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Acute Upper Gastrointestinal Bleeding–Impact of Timing of Endoscopy on Patient Outcomes: Impact of Timing of Endoscopy on Patient Outcomes

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Discussion Summaries

Abstract

Acute upper gastrointestinal bleeding (AUGIB) is one of the most common emergencies encountered by gastroenterologists across the world. Various medical and endoscopic therapies have evolved over time to improve patient outcomes. However, controversy still exists around the optimal time of endoscopy for patients with AUGIB. Recently, several studies have been published to answer this clinical question and we have reviewed one of these articles.

On 13th October 2021, @Gijournal, we discussed the latest high-impact article published to answer this clinical question. We critically appraised, ‘’Timing of endoscopy for acute upper gastrointestinal bleeding: a territory-wide cohort study’’ which was published in ‘Gut’ on Sep 21 by Cosmos L T Guo et al. This is a brief review of this article and subsequent discussion around it. This session was moderated by Shima Ghavimi, and experts were Cosmos L T Guo, Louis H S Lau, and Rashid N S Lui who were also authors of this paper.

Discussion Summary

Background

Acute Upper gastrointestinal bleeding (AUGIB) is one of the most common medical emergencies encountered by gastroenterologists. Medical and endoscopic management has improved outcomes over the years, but incidence remains high. Currently. It is recommended that endoscopy should be performed in first 24 hours (1, 2). A randomized controlled trial published by same group recently didn’t show any benefit of early endoscopy done within 6 hours (3).

To move another step forward, the authors published this study to answer key questions around timing of endoscopy and its impact on patient outcomes. This was a retrospective analysis of electronic records of all patients admitted with AUGIB from all public hospitals in Hong Kong between 2013-2019. Patients were divided into three groups based on their time of endoscopy from admission, urgent with EGD done from 0-6hrs, early group from 06-24hrs and late from 24-48 hrs. The bleeding severity was determined by modified Glasgow-Blatchford Score (GBS). The inverse probability of treatment weighting (IPTW) was employed to adjust for the baseline characteristics.

Primary outcome of the study was 30-day all-cause mortality rate. Secondary outcome was need of repeating therapeutic endoscopy within 30 days , average units of blood transfused within 30 days , Intensive care unit (ICU) admission within 30 days, in-hospital mortality rate as well as length of stay in hospital.

In total there were 6,474 patients in the study. Urgent group (<6hr) had 1,008 with mean EGD time of 4.08 hours, early group had 3,865 patients with mean EGD time of 15.6 hours and late group had 1,601 patients with mean EGD time 32.3 hours.

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In most of the results, early group was used as baseline as they had lowest mortality. Urgent group of patients showed highest mortality (aHR of 1.43 - 95% CI 1.24 to 1.65, p<0.001) and mortality was still high in late group- aHR of 1.25 (95% CI 1.078 to 1.449, p=0.003). There were more deaths seen in urgent and late group as compared to early group (Urgent - 6.2% vs early 4.3%, p=0.017 late - 5.8% vs early 4.3%, p=0.022).

In secondary outcomes, early group was again used as reference. Thirty day repeat endoscopy rates were higher in urgent and late group as well (Urgent – aHR - 1.215 p<0.001; Late – aHR - 1.040 p=0.426). Thirty-day ICU admission were higher in urgent group but lower in late group of patients (Urgent – aHR- 1.403 p <0.001 Late – aHR - 0.716 p=0.002).

Looking through the patient characteristics, urgent group had more comorbidities. However, even those without significant comorbidity had higher 30-day all-cause mortality compared to early group (aHR.1.69 p<0.001) and higher 30-day ICU admission (aHR 1.55 p<0.001).

In subgroup analysis, there were 286 patients with variceal bleeding as compared to 6188 with non-variceal. It's important to note that there were no significant outcomes in urgent and early group. Late group was associated with higher 30-day mortality in variceal group. In sub group analysis, there was no significant effect of weekend admission on the association between timing and clinical outcomes.

