, 84 to PPI group and 80 to 2nd OGD group. 8 (9.4%) in the PPI group and 5 (6.3%) in the 2nd OGD group sustained rebleeding (Chi square test $p = 0.43$; RR = 0.63, 95% CI 0.19 - 2.03). There is no difference in the probably of rebleeding within 30 days upon Kaplan Meier statistics (Log rank test $p = 0.54$) (Fig 1). The number of patients that required surgery for rebleeding was 4 (4.8%) in PPI group and 1 (1.3%) in 2nd OGD group ($p = 0.36$; RR = 0.25, 95%CI 0.03-2.32). There was no difference in the hospital stay, ICU stay, transfusion or mortality between the two groups. Conclusion Both scheduled second endoscopy and adjunctive high dose omeprazole infusion are effective strategy in prevention of peptic ulcer rebleeding after therapeutic endoscopy.

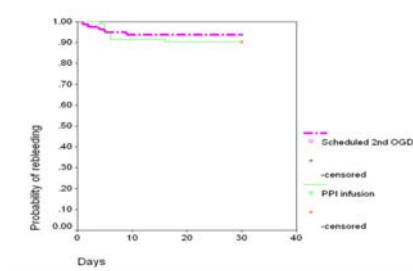


Fig 1

222326: Meta-Analysis of Bleeding With Low-Dose Aspirin and Clopidogrel In Randomized Controlled Trials. Kenneth McQuaid, Loren Laine

BACKGROUND: Prior meta-analyses of low-dose aspirin have shortcomings: doses outside the accepted 75-325mg range are included, concurrent anticoagulant use is allowed, duration of therapy is not considered, all CV prevention studies are not included, the most clinically relevant results (absolute increase in incidence, number needed to harm (NNH)) are not provided. **METHODS:** PUBMED and Cochrane CCTR were searched for RCTs of aspirin (75-325 mg qd) and/or clopidogrel therapy for prevention of CV disease. Primary endpoints were major bleeding (author-defined, or led to hospitalization, transfusion, or death) and intracranial bleeding. **RESULTS:** 25 studies were included. Study quality was good: Jadad score (0-5) was ≥ 3 in 23 studies and ≥ 4 in 19. **Aspirin vs. Placebo:** Meta-analysis of placebo-controlled aspirin trials is shown in the Table. The weighted incidence of major GI bleeding with placebo was 0.12% per year. The absolute increase in incidence with aspirin above placebo was 0.12% per yr (95% CI, 0.07-0.19% per yr) and NNH at 1 yr was 833 (526-1429). **Aspirin vs. Clopidogrel:** No study compared clopidogrel with placebo. One RCT (N=19,485) compared clopidogrel with aspirin 325mg. The RRs of major GI bleeding (RR 1.45; 1.00-2.10) and all GI bleeding (RR 1.34; 1.11-1.61) were increased in patients taking aspirin. The absolute increase in incidence of major GI bleeding was 0.12% per yr (0.00-0.28% per yr) with an NNH at 1 yr of 833 (95 % CI, 357- ∞). The cost to prevent one major GI bleeding episode from aspirin in 1 yr by substituting clopidogrel would be \$1,216,180. **Aspirin + Clopidogrel vs. Either Alone:** Two RCTs (N=20,161) revealed a decreased risk with aspirin alone (RR=0.56; 0.39-0.80) and with clopidogrel alone (RR=0.34; 0.23-0.51). **CONCLUSIONS:** Low-dose aspirin doubles the risk of major GI bleeding compared to placebo, but the absolute increase in annual incidence is modest at 1.2 patients per thousand. An increased risk with "higher" low-dose vs. "lower" low-dose aspirin was not seen. Aspirin increases major GI bleeding by 1.5-fold vs. clopidogrel, but the absolute increase is small and switching to clopidogrel to avoid a major GI bleeding episode is not likely to be cost-effective. Combined therapy significantly increases risk vs. either therapy alone.

META-ANALYSIS OF ASPIRIN VS. PLACEBO RCTS

ENDPOINTS	SUBJECTS: ASPIRIN/PLACEBO	RR (95% CI)
Major GI Bleeding (14 studies) (Lower Dose: 75-162.5mg) (Higher Dose: >162.5-325mg)	28,686/28,719 14,778/14,842 2,871/2,843	2.07 (1.61-2.66) 2.22 (1.61-3.06) 2.35 (0.98-5.66)
Any GI Bleeding (11 studies)	25,036 / 25,024	1.62 (1.25-2.09)
Fatal GI Bleeding (12 studies)	25,964/25,993	1.23 (0.45-3.41)
Dyspepsia (5 studies)	12,510/12,496	1.09 (0.97-1.22)
Any major bleeding (9 studies)	26,673/26,712	1.71 (1.41-2.08)
Intracranial bleeding (11 studies)	27,671/27,712	1.65 (1.12-2.44)

