|  |  |
| --- | --- |
| PICO 1 | Risk stratification to identify low-risk patients with LGIB who can be discharged early from the hospital with outpatient evaluation  P: People with LGIB with very low risk scores (e.g. Oakland<=8) at presentation  I: Discharge from the ED with outpatient management  C: Hospitalize  O: Safe discharge (absence of blood transfusion, rebleeding, hemostatic intervention [endoscopic hemostasis, arterial embolization, surgery], hospital readmission, death) |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Pooled diagnostic accuracy | | |  |  |
|  | Cutoff value | Sensitivity (95% CI) | Specificity (95% CI) | Comments | |
| **Oakland Score** | | | | | |
| DTA study (1) | 8 | 0.95 |  | Endpoint: Safe discharge defined as absence of rebleeding (defined as additional PRBC rec or a further decrease in Hct of 20% or more after 24 h clinical stability); RBC transfusion, therapeutic intervention to control bleeding (endoscopic, radiologic or surgical hemostasis), in-hospital death, and readmission with further LGIB within 28 days. | |
| DTA study (2) | 8 | 0.98 | 0.16 | Endpoint: Safe discharge (same as above) | |
|  | 10 | 0.96 | 0.32 | Endpoint: safe discharge (same as above) | |
| **SHA2PE score** | | | | | |
| DTA study (3) | 1 | 0.86 (0.73-0.94) | 0.66 (0.57-0.74) | Endpoint: Avoidance of hospital-based intervention (blood transfusion, endoscopic hemostasis, arterial embolization, surgery). (**Of note, rebleeding and death were not included in the definition)** | |
| DTA study (4) | 1 | 0.73 (0.58-0.84) | 0.82(0.75-0.87) | Endpoint: Same as above  \*\*14 patients misclassified as low risk who required an intervention, NPV 90% | |

1. Oakland K et al. Derivation and validation of a novel risk score for safe discharge after acute lower gastrointestinal bleeding: a modelling study. Lancet Gastroenterology and Hepatology 2017; 2: 635-643.
2. Oakland et al. External validation of the Oakland Score to assess safe hospital discharge among adult patients with acute lower gastrointestinal bleeding in the US. JAMA Netw Open 2020; 3: e209630
3. Hreinsson JP et al. The SHA2PE score: a new score for lower gastrointestinal bleeding that predicts low-risk of hospital-based intervention. Scandinavian Journal of Gastroenterology 2018; 53: 1484-1489
4. Cerruti T et al. Acute lower gastrointestinal bleeding in an Emergency Department and performance of the SHA2PE score; a retrospective observational study. Journal of Clinical Medicine 2021

|  |  |
| --- | --- |
| PICO 2 | Restrictive or liberal transfusion strategy for patients with GIB (including lower GI bleeding)  P: Patients with LGIB  I: Restrictive transfusion (e.g., hemoglobin 7-8g /dL)  C: Liberal transfusion (e.g., hemoglobin 9,10 g/dL)  O: **CRITICAL:** Further bleeding, mortality  **IMPORTANT:** Transfusion-related adverse events, cardiovascular events |

|  |  |  |  |
| --- | --- | --- | --- |
|  | Intervention: | Outcomes | Findings ***(restr vs. liber)*** |
| **Observational studies in LGIB** | | | |
| *Kherad et al* | ***Liberal*** (Hb threshold > 80 g/L or >90 g/L in ACS or major hemorrhage)  ***Restrictive*** (threshold <80 g/L or < 90 g/L in ACS or major hemorrhage) | ***Rebleeding*** (additional transfusion needs and/or decrease in Hct >20% after 24h of stability  ***Mortality***  ***Readmission*** | **Nd** in rebleeding (OR 0.9, 95%CI 0.6-1.3)  **Nd** in mortality (0.54, 95% CI 0.3-1.1)  **Nd** in readmission (OR 1.15 95% CI 0.6-2.7) |
| **Systematic review and meta-analysis of RCTs** | | | |
| *Odutayo et al* | RBC threshold of <80g/L vs. RBC threshold of 80-110 g/L for women or 80-130g/L for men | Mortality  Rebleeding  # RBC units  Ischemic events | **RR 0.65** (0.44-0.97)  **RR 0.58** (0.40-0.84)  **-1.73 diff (-**2.36—1.11)  Nd in MI or stroke |
| **Randomized Controlled Trials** | | | |
| *Jairath et al* | Restrictive (RBC threshold <80g/L)  Liberal (RBC threshold <100g/L) | # RBC units  Further bleeding  Thromboembolic/ischemic events  Mortality | **Diff -12%** (95% CI -35 – 11)  Nd seen in rebleeding or mortality |
| *Villaneuva et al* | Restrictive (RBC threshold 7g/dL)  Liberal (9g/dL) | Mortality (primary)  Further bleeding  Complications | **HR 0.55** (95%CI 0.33-0.92) **HR 0.68** (95%CI 0.47-0.98)  40% vs. 48% (**p=0.02)** |

1. Kherad O et al. Outcomes following restrictive or liberal red blood cell transfusion in patients with lower gastrointestinal bleeding. Aliment Pharmacol Ther 2019
2. Odutayo A et al. Restrictive vs. liberal blood transfusion for gastrointestinal bleeding: a systematic review and meta-analysis of randomized controlled trials. Lancet Gastroenterol Hepatol 2017
3. Jairath V, Kahan BC, Gray A, et al. Restrictive versus liberal blood transfusion for acute upper gastrointestinal bleeding (TRIGGER): a pragmatic, open-label, cluster randomised feasibility trial. Lancet. 2015;386:137-44.
4. Villanueva C et al. Transfusion strategies for acute upper gastrointestinal bleeding. New Engl J Med 2013

|  |  |
| --- | --- |
| PICO 3 | Reversal of patients who present with LGIB on vitamin K antagonists (VKA)  P: Patients with GIB (including LGIB) on VKA  I: Administration of reversal agents (including prothrombin complex concentrate, Vitamin K, Fresh frozen plasma)  C: No reversal agents (+comparison between agents)  O: Further bleeding, mortality, endoscopic hemostasis, time to endoscopy, reduction in INR |

