A Statewide Assessment of Acute Gastrointestinal Bleed

Initiative Type

Data Collection

Status

Initiate

Added

13 September 2023

Last updated

30 October 2023

URL

https://cnxp3cuvtvrn68yjaibaht5ywrxspj7m.clinicalexcellence.qld.gov.au/improvement-exchange/statewide-assessment-acute-gastrointestinal-bleed

Summary

Acute Gastrointestinal Bleed (AGIB) is a common emergency presentation associated with high morbidity and mortality. AGIB is categorised into Upper Gastrointestinal Bleed (UGIB) and Lower Gastrointestinal Bleed (LGIB) as it directs the evaluation and management of the patient. In Australia, UGIB affects 50-150 patients per 100,000 population per annum, with a mortality rate of 6-8%.

The assessment of coagulopathy in AGIB consists of conventional coagulation testing (CCT) and viscoelastic haemostatic assays (VHA). The decision to choose CCT and/or VHA is dependent on availability of VHA, local institutional protocols and clinician's experience. There is relative paucity of data pertaining to coagulopathy in the setting of AGIB. The management of AGIB, which consists of blood component transfusion with simultaneous coagulopathy correction and volume restoration, is not unified in guidelines and is dependent on the type of AGIB, presence of liver disease, exposure to anticoagulant medications, availability of an on-site endoscopic service and presence of comorbidities. The evidence supporting guidelines in the management of haemostatic resuscitation in AGIB are of low quality and suggest opportunities exist for further research. This study performs a retrospective review of patients who presented to the ED with AGIB over a 32-month period. It will report on the epidemiology and capture the current assessment and management strategies. This will help inform further studies in this space with a view to contributing to evidence-based guidelines in the future.

Key dates

Sep 2023

Dec 2024

Implementation sites

11 HHSs (West Moreton, Metro South, Metro North, Gold Coast, Sunshine Coast, Darling Downs, Townsville, Cairns, Mackay, Central QLD and Wide Bay)

Partnerships

Queensland Health Statistical Services Branch, Pathology Queensland and Clinical, Business Intelligence Unit in Queensland Health, Monash University

Key Contacts

Akmez Latona

7386

Anonymous

Staff Specialist, Emergency Medicine, Ipswich Hospital

West Moreton Hospital and Health Service

07 46166000

akmez.latona@health.qld.gov.au

Aim

To report on the epidemiology and to capture the current assessment and management strategies of Emergency Physicians in the management of Acute Gastrointestinal bleed.

Benefits

This study will provide evidence on coagulopathy and management of AGIB with blood product administration in Queensland Health. This information will help inform gaps in evidence and directions for further research to improve patient outcomes.

Background

There is no current data in the Australian setting on assessment of coagulopathy and blood product administration in AGIB. There are also no guidelines within Queensland Health in this domain, due to paucity of data. AGIB is a common emergency presentation associated with high morbidity and mortality. AGIB is categorised into Upper Gastrointestinal Bleed (UGIB) and Lower Gastrointestinal Bleed (LGIB) as it directs the evaluation and management of the patient. In Australia, UGIB affects 50-150 patients per 100,000 population per annum, with a mortality rate of 6-8%. Although there is no cost analysis of UGIB in Australia, the cost estimates in UK of £155.5 million, indicating that huge health costs are involved. There is also no Australian data for LGIB. A structured approach involving emergency care and endoscopic source control can significantly reduce mortality rates. The emergency physician collaborates with general surgeons, gastroenterologists and radiologists and oversees the initial assessment and management. Even though coagulopathy is common in AGIB, there is no universal definition for coagulopathy. Published data on the definition, assessment and management of coagulopathy in AGIB are limited and inconclusive. This is partly because coagulopathy in AGIB is related to multiple associated factors, often a combination of: iatrogenic such as anticoagulant use (vitamin K antagonist or DOACs) or massive transfusions, medical conditions such as liver disease, sepsis, multi-organ failure from shock, traumatic injury, surgical procedures and medical interventions. Coagulopathy of liver disease in patients presenting with AGIB is complex