216388: Proton Pump Inhibitor Treatment Initiated Prior to Endoscopic Diagnosis In Unselected Upper Gastrointestinal Bleeding: A Cochrane Systematic Review and Meta-Analysis. *Stephanie Dorward, Aravamuthan Sreedharan, Grigoris I Leontiadis, Colin W Howden, Paul Moayyedi, David Forman*

Background The clinical effectiveness of proton pump inhibitors (PPI) in patients with upper gastrointestinal (UGI) bleeding has been evaluated in recent meta-analyses. However, none of these has addressed the role of PPI treatment initiated prior to endoscopic diagnosis in unselected patients with UGI bleeding. Objectives We aimed to systematically review evidence from randomized controlled trials (RCTs) that studied PPI treatment initiated before endoscopy, in UGI bleeding. Methods We performed a search of CCTR, MEDLINE, EMBASE, CINAHL databases and major conference proceedings up to September 2005. RCTs comparing intravenous or oral PPIs with either placebo or H2-receptor antagonists in patients with unselected UGI bleeding were included. Two reviewers independently assessed the eligibility criteria of each study and extracted data regarding outcomes and factors affecting methodological quality. The primary outcome was 30-day mortality; secondary outcomes included 30-day re-bleeding and surgical intervention rates, stigmata of recent hemorrhage (SRH) seen at endoscopy, length of hospital stay and blood transfusion requirement. Sub-group analyses were performed for the outcomes in patients with peptic ulcer bleeding. Results Five RCTs were included for review. Four RCTs comprising 1512 patients reported data for all randomized patients. Four RCTs were published in full; one was presented in abstract form. Two RCTs reported adequate concealment of allocation. Meta-analyses were performed for all dichotomous outcomes. Adequate data were not available to perform meta-analyses for continuous outcome measures such as blood transfusion requirements and length of hospital stay. Sensitivity analyses were performed as appropriate and sources of heterogeneity were explored. The main results are presented in the Table. Conclusions PPI treatment initiated prior to endoscopy in unselected UGI bleeding significantly reduced the proportion of patients with SRH at index endoscopy. However, there was no evidence that PPI treatment improved clinically important outcomes such as mortality, re-bleeding or need for surgery.

Results

Outcome	Number of RCTs (n)	Patients (n)	Pooled event rate (% of patients) PPI Control		Pooled effect estimate OR(95% CI)	P value
Mortality	4	1512	6.1	5.5	1.12(0.72-1.73)	0.61
Rebleeding	3	1410	13.9	16.6	0.81(0.61-1.09)	0.17
Surgery	3	1454	9.9	10.2	0.96(0.68-1.35)	0.81
SRH	4	1332	37.2	46.5	0.67(0.54-0.84)	0.0005
Blood in UGI tract	3	1230	20.6	27.0	0.64(0.32-1.30)	0.22
Active bleeding	4	1332	11.3	14.7	0.74(0.54-1.02)	0.07
Blood transfusion	4	1512	53.2	54.5	0.95(0.78-1.16)	0.62

219251: Use of GI Prophylaxis In Patients Discharged From Hospital on Ulcerogenic Medicines. *Gregory A Cote, John P Norvell, John R Rice, Michael Postelnik, Colin W Howden*