|  |  |  |  |
| --- | --- | --- | --- |
|  | Population | Intervention/Outcomes | Findings |
| ***Post hoc analysis of GIB patients in two RCTs of 4F-PCC vs. Plasma for VKA reversal*** | | | |
| *Refaii et al* | Review of patients with GIB from 2 multicenter RCTs comparing 4FPCC to plasma for VKA reversal | Outcome: time to procedure (median) | 17.5 h (PCC) vs. 23.9 h, (plasma) p=0.037 |
| ***Small study comparing FFP to PCC for warfarin reversal in GIB*** | | | |
| *Karaca et al* | Prospective cohort of 40 patients with GIB receiving PCC or FFP for high INR (>2.1) | INR levels at 2 and 6 hrs  Active bleeding on endoscopy | INR levels at 2h and 6h significantly less in PCC  35% (FFP) vs. 0% (PCC), p<.01 |
| ***Meta-analyses on overall efficacy of PCC vs. FFP in reversing VKA (not specific to GIB)*** | | | |
| *Brekelmans et al* | 18 cohort studies comparing PCC to FFP, only 1 study with only GIB patients, no subgroup analysis specific to GIB outcomes | Mortality (PCC vs. plasma)  Mortality (PCC vs. nothing)  Thromboembolic complications (PCC vs. plasma) | OR 0.64 (0.27-1.48)  OR 0.41 (0.13-1.27)  0-18% (mean 2.5%) vs. 6.4% |
| *Chai-Adisaksopha et al* | 13 studies (5 RCTs), only minority of studies with GIB included | Mortality (PCC vs. plasma)  Hemostasis (PCC vs. plasma)  Rapid INR reduction (PCC vs. plasma)  Time to INR correction (PCC vs. plasma)  CHF (PCC vs. plasma) | **OR 0.56** (0.37-0.84)  **OR 2.00** (0.85-4.68)  **OR 10.80** (6.12-19.07)  **-6.50 (-9.75-3.24)**  **OR 0.27** (0.13-0.58) |

1. Refaai M et al. Four-factor Four-Factor Prothrombin Complex Concentrate Reduces Time to Procedure in Vitamin K Antagonist-Treated Patients Experiencing Gastrointestinal Bleeding: A Post Hoc Analysis of Two Randomized Controlled Trials. Emerg Med Int 2017
2. Karaca M et al. Use and effectiveness of prothrombin complex concentrates vs. fresh frozen plasma in gastrointestinal hemorrhage due to warfarin usage in the ED. Am J Emerg Med 2014; 32:660-4.
3. Brekelmans MP, Ginkel K, Daams JG, Hutten BA et al. Benefits and harms of 4-factor prothrombin complex concentrate for reversal of vitamin K antagonist associated bleeding: a systematic review and meta-analysis. J Thromb Thrombolysis 2017; 44: 118-129.
4. Chai-Adisaksopha C, Hillis C, Siegal DM et al. Prothrombin complex concentrates versus fresh frozen plasma for warfarin reversal. A systematic review and meta-analysis. Thromb Haemost 2016; 116:879-890.

|  |  |
| --- | --- |
| PICO 4 | Reversal of patients who present with LGIB on DOAC  P: Patients with severe LGIB on DOAC (dabigatran, apixaban, edoxaban, rivaroxaban)  I: Administration of reversal agent (PCC, idaracizumab, andexanet alfa)  C: No reversal agents  O: Further bleeding, mortality, endoscopic hemostasis |

|  |  |  |  |
| --- | --- | --- | --- |
|  | Population | Outcomes | Findings |
| ***Reversal of Dabigatran with Idaracizumab*** | | | |
| *Van der wall et al* | Analysis of 137 patients with GIB (43 with LGIB) in RE-VERSE AD study (Idaracizumab for hemorrhage or urgent surgery) | Complete reversal of dabigatran  Bleeding cessation within 24 hrs  90-day thrombosis/mortality | 97.5% of patients  72% (96/134) within median of 2.6h. For LGIB (n=42), bleeding cessation was 76% (32/42) at 2.1h  6 (4.4%) with post reversal thrombosis and 20 (14.6%) died |
| *Singh et al* | Analysis of 1124 patients receiving idaracizumab for dabigatran GIB | In-hospital mortality (idara given vs. not)  Transfusion rate (idara given vs. not)  VTE rate (idara given vs. not) | 3.3% (37/1124) vs. 5.9% (9/153), p=0.11  42.5% (478/1124) vs. 61% (93/153),***p<.001***  4.2% vs. 1.3%, p=.08 |
| ***Reversal with Andexanet alfa*** | | | |
| *Connolly et al* | Analysis of 352 patients with major bleeding due to a factor Xa inhibitor receiving andexanet (90 with GIB) | Hemostatic efficacy after 12 hours (independent adjudication committee)  Safety | 85% (76-94%) with excellent or good hemostasis in GIB pop  10% of cohort had thrombosis and 14% died w/in 30 days |
| *Siegel at al* | (Abstract)  Analysis of 62 patients with GIB in ANNEXA-4 (LGIB, n=21) | Hemostatic efficacy  30-day thrombosis/death | 85% with good or excellent hemostatic efficacy  6%/13% |
| *Coleman et al* | Analysis of 1453 patients with GIB on factor Xa inhibitors | Andexanet (9%, n=137)  PCC (21%, n=303)  No reversal (16%, n=228) | Inpatient mortality for GIB (andexxa, 1%; PCC, 4%; no reversal, 5%) |
| ***Meta-analyses on overall efficacy/safety of reversal agents for factor Xa inhibitors for major bleeding (not specific to GIB)*** | | | |
| *Gomez-Outes et al* | PCC (n=2688)  Idaracizumab (n=1111)  Andexanet (n=936)  Small minority of patients with GIB in studies | Mortality  Hemostatic efficacy | Extracranial hemorrhage (15.4%, 95% CI 11.9-19.2)  PCC (14.0% 5.3-25.9)  Idaracizumab (13.6%, 8.1-20.3)  Andexanet (10.3, 2.6-22.3)  PCC (81.5%, 95%CI 69.4-91.1)  Idaracizumab (76.2%, 95% CI 56.2-91.5)  Andexa (77.2%, 48.0-96.4) |
| *Jaspers et al* | PCC (n=1428)  Andexanet (n=396) | Hemostatic efficacy  Thromboembolism | PCC (0.85, 0.80-0.90)  Andexa (0.82, 0.78-0.87)  PCC (0.03, 0.02-0.04)  Andexa (0.11, 0.04-0.18) |
| *Luo et al* | 22 studies (minority with GIB) | Hemostatic efficacy in extracranial bleeding/GIB  Mortality in extracranial bleeding/GIB | Andexa (84%, 75-92)  PCC (69%, 56-82)  Andexa (22%, 3-60)  PCC (29%, 13-45) |
| *Nederpelt et al* | PCC (n=1278, 87 with GIB)  Andexa (n=438, 86 with GIB) | Hemostatic efficacy (12 hr) | Andexa (0.82, 0.77-0.86)  PCC (0.88, 0.81-0.93) |