The strength of this study was the large sample size which allowed for a robust statistical analysis. The limitations were lack of some initial data for blood pressure, pulse and clinical data of syncope which was key component of modified GBS score. The data wasn't robust to show any significant impact on variceal bleeding and time of endoscopy.

Discussion Summaries

Summary of Article: by (AA)

Timing of endoscopy for acute upper gastrointestinal bleeding: a territory-wide cohort study

Guo CLT, Wong SH, Lau LHS, et al. Gut 2021;0:1–7. doi:10.1136/gutjnl-2020-323054

@GIJournal

Objective

- The ideal time for endoscopic intervention for patients presenting with acute upper gastrointestinal bleeding (AUGIB) is unclear and there are conflicting studies about the optimal timing and its impact on patient outcomes.
- The aim of study was to assess whether endoscopy timing post-admission would affect outcomes.

Design

- A retrospective, territory-wide, cohort study with healthcare data from all public hospitals in Hong Kong was collected. Adult patients (age ≥18) that presented with AUGIB between 2013 and 2019 and received therapeutic endoscopy within 48 hours (n=6474) were recruited.
- Patients were classified based on endoscopic timing post-admission: urgent (t≤6), early (6<t≤24) and late (24<t≤48).
- Baseline characteristics were balanced with inverse probability of treatment weighting. 30-day all-cause mortality, repeated therapeutic endoscopy rate, intensive care unit (ICU) admission rate and other endpoints were compared.

Results

- Results showed that urgent timing (n=1008) had worse outcomes compared with early endoscopy (n=3865), with higher 30-day all-cause mortality (p<0.001), repeat endoscopy rates (p<0.001) and ICU admission rates (p<0.001).
- Late endoscopy (n=1601) was associated with worse outcomes, with higher 30-day mortality (p=0.003), in-hospital mortality (p=0.022) and 30-day transfusion rates (p=0.018).

Conclusion

- Compared with urgent and late endoscopy among patients who have received therapeutic endoscopies, early endoscopy was associated with superior outcomes especially among patients with non-variceal bleeding.
- This supports the notion that non-variceal AUGIB patients should receive endoscopy within 24 hours, but also emphasises the importance of prior resuscitation and pharmacotherapy.

Discussion:

First Poll (232 votes)

SG: 54 y/o male with PmHx of HTN and DM came to the ER, with c/o hematemesis, no Hx of liver diseases, has hx of NSAID use, BP:100/80, HR, 110, Hb:11 from baseline 13. \What would you do next?

- Transfuse Blood (0.9%)
- Admit to MICU (3%)
- **Resuscitate + Fluids+PPI (88.8%)**
- Endoscopy within 6 hrs (7.3%)

2nd Poll (121 votes)

SG: After resuscitation for the patient above, GI team was called. When would YOU consider EGD for this patient?

- <6 hours (10.7%)
- 6 to 12 hours (17.4%)
- **6 to 24 hours (64.5%)**
- 24 to 48 hours (7.4%)

UK(@UmairKamran11): What do experts think is the reason of difference in outcomes? If I have rightly understood, baseline pulse and BP were not different between groups so can't say that urgent group was not resuscitated properly.

RL: There may be processes like hemodynamical dysfunction, ongoing bleeding that are not fully captured by baseline vitals. Also 55% missing is quite high for using multiple imputations and is a drawback for our study.

SM:

Discussion Summaries

1. Patients can become unstable during procedure leading to aborting the procedure

2. Incomplete visualization. Erythromycin and Reglan would be great but difficult to time with endoscopy. Rarely saw them being used in practice.

3rd Poll

Does the timing of endoscopy affect clinical outcomes in patients presenting with acute upper gastrointestinal bleeding ? (80 votes)

Yes (75%)

No (20%)

Explain in comments (5%)

SM (@SultanMahmoodMD): I was beginning to think that timing doesn't make a difference based on recent RCTs. However, this study did show worse outcomes for late group.