Background: Gastrointestinal (GI) hemorrhage is responsible for 200,000-400,000 admissions in the United States annually. Up to twenty million Americans take nonsteroidal anti-inflammatory drugs (NSAIDs) on a regular basis. NSAIDs are responsible for >30% of admissions due to GI hemorrhage. Misoprostol reduces the number of upper GI events due to NSAIDs; proton pump inhibitors (PPIs) reduce the incidence of NSAID-related ulcers seen at endoscopy. Despite this, compliance with clinical practice guidelines to minimize medication-induced upper GI events may be poor. **Aim:** To measure the utilization of appropriate GI prophylaxis in patients discharged from hospital on ulcerogenic medicines **Methods:** We performed a retrospective chart review of all patients discharged from the medical service over a 3-month period on aspirin, NSAIDs, warfarin and/or corticosteroids. Data were collected on PPI or misoprostol administration at the time of discharge. Co-morbidities were documented, with particular attention on known risk factors for GI hemorrhage (age, previous hemorrhage, type of ulcerogenic medicine). Other indications for acid suppressive therapy were also documented. **Results:** 480 patients were discharged between January and March 2005 on aspirin, NSAIDs, warfarin, corticosteroids or some combination. 142 were excluded for having a current indication for PPI therapy. Of the 338 remaining patients, 154 (46%) were prescribed GI prophylaxis: 119 (35%) received daily PPI, 2 (1%) misoprostol, 15 (4%) H₂RA and 18 (12%) twice daily PPI. Of the 154 patients discharged on prophylaxis, 98 (64%) had been taking it before admission. The 338 patients were also divided into four groups based on risk factors for GI hemorrhage: age, Charlson co-morbidity index, and type of medication. 24% of low-risk (n=33), 36% of moderate risk (n=99), 48% of high-risk (n=107), and 60% of very high-risk (n=99) patients received some form of prophylaxis. Patients were also divided by Charlson score; 40% with scores of 0-1, 47% with scores 2-4, and 51% with scores ≥ 5 received prophylaxis. **Conclusions:** Although there was a trend towards higher use of prophylaxis in the highest risk patients, only 60% were discharged on appropriate therapy. Further, 24% of low-risk patients were prescribed prophylaxis without a clear indication. Although hospitalization offers an excellent opportunity to recognize and manage patients at high risk of developing GI hemorrhage, adherence with current guidelines was suboptimal. Educational efforts should be directed at residents in training to help them recognize risk factors for GI hemorrhage and understand indications for prophylaxis.

217224: Early Is Good; Is Very Early Better? Does Endoscopy Within 6 Hours of Presentation Improve Outcomes in High-Risk Patients Presenting With Acute Non-Variceal Upper Gastrointestinal Bleeding (ANVUGIB). *Leila Keyvani, Laura E Targownik, Sanjay K Murthy, Shanua Leeson*

Background: ANVUGIB is a serious cause of morbidity and mortality and is associated with a 5-10% case-fatality rate. The evidence to date suggests that performance of endoscopy within 24 hours of presentation reduces the risk of rebleeding and mortality in patients presenting with ANVUGIB. However, it is unclear whether performing endoscopy very early within this 24 hour window provides any additional benefit. The benefits of performing very early endoscopy would likely be most pronounced in high-risk patients, including the elderly, those with evidence of shock on presentation, and patients with a history of severe co-morbid illness. Therefore, we sought to determine if there were significant differences in outcomes between high-risk ANVUGIB patients who undergo endoscopies within 6h of presentation ("very early") or between 6h and 24h from presentation ("early"). **Methods:** We performed a retrospective review of all patients with ANVUGIB who presented to one of our two tertiary care medical centers in Winnipeg, Manitoba between 1999-2004. We selected the patients who were high risk based on their having a clinical Rockall score ≥ 3 . We separated subjects into two comparator groups based on whether they received endoscopy "very early" (≤ 6 hrs) or "early" (6-24 hrs). The primary outcome measure was any adverse outcomes (re-bleeding, need for surgery, mortality, readmission within 30 days of ANVUGIB). The secondary outcomes include the length of hospital stay, and receiving a blood transfusion more than 24h following the initial endoscopy. **Results:** 221 patients with a clinical Rockall score ≥ 3 underwent endoscopy within 24 hours of presentation. Of these high risk patients, 79 had "very early" endoscopy whereas 142 underwent "early" endoscopy. There were no significant differences in the baseline characteristics between the comparator groups. Patients receiving "very early" endoscopy were significantly more likely to have undergone endoscopic hemostasis (50% "very early" vs. 36% "early, $p=0.01$). There were no differences in the incidence of adverse outcomes (25% vs. 22%, $p>.0.2$). Patients undergoing "very early" endoscopy were significantly more likely to have a hospital stay exceeding 5 days (64% "very early" vs. 49%, $p=.032$). **Conclusion:** There is no difference in the rate of adverse outcomes in high risk ANVUGIB patients who undergo "very early" endoscopy and "early" endoscopy, though patients receiving "very early" endoscopy are more likely to require both endoscopic hemostasis and longer stays in hospital. The optimal timing of endoscopy within first 24 hours should be confirmed in well designed randomized controlled trial setting.