1. Van der Wall S et al. Idaracizumab for dabigatran reversal in the management of patients with gastrointestinal bleeding. Circulation 2019; 139: 748-756.
   1. *Review of GIB patients in REVERSE AD who received idaracizumab*
2. Singh S et al. Real world outcomes associated with idaracizumab: population-based retrospective cohort study. American journal of cardiovascular drugs 2020
3. Connolly SJ et al. Full study report of andexanet alpha for bleeding associated with factor Xa inhibitors. New Engl J Med 2019; 380: 1326-1335.
4. Siegal D et al. The efficacy and safety of andexanet alfa in patients with acute gastrointestinal bleeding while taking factor Xa inhibitors: an ANNEXA-4 sub analysis Am J Gastroenterol 2019; 114: S332-S333 (abstract)
5. Coleman C et al. Real-world management of oral factor Xa inhibitor -related bleeds with reversal or replacement agents including andexanet alfa and four-factor prothrombin complex concentrate: a multicenter study. Future Cardiology 2020
6. Gomez-Outes A et al. Meta-analysis of reversal agents for severe bleeding associated with direct oral anticoagulants. JACC 2021.
7. Jaspers T et al. A meta-analysis of andexanet alfa and prothrombin complex concentrate in the treatment of factor Xa inhibitor-related major bleeding. Res Pract Thromb Haemost 2021
8. Luo C et al. Prothrombin complex concentrates and andexanet for management of direct factor Xa inhibitor-related bleeding: a meta-analysis. Eur Rev Med Pharmacol Sci 2021
9. Nederpelt C et al. Andexanet alfa or prothrombin complex concentrate for factor Xa inhibitor reversal in acute major bleeding: a systematic review and meta-analysis. Crit Care Med 2021

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| PICO 5 | Administration of antifibrinolytic agents in LGIB  P: Patients with severe LGIB  I: Administration of transexemic acid  C: No administration  O: Mortality, further bleeding | | | |
|  | | Population | Comparator/Outcomes | Findings |
| **Data specific to LGIB** | | | | |
| *Miyamoto et al* | | Observational Japanese database study in diverticular bleeding comparing TXA on day of admission to no TXA (propensity matched 1:1) – 30,526 matched pairs | In hospital mortality (control vs. TXA)  Severe bleeding events (control vs. TXA)  Blood transfusion (control vs. TXA) | ND in in-hospital mortality (0.7% vs. 0.7%)  SD (17.5% vs. 16.6%, p=.003)  SD (34.3% vs. 31.4%, p<.001) |
| *Smith et al* | | Double-blind placebo controlled RCT in LGIB (n=100) randomized 1:1 to TXA and placebo | Blood loss (reduction in Hgb levels)  Transfusion rate  Intervention rate LOS  Readmission | ND in blood loss (11g/L TXA vs. 13g/L control)  ND in transfusion rate, intervention rate, LOS, 28 day mortality, readmission |
| **RCT in all-cause GIB** | | | | |
| *Roberts et al* | | Multicenter RCT in GIB of TXA (n=5994) vs. placebo (n=6015) | Death (primary) within 5 days  VTE events (TXA vs. placebo) | ND (RR 0.99, 95% CI 0.82-1.18)  **1.85 (1.15-2.98)** |
| **Systematic review and meta-analysis of RCTs evaluating TXA in GIB** | | | | |
| *Lee et al* | | 13 RCTs (n=2271). Only 2 trials were in LGIB, and 1 was undifferentiated. Highly heterogeneous results | Continued bleeding/Rebleeding (TXA vs. placebo)  Urgent Endoscopic intervention (TXA vs. placebo) | **RR 0.60** (95% CI 0.43-0.84), RR 0.84 (0.61-1.15)  **RR 0.35** (0.24-0.50)  ND in any endoscopic intervention |

1. Miyamoto Y et al. Effect of transexemic acid in patients with colonic diverticular bleeding: a nationwide inpatient database study. J Gastroenterol Hepatol 2020
2. Smith SR et al. Transexemic acid for lower GI hemorrhage: a randomized placebo-controlled trial. Dis Colon Rectum 2018
3. Roberts I et al. Effects of a high-dose 24-h infusion of transexemic acid on death and thromboembolic events in patients with acute gastrointestinal bleeding (HALT-IT): an international randomized, double-blind, placebo-controlled trial. Lancet 2020
4. Lee P et al. Tranexamic acid for gastrointestinal bleeding: a systematic review with meta-analysis of randomized controlled trials. American Journal of Emergency medicine 2021

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| PICO 6 | Role of colonoscopy in LGIB  P: Patients with suspected lower gastrointestinal bleeding  I: Performance of colonoscopy during hospitalization  C: No colonoscopy  O: Source of bleeding, further bleeding/rebleeding, frequency of endoscopic treatment/hemostasis | | | |
|  | | Population | Comparator/Outcomes | Findings |
| ***Diagnostic Yield of Colonoscopy, SRH, Frequency of endoscopic treatment*** | | | | |
| *Chung et al* | | Retrospective cohort of n=5195 (derivation) and (validation), n=914 undergoing colonoscopy for LGIB | Active bleeding  Malignant source of bleeding  Clinical prediction score to predict lesions bleeding requiring hemostasis, malignant-lesions, or active bleeding | Active bleeding found in 3.8%  2.5% malignant lesions  Threshold of 6 has a NPV of 93.8% |
| *Nagata et al* | | Multicenter retrospective cohort of 10,342 pts with hematochezia (colonoscopy performed in 87.7%. | Frequency of SRH  Diagnostic yield of colonoscopy  Frequency of endoscopic treatment  In-hospital rebleeding | SRH ~ 30.9%  Yield ~ 94.9%  Treatment ~ 30.7%  Rebleeding ~ 15.2% |
| *Oakland et al* | | Multicenter UK cohort of 2528 cases of LGIB | Diagnostic yield  Endoscopic intervention  Continued bleeding during first 24 hrs  Rebleeding | Flex sig ~ 77% (418/543)  Cscope ~ 72% (71/99)  2.1% (54/2528)  11% (279/2528)  13.6% (343/2528) |
| *Radaelli et al* | | Multicenter prospective of 1198 pts hospitalized with LGIB | Diagnostic yield of colonoscopy  Intervention rate of colonoscopy | Cscope ~ (78.8%)  Cscope<24 hrs (21.3%)  Cscope>24 hrs (10.8%)  Intervention not a/w in-hospital mortality or rebleeding |
| *Gobinet et al* | | Retrospective multicenter of 5823 patients with diverticular bleeding, comparing conservative mgmts. Vs. endoscopic intervention | Early rebleeding rates in definitive CDB treated endoscopically vs. conservatively  Late rebleeding rate in definitive CDB treated endoscopically vs. conservative | 17.4% (endoscop tx) vs. 26.7% (treated conservatively)  32.0% (endoscopic) vs. 36.1% (treated conservative) |
| ***Frequency of Endoscopic intervention*** | | | | |
| *Ron-Tal Fischer et al* | | Retrospective cohort of 3151 pts undergoing inpatient cscope for hematochezia | Frequency of endoscopic intervention  Predictors of hemostasis | ~4.6%  Angiodysplasia seen at colonoscopy (18.6, 95% CI 12.1-28.6) |
| *Nigam et al* | | Retrospective cohort of 1204 patients undergoing colonoscopy for LGIB | Colonoscopy w intervention  Predictors of intervention | 3% (n=40)  Early colon (OR 3.70), older age (1.03), and colonic AVMs (OR 26.80) |
| *Nigam et al* | | Retrospective, propensity-matched insurance claims database of 20,010, comparing early colonoscopy | Endoscopic intervention (early vs. elective) | 3% vs. 8% ,p<.0001 |