RL: I think someone brought that up before. If it's not weekends or something else, we measured, maybe it was other confounding like #ACS, sepsis, need to withhold anti-platelet agents/ anti-coagulants etc. Though it's possible that in these cases the prognosis was poor to begin with.

RI: A good and fair point. The @Gut_BMJ paper drew data from the entire #HongKong so there would be variations in practice. In our centre at @CUHKMedicine there is 24/7 urgent coverage. But we did look at the weekend effect in sensitivity analyses, there were no big surprises.

SM: Are there other studies which show that delayed endoscopy >24 hr after admission is associated with worse outcomes?

DK (@GI_Pearls): Hard to remove confounding in such (clearly non-randomized studies). In many hospitals if endoscopy is delayed, there may be a medical reason for it (active MI, some other ICU mishap, etc, which would make mortality high.

LL: Fully agree. The 'late' group could have various reasons for delaying their endoscopies, for example, other concurrent medical illness like cardiac or septic conditions, which will increase the overall mortality.

SM: My initial thought too. Before IPTW higher GBS score and more cardiac disease in late group. Makes me wonder if timing makes a difference at all. I know we were delaying endoscopy for a lot of COVID pts who did fine even without it.

SG: Patients admitted on the weekend for PUD hemorrhage have higher mortality and more frequently undergo surgery. Wait times for EGD are prolonged in patients hospitalized on the weekend, this delay does not appear to mediate the weekend effect (4).

RL: True. No matter how rigorous the matching was, non-randomised studies have their limitations.

SG: Confounding is less likely when researching rare but serious harms, which are very difficult to investigate with #RCTs. #NRS may have a valuable role in this context (5).

4th Poll

SG: Based on this study would you change your practice (33 votes)

- Yes (33.3%)
- **NO (48.5%)**
- Not Sure yet (18.2%)

SG: Details about endoscopy report is crucial.

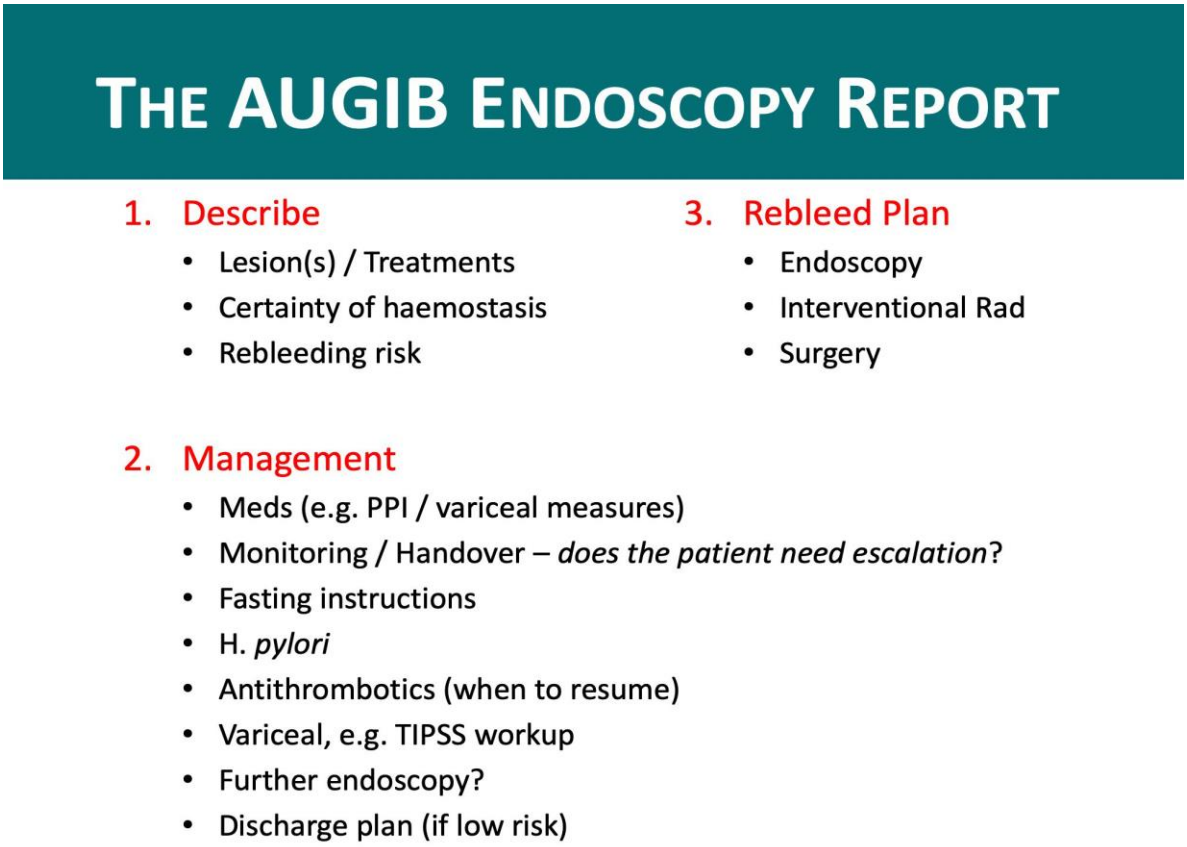
RL: Clip near the vessel for marking if needed to help our IR docs visualize better!