222841: Serum Markers of Prognosis Following Emergency Department Presentation for GI Bleed. *Sara M Echelmeyer, Latha G Stead*

Objective: To study mortality after presentation to the Emergency Department (ED) for GI bleed, and to determine whether any serum laboratory values were associated with a worse prognosis. **Methods:** All patients presenting to the ED of an academic medical center for acute GI bleed between 1/2002-6/2004 were included. Patients had standard laboratory evaluation. Time-to-

event methodology was used for the analysis of patient survival. Duration of follow-up was calculated from the date of ED visit to the date of death or last follow-up, with all events censored at 1 year. Survival estimates were based on the Kaplan-Meier method. Cox proportional hazards models were fit to evaluate the association between each of the laboratory values and death. Associations were summarized with risk ratios (RR) and 95% confidence intervals (CI). Laboratory values were evaluated univariately by fitting separate models, and then with a multivariate model using a combination of stepwise backward procedures and an inclusion criterion of $p < 0.05$. A total of 255 adults presented during the study period. Of these, 24 denied research authorization. The cohort was 55% male with a mean age of 64.2 years (SD, 18.0; median, 68; range, 18-100 years). A total of 50 patients died; 9 within 30 days, 11 within 31-90 days, 9 within 91-365 days, 17 within 1-2 years, and 4 after 2 years. Among the remaining 181 patients alive at last follow-up, the median duration of follow-up was 1.2 years (interquartile range, 0.5-2.0 years). The survival estimates at 6-months, 1-year, 18-months, and 2-years following ED presentation were 89.0%, 85.4%, 79.0% and 69.0%, respectively. Univariate analysis identified the following variables as being significantly associated with poorer patient survival: older age, leukocytosis, elevated creatinine, elevated troponin, elevated AST, elevated lactate, low platelet count, low sodium, low bicarbonate, low chloride, high potassium, high glucose, high aPTT, and high bilirubin (all $p < 0.05$). Multivariate analysis identified older age, elevated troponin, elevated creatinine, low sodium, and high aPTT as being jointly associated with poorer patient survival. Conclusion: Hyponatremia, renal insufficiency, an elevated troponin or aPTT are associated with increased risk of death at one year following ED presentation for gastrointestinal hemorrhage.

Prognostic Factor	RR (95%CI)	P-value
Age	1.4 (1.1,1.8)	0.005
Creatinine (high)	4.2 (1.1, 16.1)	0.037
Troponin (high)	3.2 (1.4, 7.0)	0.004
Sodium (low)	3.1 (1.6, 6.3)	0.001
aPTT (high)	2.8 (1.3,5.8)	0.008

225089: The Predictive Value of Admission Hematocrit in Patients Hospitalized With Acute Upper and Lower Gastrointestinal Bleeding (GIB). *Richard A Del Rio, Richard C Wong, Layla Hajjafar, Gregory S Cooper*

Background: The ability of admission hematocrit (HCT) to help identify those patients at risk of death from acute GIB is unclear. Aims: 1) To compare the in-hospital mortality rate of patients with different admission HCT values; and 2) To determine if admission HCT is an independent predictor of mortality. Methods: A retrospective cohort study was performed using 7,909 patients hospitalized with the primary diagnosis of acute GIB. In-hospital mortality rates were compared for patients with lower versus higher admission HCT for specific values: 10, 15, 20, 25, 30, 35, and 40%. A multivariate logistic regression model was performed to determine if admission HCT was an independent predictor of mortality after adjusting for: age, sex, race, admission pulse and blood pressure, admission platelet count and prothrombin time, history of GIB, and comorbidities (diabetes, CAD, cirrhosis and chronic renal failure). Results: In-hospital mortality rate was 3.3% for all GIB, 3.7% for upper GIB, and 1.8% for lower GIB. For all GI bleed, low HCT was an independent predictor of mortality for values less than 25%, with the risk of death ranging from 19% higher for HCT < 25% to 69% higher for HCT < 10% (Table). HCT values of 30, 35 and 40% were not significant predictors of mortality (data not shown). Similar results were found when evaluating upper and lower GI bleed separately (Table). Other predictors of mortality were age, gender, admission pulse and blood pressure, prothrombin time and comorbidities. Conclusion: An admission hematocrit value of less than 25% appears to be an independent predictor of in-hospital mortality and can be used with other known predictors to help identify patients at risk for poor outcomes.

In-Hospital Patient Mortality Rate for Different Admission HCT Values

HCT (%)	Site	Rate (%)	OR	95% CI
	All	13.3	1.69	(0.78, 3.70)
10	Upper	14.3	1.67	(0.76, 3.70)
	Lower	NP	NP	NP
	All	7.8	1.49	(1.11, 2.00)
15	Upper	7.3	1.35	(0.96, 1.89)
	Lower	10.7	2.50	(1.27, 5.00)

	All	5.7	1.27	(1.06, 1.49)
20	Upper	5.7	1.19	(1.00, 1.41)
	Lower	5.4	1.69	(1.03, 2.78)
	All	4.6	1.19	(1.04, 1.35)
25	Upper	5.0	1.16	(1.00, 1.33)
	Lower	2.5	1.08	(0.74, 1.35)