1. Chung W et al. A predictive model for diagnostic and therapeutic yield of colonoscopy performed for lower gastrointestinal bleeding. J Clin Gastroenterol 2021
2. Nagata N et al. Identifying Bleeding etiologies by endoscopy affected outcomes in 10,342 cases with hematochezia: CODE BLUE-J study. Am J Gastroenterol 2021
3. Oakland K et al. Acute lower GI bleeding in the UK: patient characteristics, interventions and outcomes in the first nationwide audit. Gut 2018
4. Radaelli F et al. Clinical management and patient outcomes of acute lower gastrointestinal bleeding. A multicenter, prospective, cohort study. Dig Liver Dis 2021
5. Gobinet M et al (Dec 30 2021). Treatment strategies for reducing early and late recurrence of colonic diverticular bleeding based on stigmata of recent hemorrhage: a large multicenter study
6. Ron-Tal Fischer O et al. Endoscopic hemostasis is rarely used for hematochezia: a population study from the clinical outcomes research initiative national endoscopic database. GIE 2014
7. Nigam N et al. Outcomes of early vs. delayed colonoscopy in LGIB using a hospital administrative database 2018
8. Nigam N et al. Early colonoscopy for diverticular bleeding does not reduce risk of post-discharge recurrent bleeding: a propensity scoring matching analysis. Clin Gastroenterol Hepatol 2019.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| PICO 7 | Colonoscopy vs. CTA as initial diagnostic testing in patients with severe hematochezia  P: Patients with severe LGIB  I: Performance of CT Angiography as initial diagnostic testing  C: Performance of colonoscopy  O: Source of bleeding, further bleeding, mortality, endoscopic intervention | | | |
|  | | Population | Comparator/Outcomes | Findings |
| ***Comparing colonoscopy to CTA as initial diagnostic testing*** | | | | |
| *Clerc D et al* | | Single center, retrospective analysis of 183 pts with LGIB (122 had colon first vs. 32 had CTA) | Frequency of active bleeding  Non-active bleeding source | 31.3% (CTA group) vs. 14.8% (colon group), p<.0001  21.8% (CTA group) vs. 31.1% (colon), p=0.305 |
| *Lee et al* | | Single center retrospective analysis of 382 pts with LGIB (112 with CT, 65 with colonoscopy) | Active bleeding  Etiology diagnosed | 12/112 (CTA group)  10/65 (colon group)  91/112 (CTA group)  41/65 (colon group) |
| *Lipscey et al* | | Single center retrospective analysis of 258 pts with LGIB (162 initial colon, 96 CTA). | Diverticular bleeding as source  Overall source identification  Therapeutic intervention  \*\*CTA had higher unadjusted rate of source identification and intervention in diverticular subgroup | CTA group (63.6%), colonoscopy group (32.1%)  Colonoscopy group (64.2%)  CTA group (45.3%), **p=.004**  Colonoscopy group (30.9%)  CTA group (17.6%), **p=.03** |
| ***Performance of CTA prior to Colonoscopy*** | | | | |
| *Ichiba T et al* | | Retrospective analysis of 257 consecutive pts with diverticular hemorrhage undergoing CTA prior to colonoscopy | Definitive diverticular hemorrhage (CTA or colon)  Agreement rate of CTA vs. colon localization | CTA (71.6%)  Colonoscopy (50.6%)  67.3% (26.5% identified only on CTA , 5.4% identified only on colon) |
| *Nagata et al* | | Retrospective analysis of 223 pts with acute LGIB (126 underwent CT prior to early colon vs. 97 undergoing early colon alone) | Vascular lesion detection rate  Endoscopic interventions | CTA prior to colon (35.7 vs. 26%, p**=0.01**  CTA prior to colon (34.9 vs. 13.4, **p=<.01** |
| *Nakatsu et al* | | Retrospective analysis of 1604 pts with LGIB who underwent colonoscopy within 3 mos (879 also underwent CT). Urgent colonoscopy performed after CTA in 640 cases. | Rate of detection of bleeding source on colonoscopy in those with contrast extravasaton (CE) on CT vs. no CE | CE-CT (68%) vs. no CE-CT (20%), **p<.001** |
| Umezawa S et al | | Prospective multicenter of 202 patients with diverticular bleeding undergoing CT prior to colonoscopy | Positive extravasation rate on CT  Sensitivity/specificity of finding SRH on colonoscopy after extravsation on preceding CT | 24.7% (50/202)  57.6% (38/66) (sens)  91.2% (124/136) (spec) |

References:

1. Clerc D et al. Lower gastrointestinal bleeding – computed tomographic angiography, colonoscopy, or both? World J Emerg Surg 2017
2. Lee H et al. Computed tomography versus lower endoscopy as initial diagnostic method for evaluating patients with hematochezia at emergency room. Medicine 2020
3. Lipcsey M et al. Primary CT Angiography vs. colonoscopy in acute lower gastrointestinal hemorrhage. Techniques and innovations in Gastrointestinal Endoscopy 2021
4. Ichiba T et al. Impact of computed tomography evaluation before colonoscopy for the management of colonic diverticular hemorrhage. J clin Gastroenterol 2019.
5. Nagata N et al. Role of urgent contrast-enhanced multidetector CT for acute lower gastrointestinal bleeding in patients undergoing early colonoscopy J Gastroenterol 2015
6. Nakatsu S et al. Urgent computed tomography for determining the optimal timing of colonoscopy in patients with acute lower gastrointestinal bleeding. Intern Med 2015
7. Umezawa S et al. Contrast-enhanced CT for colonic diverticular bleeding before colonoscopy: a prospective multicenter study Radiology 2018