SG: Be specific w lesions: size, depth, classification if ulcers, red wale or SRH if varices, and difficulty (Unapproachable post bulbar location? Big clot in fundus? Should be intubated if rebleeds?) Things that would help others pick up where you left off, why, what to do.

SG: Under the rebleed plan, I would briefly document any discussions that have already taken place with surgeons or IR to make it easier for the next person who gets called about the rebleed.

SG: Also, put in instructions to avoid medications like NSAIDs for ulcer disease and mark specimen/site of sample.

Image 1: Essentials of AUGIB endoscopy report (Courtesy of @drkeithsiau)



5th Poll

Which of the following is the most common cause of #NVUGIB? (38 votes)

Dieulafoy's lesion (0%)

GAVE (0%)

Mallory-Weiss tear (7.9%)

Peptic Ulcer Disease (92.1%)

Discussion Summaries

LL: With the increasing awareness of HP eradication and NSAID's harm, we observed an increasing trend in idiopathic ulcers. They are more prone to rebleed and more lethal (6).

LL: Our previous RCT on this condition showed a numerically lower rebleeding rate in PPI group (0.88% vs 2.62%) over a follow-up period of 24 months (7).

SG: There are many well-established causes and some associated factors related to its development, the most important being: NSAIDs/aspirin, direct chemical/erosive agents, H. pylori and neoplasm.

SG: Image 2 (8)

Etiologies of Peptic Ulcer Disease (Courtesy of @RashidLui)

Discussion Summaries

Etiologies of peptic ulcer disease	
Drugs	**NSAIDs/Aspirin** Bisphosphonates SSRIs Iron tablets Potassium chloride Spironolactone etc.
Infection	**H. Pylori** CMV infection Candida
Neoplasm	**Gastric cancer** Small bowel cancer Lymphomas (MALTomas)
Stress	Raised intracranial pressure (Cushing's ulcer) Burns (Curling's ulcer)
Mechanical	Cameron's
Autoimmune	Crohn's Vasculitis
Hypersecretory state	Zollinger-Ellison syndrome (gastrinoma) Hyperparathyroidism
Iatrogenic	Post-ESD/EMR Irradiation
Idiopathic	

@RashidLui

SG: "Risk stratification is important to determine the indication for treatment and predict clinical outcome. Early identification of high-risk patients is essential for intensive management and pre-emptive intervention" (9).