HCT = admission hematocrit; NP = no patients in group; OR = odds ratio; CI = confidence interval

Additional Reading: GI Bleeding

222145: The Value of Baylor and Rockall Scores In Inpatients With Non Variceal Upper Gastrointestinal Bleeding *Jose A Gonzalez-Gonzalez, Juan O Gaytan-Torres, Dora A Garcia-Cantu, Hector J Maldonado-Garza Arnoldo Guerrero-Chapa*

Introduction: Differences in etiologies have emerged in recent studies in both outpatients (OUTPTs) and inpatients (INPTs) with non variceal bleeding (NVB). Little data about the use of Baylor score and Rockall score in INPTs is available Objectives: To compare the clinical characteristics, bleeding etiologies, co-morbidities, Baylor score and Rockall score among OUTPTs and INPTs with NVB. Material and Methods: We prospectively studied all pts admitted to our institution with NVB (2001-2005) with information obtained from our database. We studied age, gender, co-morbidities, alcohol, tobacco and NSAIDs use, history of previous GI bleeding and Hp. status. We compared bleeding manifestations, diagnoses, treatment, transfusions required, rebleeding, Baylor score and Rockall score, surgery and mortality. Statistical Analysis: The variables are expressed as mean, range. Chi-square and Fishers exact test were used for comparisons. Results. 653 pts: 85% OUTPTs; M/F 360/197, mean age 58 vs 15% INPT; M/F 61/36 mean age 57. Risk factors as DM, CRF, HTN, pulmonary and liver disease, OH, tobacco, NSAIDs use, Hp status and previous GI bleeding was not different among OUTPTs and INPTs, only cardiac disease 9% (16%) was significant in INPTs (p = 0.03). Presence of bright red blood hematemesis 36% (19%) and melena 64% (50%) was significant in OUTPTs (p= 0.001, p = 0.01). The gastric and duodenal ulcer, tumors and erosive duodenitis, was not different. Only erosive gastritis was significant in INPTs 23 % (33%) p = 0.04. The need for endoscopic treatment, units of blood requirement, rebleeding rate and surgery was not different, only the mortality rate was more frequent in the INPTs (p= 0.02). In the OUTPTs the Baylor score was useful to predict rebleeding and mortality (p= 0.0001, p= 0.003) and the Rockall score was only significant for mortality (p= 0.0001). Both scores for INPTs are shown in Table 1 Conclusions: In our study, INPTs with NVB had more coronary disease, erosive gastritis and higher mortality when compared to OUTPTs who usually presented with either melena or bright red blood hematemesis. In OUTPTs, the Baylor score was useful in predicting re-bleeding rates and mortality but was not useful in INPTs, whereas the Rockall score was helpful in predicting mortality in both groups.

INPTs	N	Rebleeding	Death
Rockall ≤ 2	22	0 OR 1.28 IC 95% (0.89 -1.84)	1 (5%) OR 0.12 IC 95% (0.01-0.96)
Rockall > 2	75	7 (9%) OR 0.77 IC95% (0.54-1.11)	21 (28%) OR 8.1 IC 95% (1.03-64.6)
p		0.19	0.02
Baylor ≤ 10	68	5 (7%) OR 1.07 IC 95%(0.19-5.86)	12 (18%) OR 0.40 IC 95% (0.15-1.09)
Baylor > 10	29	2 (7%) OR 0.93 IC 95% (0.17-5.11)	10 (34%) OR 2.45 IC 95% (0.91-6.59)
p		0.99	0.11

220024: Therapeutic Efficacy of Balloon-Occluded Retrograde Transvenous Obliteration in Patients with Gastric Variceal Bleeding. *Kyungsik Park, Byoungkuk Jang Woojin Chung, Kwangbum Cho, Jaeseok Hwang, Sunghoon Ahn, Younghwan Kim, Jinsu Choi, Junyoung Hwang*

Background/Aims: Gastric variceal bleeding is fatal complication of portal hypertension caused by end stage liver disease which is common in east Asia. But endoscopic treatment of the condition is sometimes very difficult as its hemodynamics and accessibility are different with those of esophageal varix. Though transjugular intrahepatic portosystemic shunt is another important therapeutic option in gastric varix, it also has some limitations such as aggravation of hepatic encephalopathy or deterioration of hepatic function. Recently balloon-occluded retrograde transvenous obliteration(BRTO) has been used as a new procedure for gastric variceal bleeding with minimal invasiveness but reports about the results of this procedure are not enough. So we analyzed the results of our cases which we have experienced for recent 39 months. Methods: Twenty eight patients who