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| PICO 8 | Management of patients with a positive CTA  P: Patients with severe hematochezia who have a positive CTA localizing a source of bleeding in the colon  I: Performance of mesenteric angiography with embolization  C: Colonoscopy  O: Endoscopic hemostasis, Rebleeding, Source of bleeding | | | |
|  | | Population | Comparator/Outcomes | Findings |
| ***Comparing outcomes of angiography to embolization*** | | | | |
| *Miyakuni et al* | | Retrospective analysis of 6546 pts with LGIB undergoing colonoscopy (n=5737) or angiography (n=809)within 1 day of admission for severe LGIB. After 1:4 propensity matching, colonoscopy (n=3220) compared to angiography (n=809) | In-hospital mortality (angio vs. colon)  Need for surgery w/in 1 day (angio vs. colon) | RR 1.14 (95% CI 0.95-1.36)  RR 0.44 (95% CI 0.29-0.67; **p<.001**) |
| *Tse et al (****Published 2/22****)* | | Retrospective analysis of 71 pts with LGIB who had a positive CTA undergoing either colonoscopy (n=27) or angiography (n-44) | Yield of detecting active bleeding  Rates of therapeutic intervention  Predictors of either confirmation of bleeding or therapeutic intervention  Rebleeding and adverse events | Angio > colonoscopy (**55% v. 26%, p=.03)**  ND (70% vs. 56%, p=.21)  Shorter time to procedure (median 5h for CA vs. 15h for colon)  ND between angio or colon groups |
| ***Efficacy/Technical success of Angiography/Embolization*** | | | | |
| Chevallier O et al. | | Systematic review/meta-analysis of TAE with NBCA. Analysis included 243 patients with LGIB. Tech success defined as occlusion of vessel, clinical success defined as no rebleeding within 30 days | Technical success  Clinical success  30-day rebleeding  30-day mortality  Complications | 99%  78% (145/189), 95% CI 68.3-86.3%)  15.7% (33/218), (95% CI 11.2-20.8%)  12.7% (95% CI 0.7-36.1%)  13% (25/228) (major complications in 19 pts) |
| *Hur S et al* | | Single-center retrospective analysis of 112 pts with LGIB undergoing embolization with NBCA (n=84), gelatin sponge (n=20), microcoils | Technical success  Recurrent bleeding w/in 30 days  Major complications due to ischemia | 96.4%  17.4% (15/86)  4.6% (n=5) |
| *Hwa Kim et al* | | Meta-analysis of 179 patients with LGIB undergoing TAE with NBCA embolization | Technical success  Pooled Clinical success  Major complications | 97.8% (175/179)  86.1% (95% CI 79.9-90.6%)  6.1% (95% CI 3.1-11.6%) |
| ***Positive CTA prior to Angiography*** | | | | |
| *Jacovides CL et al* | | Retrospective analysis of 161 angiographies for LGIB over study period (78 before, and 83 after protocol incorporating CTA into management). Analysis compared CTA prior to VA (n=49) compared to VA alone (n=21) | Utilization of CTA pre and post protocol implementation  Positive study rate (VA first vs. CTA prior to VA) | Increase from 3.8% to 56.6%, (decrease in nuclear scintigraphy)  42.9% (9/21) vs. 93.9% (46/49), p<.001 |
| *Senadeera S et al* | | Retrospective analysis of 104 pts with positive CTA for LGIB who underwent TA. Analysis of 77 pts who underwent embolization | Clinical success  Bowel ischemia  Predictors of clinical success | 81% (n=63/77)  5.2% (n=4/77)  More common in diverticular bleeding (61.9% vs. 38.1%, p=0.04) |
| *Thavanesan N et al* | | Retrospective analysis of 123 pts with LGIB undergoing angiography (DSA) after preceding CTA. DSA localized bleeding in 64.2% (n=79/123). Technical success in 64/79 pts. | Frequency of positive CTA in technical successful DSA vs. unsuccessful DSA  MV analysis of variables predictive of negative DSA | 98.3% (60/61) vs. 87.5% (42/48)  Probability of success highest if CTA to DSA time <120 min  **Time between CT and DSA** (>126 min, OR 9.53, 95% CI 1.75-51.9)  **Hemodynamic instability** (OR 0.13, 95% CI 0.03-0.66) |
| *Koh FH et al* | | Retrospective analysis of 48 angiography performed after positive CTA for LGIB | Median delay from positive CTA to MA  Positive MA rate  Time lapse between CTA and MA (<90 min vs. >90 minutes) | 144 minutes (32-587)  52% (25/48)  OR 8.56 (95% CI 0.96-76.1), p=.05 |
| ***Positive CTA prior to Colonoscopy*** | | | | |
| *Ochi M et al* | | Retrospective analysis of 182 pts with diverticular bleeding undergoing CTA and colonoscopy. Urgent CT (<4 hrs), n=100 vs. elective CT (>4 h), n=82 | Identification of SRH on colonoscopy (urgent CT vs. elective CT)  Identification of SRH in positive CTA | 35% (35/100) vs. 7.3% (6/82), p<.01  66%, 31/47 (urgent CT) vs. 20%, 4/20 (elective CT) |
| *Takada H et al* | | Retrospective analysis of 132 pts with diverticular bleeding. CT extravsation seen in 19% of pts | Factors predicting SRH during colonoscopy (univariate analysis) | Extravsation/fluid collection on CT (OR 17, p<.001) |
| *Nagata et al* | | Retrospective analysis of 223 pts with acute LGIB (126 underwent CT prior to early colon vs. 97 undergoing early colon alone) | Vascular lesion detection rate  Endoscopic interventions | CTA prior to colon (35.7 vs. 26%, p**=0.01**  CTA prior to colon (34.9 vs. 13.4, **p=<.01** |
| *Nakatsu et al* | | Retrospective analysis of 1604 pts with LGIB who underwent colonoscopy within 3 mos (879 also underwent CT). Urgent colonoscopy performed after CTA in 640 cases. | Rate of detection of bleeding source on colonoscopy in those with contrast extravasaton (CE) on CT vs. no CE | CE-CT (68%) vs. no CE-CT (20%), **p<.001** |
| *Umezawa et al* | | Prospective multicenter of 202 patients with diverticular bleeding undergoing CT prior to colonoscopy | Positive extravasation rate on CT  Sensitivity/specificity of finding SRH on colonoscopy after extravsation on preceding CT | 24.7% (50/202)  57.6% (38/66) (sens)  91.2% (124/136) (spec) |