and an increased INR does not reflect coagulopathy or bleeding. Despite the INR being the most used coagulation test, it has only been validated for warfarinised patients. Some studies have defined coagulopathy as an INR>1.5 and many have defined severe coagulopathy as defined as an INR >1.8 and/or platelet count <50,000/µL. Coagulation tests routinely available to the emergency physician does not guide assessment of haemostatic efficacy in DOAC-related bleeding. Similar to UGIB, coagulopathy for LGIB is not defined in the literature and is discussed only in the context of anticoagulant reversal; evidence behind the management of coagulopathy in LGIB is of low quality. Viscoelastic Haemostatic Assays (VHA) used in Queensland, Australia, include Rotational thromboelastography (ROTEM) (ROTEM®; TEM International, Munich, Germany) and thromboelastography (TEG) (TEG® ; Haemonetics, Braintree, MA). Both are point of care (POC) viscoelastic tests of haemostasis in whole blood, which allow measurement of global clot formation and dissolution in real time. Both ROTEM and TEG assess clot formation/dissolution kinetics and strength by measuring and displaying the amount of a continuously applied rotational force that is transmitted to an electromechanical transduction system by developing clot. In the TEG system, a cuvette is filled with native whole blood and a pin is immersed in the sample by a torsion wire. The cup is rotated through 4° 45? over five seconds with a one second rest period at each end. As long as the blood is liquid, movement of the cup is unrestricted. As the blood clots and fibrin strands begin to form between the cup and the pin, the rotational movement of the pin is restricted, which is detected optically and displayed as a TEG tracing. In ROTEM, the pin is rotated. The movement of the pin is detected by an optical detection system which is transmitted to and processed by a computer with a specific ROTEM software. ROTEM and TEG provide essentially the same information on clot formation kinetics and strength. Because of differences in operating characteristics, the results are not interchangeable. Monitoring dynamic changes of haemostasis VHA may enable distinction between a surgical cause of bleeding or coagulopathy, diagnosis of the specific type of coagulopathic impairment, and guidance in the choice of haemostatic treatment. This may reduce the use of blood products and reduce bleeding, the need for re-operations and complications associated with hypovolaemic shock. The assessment of coagulopathy in AGIB consists of conventional coagulation testing (CCT) and Viscoelastic Haemostatic Assays (VHA). The decision to choose CCT and/or VHA is dependent on availability of VHA, local institutional protocols and clinician's experience. Hospitals with ROTEM availability in Queensland are Cairns, Rockhampton, Toowoomba, Gold Coast, Robina, Mackay, Caboolture, RBWH, Redcliffe, Prince Charles, Princess Alexandra, Redland, Townsville, Ipswich, Bundaberg, Hervey Bay and QEII. Hospitals where TEG is available are Logan, Nambour and Sunshine Coast. There is relative paucity of data pertaining to assessment of coagulopathy in the setting of AGIB. CCTs have been traditionally used to assess coagulation in gastrointestinal bleed. However, the difficulty with CCT is that it measures only procoagulant activity, and not the anticoagulant activity. It is time-consuming and tend to be omitted in situations where rapid treatment is needed, such as severe bleeding. Furthermore, the INR and apTT measurements in CCT are centrifuged and consist solely of the patient‘s serum. This results in a lack representation of the cellular parts of coagulation. The in vitro nature of CCT results in lack of information about the vessel bound parts of the coagulation cascade, particularly thrombomodulin which increases thrombin-induced activation of protein C and thus causes anticoagulation; this leads to different results compared with in vivo conditions. Therefore, the interaction between procoagulant factors (2,7,9,10) and anticoagulant components (protein C and S) and platelets cannot be assessed with CCT. In contrast to CCT, VHA provide a dynamic picture of the entire coagulation process. Gastroesophageal variceal bleeding occurs in 30% of patients with cirrhosis and carries a significant health burden. Liver disease patients exhibit rebalanced haemostasis, and the abnormal CCT is not indicative of bleeding. VHA-guided assessment of coagulopathy in liver disease provides a better overview of the coagulation system, improves overall number of patients exposed to blood product transfusions, quantity of transfusions and bleeding events compared to CCT. The appeal of VHA to assess coagulopathy and guide haemostatic blood