were received BRTO for the purpose of primary hemostasis or secondary prevention from December 2001 to March 2005 were analyzed retrospectively. Size of gastric and esophageal varix, clinical presentations, laboratory findings were compared before and after procedure. Cumulative rebleeding and survival rate were also analyzed with Kaplan-Meier curve. Results: Twenty three men and five women were involved and mean age was 53.7 ± 9.6 years. Technical and clinical success rates were 89.3% and 85.7%, respectively. Follow up were continued for 17.5 ± 12.5 months in 23 patients. Gastric varices were disappeared in 78.3% and decreased in size more than 50% in 21.7%. Relapse was occurred in a(4.3%) patient. Preexisting hepatic encephalopathy was improved in all patients. Aggravation or development of ascites, esophageal varices, portal hypertensive gastropathy were observed in 45.8%, 30.4%, 56.5%, respectively. Temporary decreased albumin concentration($p=0.002$), increased bilirubin concentration($p<0.001$) and Child-Pugh score($p<0.001$)was observed at 3 days after procedure but resolved at 7 days after procedure. Increased albumin concentration and decreased Child-Pugh score were maintained thereafter. Rebleeding was occurred in 3 patients and all cases were esophageal variceal bleeding. There were no factors related with rebleeding. Two-year survival rate was 54.6%. Presence of hepatocellular carcinoma(HCC)($p=0.001$) and Child-Pugh grade B($p=0.036$) and C($p=0.012$) affected survival in univariate analysis and presence of HCC was independent risk factor($p=0.010$, OR=15.837) in multivariate analysis. Conclusions: BRTO is effective therapeutic procedure for primary hemostasis, secondary prevention, and improvement of survival in gastric variceal bleeding patients.

226434: How Reliable is the Clinical History of NSAID Use in Patients who Present with Upper Gastrointestinal Hemorrhage? *John M Runnels, Anil Minocha*

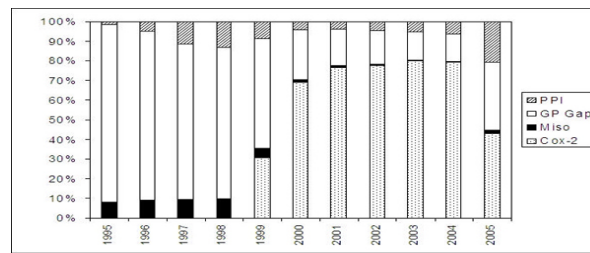
There is paucity of literature regarding the reliability of clinical history for assessing the use of nonsteroidal anti-inflammatory drugs (NSAIDs) in patients presenting with upper GI hemorrhage. Platelet function testing using the PFA-100 has been used to detect the effects of NSAIDs on platelets. We hypothesized that surreptitious use of NSAIDs occurs only in a small minority of such patients. Study Design Adult hospitalized patients undergoing endoscopy for evaluation of melena, hematemesis or coffee ground emesis were included in the study. Exclusion criteria included hematocrit less than 25% or platelet count less than 100,000/mm³, as these factors cause invalid measurements by the platelet function analyzer. Results Sixty three patients met inclusion criteria. Sixteen patients were excluded due to anemia and thrombocytopenia as above. The average (SD) age of patients was 53.65(15.55) years. Caucasians formed 40% of the study population, whereas the remaining were African-Americans. Patients were predominantly males (64%). Twenty one percent of the patients tested had positive PFA-100 measurements that suggested NSAID use. However, 60% of those with positive PFA-100 test had denied a history of prior NSAID use. Conversely, only 25% of the patients that gave a history of prior NSAID usage had positive PFA-100 test results confirming prior NSAID use. Conclusions Clinical history is not a reliable indicator of prior NSAID use in patients presenting with upper gastrointestinal bleeding. Alternate testing to evaluate for surreptitious use of NSAIDs should be considered in patients with bleeding due to non-HP, non-NSAID ulcers.

226878: Longterm Prevention of Esophageal Variceal Bleeding With Rabeprazole : Results of A 5 Year Study In Japan. *Kuwayama Hajime, Nishiki Ryoichi*