1. Miyakuni Y et al. Angiography vs. colonoscopy in patients with severe lower gastrointestinal bleeding: a nation-wide observational study. Acute Medicine and Surgery 2020
2. Tse et al. Colonoscopy vs. catheter angiography for lower gastrointestinal bleeding after localization on CT angiography. J Am Coll Radiol 2022.
3. Chevallier O et al. Efficacy, safety and outcomes of transcatheter arterial embolization with N-butyl cyanoacrylate glue for non-variceal gastrointestinal bleeding: A systematic review and meta-analysis. Diagn Interv Imaging 2021; 102: 479-487.
4. Hur S et al. Safety and efficacy of transcatheter arterial embolization for lower gastrointestinal bleeding: a single-center experience with 112 patients. J Vasc Interv Radiol 2014; 25
5. Hwa Kim P et al. Transcatheter Arterial Embolization of Gastrointestinal Bleeding with N-Butyl Cyanoacrylate: A Systematic Review and Meta-Analysis of Safety and Efficacy. J Vasc Interv Radiol 2017
6. Jacovides CL et al. Arteriography for lower gastrointestinal hemorrhage: role of preceding abdominal computed tomographic angiogram in diagnosis and localization. JAMA Surg 2015.
7. Senadeera S et al. Role of super-selective embolization in lower gastrointestinal bleeding. ANZ J Surg 2018; 88: E644-E648.
8. Thavanesan N et al. Clinical factors associated with successful embolization of lower gastrointestinal bleeding. ANZ J Surg 2021
9. Koh FH et al. Does the timing of an invasive mesenteric angiography following a positive CT mesenteric angiography make a difference? Int J Colorectal Dis 2015
10. Ochi M et al*.* Early colonoscopy and urgent contrast enhanced computed tomography for colonic diverticular bleeding reduces risk of rebleeding. World Journal of Clinical Cases 2021
11. Takada H et al. Extravasation and fluid collection on computed tomography imaging in patients with colonic diverticular bleeding. PLoS One 2020; 15: e0229884.
12. Nagata N et al. Role of urgent contrast-enhanced multidetector CT for acute lower gastrointestinal bleeding in patients undergoing early colonoscopy J Gastroenterol 2015
13. Nakatsu S et al. Urgent computed tomography for determining the optimal timing of colonoscopy in patients with acute lower gastrointestinal bleeding. Intern Med 2015
14. Umezawa S et al. Contrast-enhanced CT for colonic diverticular bleeding before colonoscopy: a prospective multicenter study Radiology 2018

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| PICO 9 | Timing of colonoscopy  P: Patients hospitalized with severe hematochezia undergoing colonoscopy  I: Performance of early colonoscopy (within 24 hours)  C: Performance of elective colonoscopy (beyond 24 hours)  O: Rebleeding, endoscopic intervention, source of bleeding, LOS, mortality, need for IR/surgery | | | |
|  | | Population | Comparator/Outcomes | Findings |
| **Meta-analyses** | | | | |
| *Kherad O et al* | | Systematic review of 4 RCTs (n=466) and 13 observational studies comparing elective (>24h) colonoscopy to early colonoscopy | Rebleeding rate (RCT only), early vs elective  Secondary outcomes (mortality, LOS, definite cause of LGIB (early vs. elective), adverse events, need for surg  Limiting analysis to observational studies only, early vs. elective colonoscopy | ND (OR 1.70, 95% 0.79-3.64)  ND in any secondary outcome when limited to RCT, except definite cause of bleeding (OR 1.71, 95% CI 1.00-2.93)  Mortality (OR 0.86, 95% CI 0.75-0.98)  Surgery (OR 0.52, 95%CI 0.42-0.64),  Transfusion (OR 0.81) |
| *Anvari S et al* | | Systematic review of 4 RCTs (n=463) comparing urgent to standard colonoscopy in LGIB | Length of stay, rate of additional intervention, mortality  When including observational studies (9 studies, n=111,950), comparing standard vs urgent colonoscopy | ND  Shorter LOS in urgent group  Higher mortality in standard group |
| *Tsay et al* | | Systematic review of 4 RCTs comparing early colonoscopy to elective colonoscopy in LGIB | Further bleeding (Persistent or recurrent bleeding)  Secondary outcomes (mortality, diagnostic yield, endoscopic intervention, any hemostatic intervention | ND  ND in any secondary outcome |
| *Roshan Afshar et al* | | Systematic review of 19 observational studies and 2 RCTs of early vs. late colonoscopy | Rebleeding  Mortality, surgery,  Definite cause of LGIB (early vs late)  LOS (early vs. late) | ND (total analysis + RCT only)  ND  **OR 4.12 (2.00-8.49)**  **-1.52 D** (95% -2.54-0.50) |
| *Seth A et al* | | Systematic review of 2 RCTs and 4 observational studies comparing urgent vs. elective colonoscopy | SRH (urgent vs. elective)  Bleeding source, Mortality, Rebleeding, Surgery, LOS, endoscopic intervention | **OR 2.85 (1.90-4.28)**  ND |
| *Kouanda et al* | | Systematic review of 12 studies (10 observational, and 2 RCTs) comparing urgent to elective colonoscopy | Endscopic intervention rate (urgent vs. elective)  Bleeding source, adverse events, rebleeding, transfusion, mortality | **RR 1.70, 95%CI 1.08-2.67)**  ND |
| *Sengupta et al* | | Systematic review of 6 studies (2 RCTs) | Bleeding source (urgent vs. elective)  Endoscopic intervention (urgent vs. elective)  Mortality, rebleeding, surgery, LOS | **OR 2.97,** 95% 2.11-4.19  **OR 3.99,** 95% CI 2.59-6.13  ND |
| **RCTs** (published since 2015) | | | | |
| *Niikura et al* | | Multicenter RCT of 170 pts with LGIB assigned 1:1 (early colon<24 hrs or elective colon, 24-96 hrs) | Primary outcome: SRH  Rebleeding within 30 d  Endoscopic treatment  Transfusion  LOS  Mortality | 21.5%, 17/79 (early group) vs. 21.3%, 17/80 (elective group), **p=0.967**  ND  ND  ND  ND  ND |
| *Van Rongen et al* | | RCT of 132 pts randomized to early (n=63) vs. standard colon (n=69). | Primary outcome: LOS (early vs. standard)  Recurrent bleeding (early vs. standard)  Bleeding source, transfusion, mortality | 2.0 (IQR 2-4) vs. 3.0 (IQR 2-4), **p=.009**  **13% vs. 3%, p=0.04**  ND |