transfusion is that the faster availability of results may assist clinical decisions of what, when and how much blood products to transfuse. This is in addition to their ability to provide a global and functional assessment of coagulation. Outside liver disease, there is limited data on VHA tests in AGIB. In Australasia, there are no studies on VHA in AGIB. The management of AGIB with blood product transfusion with simultaneous coagulopathy correction and volume restoration is not unified in guidelines and is dependent on the type of AGIB, presence of liver disease, anticoagulants, availability of an on-site endoscopic service and presence of comorbidities. Randomized trials of transfusion thresholds have not included patients with LGIB. Some institutions use VHA to guide blood products and others use CCT. The evidence supporting guidelines in the management of haemostatic resuscitation in AGIB are low quality and suggest opportunities exist for further research. The aim of this study is to report the epidemiology and to capture the current assessment and management strategies of emergency physicians. This will help inform gaps in evidence and directions for further research to improve patient outcomes.

Evaluation and Results

We plan to use a combination of local data collection and statewide data collection through the in scope HHSs to obtain results. Descriptive statistical analyses will be undertaken for each variable. They will be summarised using mean (SD), median (IQR) or counts (proportions) as appropriate. The patients will be sub grouped into those with a coagulopathy and those without. The proportion of patients with coagulopathy will be the primary outcome measure and reported with 95% confidence intervals. Comparisons of variables between the two groups will be performed using the Student’s t-test, Wilcoxon Rank Sum test or the chi-square or Fisher’s exact test as appropriate. Associations of variables with coagulopathy will be assessed using logistic regression and reported using odds ratios and 95% confidence intervals. A p-value of <0.05 will be defined to be statistically significant. All analyses will be performed using Stata v 17.0 (College Station, TX, USA).

References

[1] Villanueva C, Colomo A, Bosch A, Concepción M, Hernandez-Gea V, Aracil C, Graupera I, Poca M, Alvarez-Urturi C, Gordillo J, Guarner-Argente C, Santaló M, Muñiz E, Guarner C. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013 Jan 3;368(1):11-21. doi: 10.1056/NEJMoa1211801. Erratum in: N Engl J Med. 2013 Jun 13;368(24):2341. PMID: 23281973. [1] Sabat N, McSweeney W, Konno T, Gilberd MA, Molloy C, Pretorius C. Upper GI bleeding in rural Australia: general surgery still alive and well! ANZ J Surg. 2023 Apr 12. doi: 10.1111/ans.18454. Epub ahead of print. PMID: 37043717. [1] Gralnek IM, Neeman Z, Strate LL. Acute Lower Gastrointestinal Bleeding. N Engl J Med. 2017 Mar 16;376(11):1054-1063. doi: 10.1056/NEJMcp1603455. PMID: 28296600. [1] Kumar M, Ahmad J, Maiwall R, Choudhury A, Bajpai M, Mitra LG, Saluja V, Mohan Agarwal P, Bihari C, Shasthry SM, Jindal A, Bhardwaj A, Kumar G, Sarin SK. Thromboelastography-Guided Blood Component Use in Patients With Cirrhosis With Nonvariceal Bleeding: A Randomized Controlled Trial. Hepatology. 2020 Jan;71(1):235-246. doi: 10.1002/hep.30794. Epub 2019 Aug 27. PMID: 31148204. [1] Kovalic AJ, Khan MA, Malaver D, Whitson MJ, Teperman LW, Bernstein DE, Singal A, Satapathy SK. Thromboelastography versus standard coagulation testing in the assessment and reversal of coagulopathy among cirrhotics: a

systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2020 Mar;32(3):291-302. doi: 10.1097/MEG.0000000000001588. PMID: 32012141. [1] Tokar JL, Higa JT. Acute Gastrointestinal Bleeding. Ann Intern Med. 2022 Feb;175(2):ITC17-ITC32. doi: 10.7326/AITC202202150. Epub 2022 Feb 8. PMID: 35130044. [1] Tokar JL, Higa JT. Acute Gastrointestinal Bleeding. Ann Intern Med. 2022 Feb;175(2):ITC17-ITC32. doi: 10.7326/AITC202202150. Epub 2022 Feb 8. PMID: 35130044. [1] Sverdén E, Markar SR, Agreus L, Lagergren J. Acute upper gastrointestinal bleeding. BMJ. 2018 Oct 25;363:k4023. doi: 10.1136/bmj.k4023. PMID: 30361444. [1] Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG Clinical Guideline: Upper Gastrointestinal and Ulcer Bleeding. Am J Gastroenterol. 2021 May 1;116(5):899-917. doi: 10.14309/ajg.0000000000001245. Erratum in: Am J Gastroenterol. 2021 Nov 1;116(11):2309. PMID: 33929377. [1] Villanueva C, Colomo A, Bosch A, Concepción M, Hernandez-Gea V, Aracil C, Graupera I, Poca M, Alvarez-Urturi C, Gordillo J, Guarner-Argente C, Santaló M, Muñiz E, Guarner C. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013 Jan 3;368(1):11-21. doi: 10.1056/NEJMoa1211801. Erratum in: N Engl J Med. 2013 Jun 13;368(24):2341. PMID: 23281973. [1] Kim ER, Chang DK. Management of Complications of Colorectal Submucosal Dissection. Clin Endosc. 2019 Mar;52(2):114-119. doi: 10.5946/ce.2019.063. Epub 2019 Mar 29. PMID: 30959586; PMCID: PMC6453857. [1] Sabat N, McSweeney W, Konno T, Gilberd MA, Molloy C, Pretorius C. Upper GI bleeding in rural Australia: general surgery still alive and well! ANZ J Surg. 2023 Apr 12. doi: 10.1111/ans.18454. Epub ahead of print. PMID: 37043717. [1] Campbell HE, Stokes EA, Bargo D on behalf of TRIGGER investigators*, et al* Costs and quality of life associated with acute upper gastrointestinal bleeding in the UK: cohort analysis of patients in a cluster randomised trial *BMJ Open* 2015;**5:**e007230. doi: 10.1136/bmjopen-2014-007230 [1] Gaiani F, De'Angelis N, Kayali S, Manfredi M, Di Mario F, Leandro G, Ghiselli A, Fornaroli F, De'Angelis GL. Clinical approach to the patient with acute gastrointestinal bleeding. Acta Biomed. 2018 Dec 17;89(8-S):12-19. doi: 10.23750/abm.v89i8-S.7861. PMID: 30561412; PMCID: PMC6502216. [1] Gralnek IM, Dumonceau JM, Kuipers EJ, Lanas A, Sanders DS, Kurien M, Rotondano G, Hucl T, Dinis-Ribeiro M, Marmo R, Racz I, Arezzo A, Hoffmann RT, Lesur G, de Franchis R, Aabakken L, Veitch A, Radaelli F, Salgueiro P, Cardoso R, Maia L, Zullo A, Cipolletta L, Hassan C. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2015 Oct;47(10):a1-46. doi: 10.1055/s-0034-1393172. Epub 2015 Sep 29. PMID: 26417980. [1] Hofer S, Schlimp CJ, Casu S, Grouzi E. Management of Coagulopathy in Bleeding Patients. J Clin Med. 2021 Dec 21;11(1):1. doi: 10.3390/jcm11010001. PMID: 35011742; PMCID: PMC8745606. [1] Latona A, Hill K, Connelly A, Stuart K, Wood P. Prothrombinex®-VF in chronic liver disease: Friend or foe? Emerg Med Australas. 2023 Feb;35(1):89-96. doi: 10.1111/1742-6723.14058. Epub 2022 Aug 22. PMID: 35993256; PMCID: PMC10087488. [1] Dorgalaleh A, Favaloro EJ, Bahraini M, Rad F. Standardization of Prothrombin Time/International Normalized Ratio (PT/INR). Int J Lab Hematol. 2021 Feb;43(1):21-28. doi: 10.1111/ijlh.13349. Epub 2020 Sep 26. PMID: 32979036. [1] Gish RG, Stravitz RT. Correction of Coagulopathy of Liver Disease Prior to Procedures. Gastroenterol Hepatol (N Y). 2021 Jan;17(1 Suppl 1):16-23. PMID: 34135700; PMCID: PMC8191819. [1] Gralnek IM, Dumonceau JM, Kuipers EJ, Lanas A, Sanders DS, Kurien M, Rotondano G, Hucl T, Dinis-Ribeiro M, Marmo R, Racz I, Arezzo A, Hoffmann RT, Lesur G, de Franchis R, Aabakken L, Veitch A, Radaelli F, Salgueiro P, Cardoso R, Maia L, Zullo A, Cipolletta L, Hassan C. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2015 Oct;47(10):a1-46. doi: 10.1055/s-0034-1393172. Epub 2015 Sep 29. PMID: 26417980. [1] Bajaj JS, Wong F, Kamath PS, Lai JC, O'Leary JG. Acute-on-Chronic Liver Failure. Am J Gastroenterol. 2022 Jun 1;117(6):831-834. doi: 10.14309/ajg.0000000000001748. Epub 2022 Mar 25. PMID: 35333779. [1] Connors JM. Testing and monitoring direct oral anticoagulants. Blood. 2018 Nov 8;132(19):2009-2015. doi: 10.1182/blood-2018-04-791541. Epub 2018 Sep 10. PMID: 30201757. [1] Sengupta N, Cifu AS. Management of Patients With Acute Lower Gastrointestinal Tract Bleeding.