Our previous reported that the PPI treatment was effective in prevention of esophageal variceal bleeding and recurrent variceal bleeding in cirrhotic patients. We investigated the effect of rabeprazole (RPZ) in prevention of esophageal variceal bleeding in 5 years using a randomized controlled trial design. Subjects & Methods: We enrolled 134 patients with confirmed cirrhosis and esophageal varices. 41 of these patients had at least one previous episode of confirmed variceal bleeding, and had been treated with endoscopic ligation. The 134 patients were randomized to receive either PPI (oral rabeprazole 20mg/day, N=73) or no anti-secretory treatment (N=61), and followed for up to 5 years. Patient demographics (age, gender, Child-Pugh score, variceal size, red color signs, and previous variceal bleeding) were not significantly difference in both groups. The evaluated association between varices bleeding and patients risk factors, odds ratios (OR) and the corresponding 95% CI were computed by means of logistic regression models. Results: The rate of variceal bleeding was significant lower in the PPI-treated group (6.8%, 5/73) than the untreated group (26.2%, 16/61, $P=0.0034$). Five- year rate for occurrence of variceal bleeding, calculated by Kaplan-Mayer analysis, was 14.0% in the PPI-treated group, which was significantly lower than the rate of 29.0% in the untreated group, $P=0.0019$ by log rank test. Subanalysis of patients with pre-study variceal bleeding (secondary prevention) showed that variceal re-bleeding rate was significant lower in PPI-treated pts (10.0%, 2/10) than untreated patients (52.4%, 11/21, $P=0.0063$). Five-year rate for recurrence of variceal bleeding, calculated by Kaplan-Mayer analysis, was 11.3 % in PPI-treated patients, significantly lower than the 56.5% rate in untreated patients, $P=0.0091$ by log rank test. Rabeprazole use was found to be significant factor for varices bleeding (OR: 0.207, 95%CI:0.071-0.604, $P=0.0004$). Conclusion: Rabeprazole treatment was effective in prevention of esophageal variceal bleeding and recurrent variceal bleeding for 5 years.

218835: Gastroprotection Gap: A rising and dangerous omission for elderly users of NSAIDs with arthritis. *Gurkirpal Singh, Huijian Wang, Eiichi Tanaka, Alka Mithal,² Lauren Gerson, George Triadafilopoulos*

Background: GI complications from NSAIDs have been well-recognized since early 1990s, and were significantly reduced by the use of selective cox-2 inhibitors, concomitant proton pump inhibitors (PPIs) or misoprostol in the early 2000s. Recent media attention on the potential association of cardiovascular events with selective cox-2 inhibitors and market withdrawals resulted in a large decline in the use of these drugs. We report change in prescription patterns in a large cohort of elderly arthritis patients from January 1, 1995 to June 30, 2005. Methods: MediCal, the Medicaid program for California, is the largest Medicaid program in the US, with over 7 million participants per year. All study drugs were available without formulary restrictions or copayments. We studied individuals with physician-diagnosed arthritis who were over 65 years of age and treated with NSAIDs for at least 30 days. Results: Of the total 5,194,765 prescriptions for NSAIDs, 2,634,345 (50.7%) were for selective cox-2 inhibitors. Among the 2,560,420 prescriptions for non-selective NSAIDs, only 1,215,762 (47.5%) had concomitant use of PPI or misoprostol. Figure shows the use of selective cox-2 inhibitors and concomitant PPIs or misoprostol, as a percentage of all NSAID use. The increasing implementation of gastroprotection strategies over the past several years reached a peak in 2004 when the percent of patients not receiving gastroprotection (Gastroprotection Gap) decreased to 14% from 91% in 1995. However, this gap more than doubled to 35% in 2005, following a decline in selective cox-2 inhibitor use, without a commensurate increase in other gastroprotective therapies. Conclusions: An increasing number of elderly users of NSAIDs are again left without gastroprotection. This trend, if left unchanged, will undoubtedly increase morbidity and mortality from NSAID-related complications to levels unacceptable for optimal medical care and deserves immediate public attention.



Gastroprotection (GP) gap in elderly patients 1995-2005. PPI=proton-pump inhibitors, miso=misoprostol, cox-2=selective cox-2 inhibitors

205402: Upper Gastrointestinal Bleeding in Hemophiliacs: Incidence and Relationship to Non-steroidal Anti-inflammatory Drugs. *M. Elaine Eyster, Shonda M Asaad, Silvia E Cohn Mary-Anne Ardini, James J Goedert*