1. Kherad O et al. Systematic review with meta-analysis: limited benefits from early colonoscopy in acute lower gastrointestinal bleeding. Aliment Pharmacol Ther 2020
2. Anvari S et al. Urgent vs standard colonoscopy for management of acute lower gastrointestinal bleeding: a systematic review and meta-analysis of randomized controlled trials. J Clin Gastroenterol 2020
3. Tsay C et al. Early colonoscopy does not improve outcomes of patients with lower gastrointestinal bleeding: systematic review of randomized trials. Clin Gastroenterol Hepatol 2020
4. Roshan Afshar I et al. The role of early colonoscopy in patients presenting with acute lower gastrointestinal bleeding: a systematic review and meta-analysis. Therap Adv Gastroenterol 2018
5. Seth A et al. Does urgent colonoscopy improve outcomes in the management of lower gastrointestinal bleeding? Am J Med Sci 2017
6. Kouanda AM et al. urgent colonoscopy in patients with lower GI bleeding: a systematic review and meta-analysis Gastrointestinal Endoscopy 2017
7. Sengupta N et al. Early vs. delayed colonoscopy in patients with lower gastrointestinal bleeding: a meta-analysis Journal of Clinical Gastroenterology 2017
8. Niikura R et al. Efficacy and safety of early vs. elective colonoscopy for acute lower gastrointestinal bleeding. Gastroenterology 2020
9. van Rongen I et al. Early versus standard colonoscopy: a randomized controlled trial in patients with acute lower gastrointestinal bleeding: results of BLEED study. J Clin Gastroenterol 2019

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| PICO 10 | Treatment of Diverticular Bleeding  P: Patients with LGIB with stigmata of hemorrhage from diverticulosis  I: Performance of mechanical therapy, thermal therapy, epinephrine, hemostatic powders  C: Comparison between therapies  O: Endoscopic hemostasis, Rebleeding | | | |
|  | | Population | Comparator/Outcomes | Findings |
| ***Systematic reviews/Meta-analyses on endoscopic treatment for Diverticular bleeding*** | | | | |
| *Ishii N et al* | | Systematic review meta-analysis of 16 studies (n=384 with diverticular bleeding) comparing treatment options. Pooled estimates were provided for each outcome | Initial hemostasis  Coagulation  Clipping  Ligation  Early recurrent bleeding  Coagulation  Clipping  Ligation  Need for TAE or surgery  Coagulation  Clipping  Ligation  Need for TAE or surgery lower in ligation vs clipping | 1. (0.91-1.00)   0.99 (0.97-1.00)  0.99 (0.95-1.00)  0.21 (0.01-0.51)  0.19 (0.07-0.35)  0.09 (0.04-0.15)  0.18 (0-0.61)  0.08 (0.03-0.16)  0 (0-01)  **P=0.03** |
| *Nagata N et al.* | | Systematic review meta-analysis of 16 studies (n=790) comparing clipping vs. band ligation in rebleeding | Pooled prevalence of early rebleeding (<30 d)  Pooled prevalence of late rebleeding (<1yr)  Initial hemostasis rate  Pooled prevalence of TAE/surgery  Complications | 0.08 (EBL) vs. 0.19 (clips), **p=.012**  0.09 (EBL) vs. 0.29 (clips), **p=.024**  ND  0.01 (EBL) vs. 0.02 (clips), **p=.031**  Two cases of diverticulitis w/ EBL vs. 0 for clips |
| ***Data from Retrospective Cohorts*** | | | | |
| *Nagata N et al* | | Retrospective cohort of 108 pts with diverticular bleeding undergoing EBL vs. clipping (direct or indirect) | Recurrent bleeding at 1 yr | 0.115(0.057-0.227) (EBL) vs. 0.37 (.25-.53) (clips), **p=0.02** ND b/w direct or indirect clipping |
| *Kobayashi et al* | | Retrospective multicenter cohort of 1679 pts with CDH treated with EBL (n=638) or clipping (N=1041) | Early rebleeding (within 30 days), EBL vs. clipping  Late rebleeding, EBL vs. clipping  Initial hemostasis and mortality  Need for IR interv, EBL vs clipping  Need for surgery, transfusion | AOR 0.46 (0.34-0.62), **p<.001**  AOR 0.62 (0.49-0.79), **p<.001**  ND  AOR 0.37 (0.19-0.76), **p=.006**  ND |
| *Okamoto et al* | | Retrospective cohort of pts with CDH treated with EBL (n=67) and clips (n=68) | Rebleeding rate (EBL vs. clips)  Rebleeding rate from same diverticulum initially treated (EBL vs. clips) | 10% vs. 31%, **p<.01**  6% vs. 22%, **p<.01** |
| *Nakano et al* | | Retrospective cohort of pts with CDH treated with EBL (n=61) and clips (n=39) | Initial rebleeding  Cumulative 1 yr incidence of rebleeding (EBL vs. clips) | 34%, 21/61 (EBL) vs. 67%, 26/39 (clips)  23% (EBL) vs. 49% (clips), **p=.004** |
| *Kobayashi et al* | | Retrospective cohort of pts with CDH treated with clips (n=87) vs. endoscopic detachable snare ligation (EDSL), n=44 | Early rebleeding rate (w/in 30 day) | 6.8% (EDSL) vs. 23% (clips), **p=0.03** |

1. Ishii N et al. Effectiveness of endoscopic treatments for colonic diverticular bleeding. (systematic review and meta-analysis). Gastrointest Endosc 2018
2. Nagata N et al. Cumulative evidence for reducing recurrence of colonic diverticular bleeding using endoscopic clipping vs. band ligation: systematic review and meta-analysis. J Gastroenterol Hepatol 2021
3. Nagata N et al. Long-term recurrent bleeding risk after endoscopic therapy for definitive colonic diverticular bleeding: band ligation vs. clipping. Gastrointest Endosc 2018
4. Kobayashi K et al. Effectiveness and adverse events of endoscopic clipping versus band ligation for colonic diverticular hemorrhage: A large-scale multicenter cohort study. Endoscopy 2021
5. Okamoto N et al. Lower Rebleeding Rate after Endoscopic Band Ligation than Endoscopic Clipping of the Same Colonic Diverticular Hemorrhagic Lesion: A Historical Multicenter Trial in Saga, Japan. Intern Med 2019
6. Nakano K et al. Comparison of long-term outcomes between endoscopic band ligation and endoscopic clipping for colonic diverticular hemorrhage. Endosc Int Open 2015; 3.
7. Kobayashi K et al. Endoscopic detachable snare ligation improves the treatment for colonic diverticular hemorrhage. Digestion 2020; 101