JAMA. 2018 Jul 3;320(1):86-87. doi: 10.1001/jama.2018.5684. PMID: 29971385. [1] Akay OM. The Double Hazard of Bleeding and Thrombosis in Hemostasis From a Clinical Point of View: A Global Assessment by Rotational Thromboelastometry (ROTEM). Clin Appl Thromb Hemost. 2018 Sep;24(6):850-858. doi: 10.1177/1076029618772336. Epub 2018 May 14. PMID: 29758989; PMCID: PMC6714726. [1] Whiting D, DiNardo JA. TEG and ROTEM: technology and clinical applications. Am J Hematol. 2014 Feb;89(2):228-32. doi: 10.1002/ajh.23599. PMID: 24123050. [1] Nielsen VG. A comparison of the thrombelastograph and the ROTEM. *Blood Coagul Fibrinolysis* 2007; **18**: 247– 252 [1] Wikkelsø A, Wetterslev J, Møller AM, Afshari A. Thromboelastography (TEG) or rotational thromboelastometry (ROTEM) to monitor haemostatic treatment in bleeding patients: a systematic review with meta-analysis and trial sequential analysis. Anaesthesia. 2017 Apr;72(4):519-531. doi: 10.1111/anae.13765. Epub 2017 Jan 4. PMID: 28052313. [1] Gralnek IM, Neeman Z, Strate LL. Acute Lower Gastrointestinal Bleeding. N Engl J Med. 2017 Mar 16;376(11):1054-1063. doi: 10.1056/NEJMcp1603455. PMID: 28296600. [1] Kumar M, Ahmad J, Maiwall R, Choudhury A, Bajpai M, Mitra LG, Saluja V, Mohan Agarwal P, Bihari C, Shasthry SM, Jindal A, Bhardwaj A, Kumar G, Sarin SK. Thromboelastography-Guided Blood Component Use in Patients With Cirrhosis With Nonvariceal Bleeding: A Randomized Controlled Trial. Hepatology. 2020 Jan;71(1):235-246. doi: 10.1002/hep.30794. Epub 2019 Aug 27. PMID: 31148204. [1] Kovalic AJ, Khan MA, Malaver D, Whitson MJ, Teperman LW, Bernstein DE, Singal A, Satapathy SK. Thromboelastography versus standard coagulation testing in the assessment and reversal of coagulopathy among cirrhotics: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2020 Mar;32(3):291-302. doi: 10.1097/MEG.0000000000001588. PMID: 32012141. [1] Tokar JL, Higa JT. Acute Gastrointestinal Bleeding. Ann Intern Med. 2022 Feb;175(2):ITC17-ITC32. doi: 10.7326/AITC202202150. Epub 2022 Feb 8. PMID: 35130044. [1] Haas, T.; Fries, D.; Tanaka, K.A.; Asmis, L.; Curry, N.S.; Schöchl, H. Usefulness of standard plasma coagulation tests in the management of perioperative coagulopathic bleeding: Is there any evidence? Br. J. Anaesth. 2015, 114, 217–224. [[1] Tripodi A, Salerno F, Chantarangkul V, Clerici M, Cazzaniga M, Primignani M, et al. Evidence of normal thrombin generation in cirrhosis despite abnormal conventional coagulation tests. Hepatology. 2005;41:553–8. [1] Lisman T, Porte RJ. Rebalanced hemostasis in patients with liver disease: evidence and clinical consequences. Blood. 2010;116:878–85. [1] Seeßle, J., Löhr, J., Kirchner, M. *et al.