The use of non-steroidal anti-inflammatory drugs (NSAIDs) in persons with hemophilic arthropathy is controversial because of bleeding concerns, especially upper gastrointestinal (UGI) bleeding. PURPOSE: To determine the incidence of UGI bleeding and its relationship to the use of conventional nonselective non-steroidal anti-inflammatory drugs (nsNSAIDs or COX-1 inhibitors) and cyclooxygenase selective (COX-2) inhibitors in persons with hemophilia (PWH). METHODS: From May 2002 through May 2005, all PWH enrolled at the 51 centers participating in the second Multicenter Hemophilia Cohort Study were queried annually about use of COX-1 and COX-2 inhibitors in the previous month and for up to or more than 12 months. These questions were repeated when a UGI bleed occurred. UGI bleeding was defined as hematemesis, detection of occult blood in the stools with endoscopically verified ulcer, or melena accompanied by a drop in hemoglobin of at least 2 grams or requiring red cell transfusion. Cox models were used to estimate relative hazards (RH) with 95% confidence intervals (CI) for fixed and time-dependent covariates postulated as risk factors. RESULTS: During a mean of 17.4 months (range 2-34), 2285 participants, ages 13 to 89 (mean 36.5) were followed for a total of 3309 person-years (py). Forty-two (42) experienced a UGI bleeding event, for an annual incidence of 1.27%. Identified sites were ulcer (11), gastritis (4), varices (5), Mallory Weiss tears (8), esophagitis (1), and angiodysplasia (1). Likelihood of bleeding was significantly increased in those who used COX-1 inhibitors for < 1 month (n=3 events; OR 3.66; 95% CI 1.1-11.9), but not for extended periods of time (n=2 events). Likelihood of bleeding was not increased in those who used COX-2 inhibitors (n=6 events). In the multivariable model, likelihood of bleeding was significantly and independently increased with age >46 yrs (RH 3.4; 95% CI 1.1-10.5), platelet counts of <100,000/cu mm (RH 2.4; 95%CI 1.0-5.5) and hepatic decompensation (RH 3.9; 95% CI 1.5-10.1). Adjusted for these, use of a COX-1 inhibitor was not significantly associated with bleeding (RH 2.7; 95% CI 0.7-11.5). CONCLUSIONS: The annual incidence of clinically important UGI bleeding events in PWH was 1.27%, similar to the 1-2% rate reported in non-hemophilic users of nsNSAIDs. After 3309 py, use of a COX-1 inhibitor for < 1 month was associated with a significant increase in UGI bleeding in univariate analysis, although older age, thrombocytopenia and hepatic decompensation were major risk factors. Use of a COX-2 inhibitor was not associated with UGI bleeding.

218211: High-dose Oral Proton Pump Inhibitor is as Effective as Intravenous Administration in the Aspect of Increasing Intra-gastric pH and Reducing Rebleeding after Endoscopic Treatment of Bleeding Peptic Ulcers. *Jae-Young*

Jang, Seok Ho Dong, Ji Heon Jung, Myung Jong Chae, Nam Hoon Kim, Sang Kil Lee, Kwang Ro Joo, Hyo Jong Kim, Byung-Ho Kim, Young-Woon Chang, Joung Il Lee, Rin Chang

Background/Aims: The use of proton pump inhibitor (PPI) prevents rebleeding by elevating intragastric pH in patients with bleeding peptic ulcers after hemostasis has been achieved. We assessed that the high-dose oral pantoprazole is as effective as high-dose intravenous pantoprazole on 24-hour intragastric pH and determined their ability to prevent rebleeding after having achieved initial hemostasis in patients with active bleeding or nonbleeding visible vessels. **Methods:** Forty patients with bleeding peptic ulcers, who had obtained initial hemostasis, were enrolled in this randomized controlled trial. In the high-dose oral pantoprazole group (n=20), 40 mg of pantoprazole was given orally twice daily for 5 days. In the high-dose intravenous pantoprazole group (n=20), 80 mg intravenous bolus of pantoprazole was given, followed by 8 mg/hour of continuous infusion daily for 3 days. Thereafter, 40 mg of pantoprazole was given orally once daily for 8 weeks. A pH meter was inserted in each patients' fundus and then the pantoprazole was administered within 5 minutes (10 patients in oral group and intravenous group, respectively). **Results:** The two groups were similar with respect to all background variables. Rebleeding occurred in 2 patients (10.0%) in the intravenous group and did not occur in the oral group by day 30 after enrollment (p=0.154). There was no significant difference in terms of therapeutic endoscopic sessions (1 vs. 1.18±0.53), surgery (0% vs. 0%), mortality (0% vs. 5.9%), and mean number of units of blood transfused (1.9 vs. 1.9 pints). Pantoprazole maintained the mean gastric pH for 24 hours at the level of 4.8±1.4 in the oral group, as compared with 5.7±0.3 in the intravenous group (p<0.001). The duration of intragastric pH higher than 6.0 was longer in the intravenous group (64.4%±38.3%) than that of the oral group (43.7%±26.2%, p<0.005). But, after 7 hours of administration, there was no significant difference in the mean gastric pH (oral; 5.6±0.6 vs. intravenous; 5.8±0.2, p=0.554). **Conclusions:** The high-dose oral pantoprazole is as effective as intravenous administration in increasing intragastric pH and reducing rebleeding episodes in patients with bleeding peptic ulcers after successful endoscopic therapy.