6th Poll (13 votes)

Do you know about Care Bundles?

Yes (23.1%)

No (76.9%)

Discussion Summaries

SG: Care bundles comprise a pragmatic series of evidence-based interventions, which when performed together, lead to a better outcome than if performed individually (10).

https://fg.bmj.com/content/11/4/311

SG: We classify the endoscopic appearance of ulcers by the Forrest classification with great examples by @EndoscopyCampus https://www.endoscopy-campus.com/en/classifications/forrest-classification/

Image 3 (11): Forrest Classification of Upper GI Bleeding

Grade	Endoscopic picture	Rebleed risk (%)
I	Active hemorrhage	
IA	Spurting	85-100
IB	Oozing	10-27
II	Signs of recent hemorrhage	
IIA	Visible vessel	50
IIB	Adherent clot	30-35
IIC	Hematin covered flat spot	<8
III	No signs of hemorrhage-clean base ulcer	<3

Other Key elements of discussion:

SM: I think for the most part this study adds more data backing up the current practice of avoiding emergent endoscopy which is unlikely to improve outcomes

RL: Vast majority of cases really don't require urgent endoscopy. Need to consider separately for those that do not respond to resuscitation, active hematemesis, or variceal bleeders (i.e. known advanced fibrosis/cirrhosis/HCC, portal HT, portal vein thromboses etc.

IA (@ijlalakbar): I have a question re PPI. Current guidelines suggest BID PPI before EGD and then drip if intervention done. @NEJM paper had drip for everyone to start with. What was the case here and what is your practice?

RL: Good Q. I can only guess that more severe bleeds likely had IV infusions. Less severe the practice is more variable. In #HongKong we like our pre-endoscopy PPI infusions The latest guidelines suggest against routine use because another RCT in @NEJM only showed downstaging of Endoscopic lesions. But the lack of evidence is not evidence that it doesn't work. And I personally think that downstaging lesions is great. More time to diagnose, take biopsies etc.

Especially pertinent in rural settings or in vast countries. Maybe less impactful in metropolitan areas

DS (@drdalbir): I would add that in addition to IV fluids, resuscitation in patients with active/witnessed hematemesis, I have low threshold for admitting these patients to MICU and elective intubation.

SG: Patients with recurrent bleeding generally respond favourably to repeat endoscopic therapy. Routine second-look endoscopy, defined as a planned endoscopy within 24 hours of the initial endoscopy, is not recommended.

AT (@DrBloodandGuts): Hemostatic powder applied as a primary modality for active bleeding PUD (Forrest 1), will only reduce rebleed to that of an adherent clot (Forrest 2b, 30%) I recommend relook in these cases for mechanical/ thermal durable hemostasis or IR mesenteric angioembolization.

SM: Question for the authors. A majority of the patients >50% were getting early endoscopy (<6h). This is definitely not the standard practice in the United States anymore. What is the current protocol in China.

AA: Also noticed that more than 50% pts didn't have initial BP and pulse recorded. These are important parameters in hemodynamic stability. How would these impact results in real life?

CG: The greatest concern here was whether the data was "missing not at random" (MNAR), which would imply that the missing data could have been associated the patient's condition, such as the severity of the bleeding. This would affect the validity of the imputation of data.

SG: Great point @CosmosGuo “if the results obtained #MNAR assumptions are similar, one can conclude that the presence of unobserved factors does not affect the conclusion.

Conclusion:

In patients with non-variceal acute upper gastrointestinal bleeding, upper endoscopy performed within 6 to 24 hours had significantly better outcomes, less 30-day mortality rate and less ICU admission as compared to those who had endoscopy performed in less than 6 hrs or when endoscopy was performed after 24 hrs. This research also highlights the importance of

resuscitation and pharmacotherapy intervention before gastroenterology consultation for upper GI endoscopy.

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