* Rotational thrombelastometry (ROTEM) improves hemostasis assessment compared to conventional coagulation test in ACLF and Non-ACLF patients. *BMC Gastroenterol* **20**, 271 (2020). https://doi.org/10.1186/s12876-020-01413-w [1] Kumar AS, Sibia RS. Predictors of in-hospital mortality among patients presenting with variceal gastrointestinal bleeding. Saudi J Gastroenterol. 2015 Jan-Feb;21(1):43-6. doi: 10.4103/1319-3767.151226. PMID: 25672238; PMCID: PMC4355862. [1] Latona A, Hill K, Connelly A, Stuart K, Wood P. Prothrombinex®-VF in chronic liver disease: Friend or foe? Emerg Med Australas. 2023 Feb;35(1):89-96. doi: 10.1111/1742-6723.14058. Epub 2022 Aug 22. PMID: 35993256; PMCID: PMC10087488. [1] Kovalic AJ, Khan MA, Malaver D, Whitson MJ, Teperman LW, Bernstein DE, Singal A, Satapathy SK. Thromboelastography versus standard coagulation testing in the assessment and reversal of coagulopathy among cirrhotics: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2020 Mar;32(3):291-302. doi: 10.1097/MEG.0000000000001588. PMID: 32012141. [1] Premkumar M, Mehtani R, Divyaveer S, Kajal K, Kulkarni AV, Ahmed S, *et al*. Clinical Validation of Global Coagulation Tests to Guide Blood Component Transfusions in Cirrhosis and ACLF. *J Clin Transl Hepatol*. 2021;9(2):210-219. doi: 10.14218/JCTH.2020.00121. [1] Bajaj JS, O'Leary JG, Lai JC, Wong F, Long MD, Wong RJ, Kamath PS. Acute-on-Chronic Liver Failure Clinical Guidelines. Am J Gastroenterol. 2022 Feb 1;117(2):225-252. doi: 10.14309/ajg.0000000000001595. PMID: 35006099. [1] Johansson PI, Stensballe J. Effect of Haemostatic Control Resuscitation on mortality in massively bleeding patients: a before and after study. Vox Sang. 2009 Feb;96(2):111-8. doi: 10.1111/j.1423-0410.2008.01130.x. PMID: 19152603; PMCID: PMC2667686. [1] Sankarankutty, A., Nascimento, B., Teodoro da Luz, L. *et al.* TEG® and ROTEM® in trauma: similar test but different results?. *World J Emerg Surg* **7** (Suppl

1), S3 (2012). https://doi.org/10.1186/1749-7922-7-S1-S3 [1] Tokar JL, Higa JT. Acute Gastrointestinal Bleeding. Ann Intern Med. 2022 Feb;175(2):ITC17-ITC32. doi: 10.7326/AITC202202150. Epub 2022 Feb 8. PMID: 35130044. [1] Sverdén E, Markar SR, Agreus L, Lagergren J. Acute upper gastrointestinal bleeding. BMJ. 2018 Oct 25;363:k4023. doi: 10.1136/bmj.k4023. PMID: 30361444. [1] Gralnek IM, Neeman Z, Strate LL. Acute Lower Gastrointestinal Bleeding. N Engl J Med. 2017 Mar 16;376(11):1054-1063. doi: 10.1056/NEJMcp1603455. PMID: 28296600. [1] Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG Clinical Guideline: Upper Gastrointestinal and Ulcer Bleeding. Am J Gastroenterol. 2021 May 1;116(5):899-917. doi: 10.14309/ajg.0000000000001245. Erratum in: Am J Gastroenterol. 2021 Nov 1;116(11):2309. PMID: 33929377.