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| PICO 11 | Resumption of Antiplatelets following LGIB  P: Patients with LGIB (including diverticular hemorrhage) who are on antiplatelets/NSAIDs  I: Resumption of aspirin, non-aspirin antiplatelets, or NSAIDs  C: No resumption of these medications  O: Recurrent bleeding, Ischemic complications | | | |
|  | | Population | Comparator/Outcomes | Findings |
| ***Data from LGIB cohorts*** | | | | |
| *Aoki et al* | | Retrospective cohort of 342 pts with LGIB, including pts on NSAIDs (n=53), ASA (n=88), non-ASA antiplatelets (n=47), DAPT (n=43) | Predictors of recurrent bleeding on MV analysis  Cumulative prob of rebleeding (survival) | NSAIDs (HR 2.0, 1.2-3.3)  Non-aspirin antiplatelet (HR 1.8, 1.0-2.3)  NSAIDs (HR 1.9, p=.01)  Non-aspirin antiplatelet (HR 2.1, p<.01)  DAPT vs. single (HR 1.8, p<.05) |
| *Chan et al* | | Retrospective cohort of 205 aspirin users hospitalized with LGIB. Outcomes were compared b/w aspirin non-users during 5 yr follow-up (n=121) vs. aspirin users (n=174) | Recurrent LGIB in aspirin users vs. non-users  Serious CV events (ASA users vs. non-users)  MV predictor of rebleeding (users vs. non-users)  Serious CV events (users vs. non-users) | 18.9% (13.3-25.3%) vs. 6.9% (3.2-12.5%), p=.007  22.8% (16.6-29.6) vs. 36.5% (27.4-45.6)  **AOR 2.76 (1.26-6.07)**  **AOR 0.59 (0.37-0.91)** |
| *Vajravelu et al* | | Retrospective insurance database of 14,925 with initial CDB. Hazard ratios for recurrent CDB associated with platelet aggregation inhibitors (PAI, non-ASA antiplatelets) estimated | Risk of second diverticular hemorrhage based on PAI exposure or not | HR 1.47 (1.15-1.88) (PAI exposure to none)  HR 1.84 (1.13-3.00) (PAI with aspirin) |
| *Oakland et al* | | Retrospective multicenter cohort of 2528 pts with LGIB, of whom n=504 on single AP, and n=79 on DAPT. Analysis compared to unexposed patients (n=1218) | Rebleeding rates (DAPT vs. unexposed)  (single AP vs. unexposed)  Mortality | HR 5.38 (1.56-18.54)  HR 3.57 (1.13-11.28)  ND |
| *Nagata et al* | | Retrospective cohort of 132 pts with CDB, including 41 NSAID users | Recurrent bleeding risk on MV analysis with continued NSAID use  Probability of rebleeding at 12 months | **HR 4.6 (2.2-9.4), p<.01**  9.4% (2.4-33) (NSAID discontinued) vs. 77% (52-94%) (NSAID continued), p<.01 |
| *Sato et al* | | Retrospective cohort of 519 pts with CDB , analysis separted into elderly (n=273) vs. not. | Independent risk factors for late rebleeding (>30 d)  Independent risk factors for late rebleeding in elderly | NSAIDs (OR 2.27, 1.37-3.78)  NSAIDs (OR 3.55, 1.86-6.76) |
| *Sostres et al* | | Retrospective cohort of 382 pts LGIB. Analysis included resumption of antiplatelets (n=192) | **Resuming AP vs. not**  Ischemic event  Recurrent GI bleeding  Mortality | HR 0.45, 0.197-1.05  HR 1.59, 0.62-4.06  **HR 0.44, 0.23-0.85** |

1. Aoki T et al. Recurrence and mortality among patients hospitalized for acute lower gastrointestinal bleeding. Clin Gastroenterol Hepatol 2015
2. Chan FK et al. Risks of bleeding recurrence and cardiovascular events with continued aspirin use after lower gastrointestinal hemorrhage Gastroenterology 2016
3. Vajravelu R et al. Incidence, risk factors, and clinical effects of recurrent diverticular hemorrhage: a large cohort study Gastroenterology 2018
4. Oakland K et al. Rebleeding and mortality after lower gastrointestinal bleeding in patients taking antiplatelets or anticoagulants Clin Gastroenterol Hepatol 2019
5. Nagata N et al. Impact of discontinuing non-steroidal antiinflammatory drugs on long-term recurrence in colonic diverticular bleeding. World J Gastroenterol 2015; 21:1292-8.
6. Sato Y et al. Risk Factors for Late Rebleeding of Colonic Diverticular Bleeding in Elderly Individuals. J Anus Rectum Colon 2021; 5(2): 148-157.
7. Sostres C et al. Risk of rebleeding, vascular events and death after gastrointestinal bleeding in anticoagulant and/or antiplatelet users. Aliment Pharmacol Ther 2019

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| PICO 12 | Resumption of Anticoagulants following LGIB  P: Patients with LGIB (including diverticular hemorrhage) on anticoagulants  I: Resumption of anticoagulant medication  C: No resumption of anticoagulant medication  O: Rebleeding, Prevention of Thromboembolism/Ischemic complications, mortality | | | | |
|  | | Population | | Comparator/Outcomes | Findings |
| ***Systematic review/Meta-analysis of any anticoagulant resumption in all GIB*** | | | | | |
| *Bingzheng X et al.* | | Systematic review, meta analysis of 7 observational studies (n=2532) evaluating GIB hospitalization, and risks of subsequent anticoagulant cessation | | Continuing vs. discontinuing AC  Recurrent bleeding  Thromboembolism  Mortality | OR 2.40 (1.62-3.56)  OR 0.22 (0.10-0.49)  OR 0.39 (0.22-0.71) |
| *Chai-Adisaksopha et al* | | Systematic review meta analysis of 3 observational studies evaluating GIB, and risks of anticoag cessation | | Continuing vs. discontinuing AC  Recurrent bleeding  Thromboembolism  Mortality | OR 1.20 (0.97-1.48)  **OR 0.68 (0.52-0.88)**  **OR 0.76 (0.66-0.88)** |
| *Little D et al* | | Systematic review meta analysis of 12 observational studies evaluating GIB, and risks of anticoag cessation | | Continuing vs. discontinuing AC  Recurrent bleeding  Thromboembolism  Mortality | **RR 1.91 (1.47-2.48)**  **RR 0.30 (0.13-0.68)**  **RR 0.51 (0.38-0.70)** |
| *Tapaskar et al* | | Systematic review meta analysis of 10 observational studies evaluating GIB, and risks of anticoag cessation | | Continuing vs. discontinuing AC  Recurrent bleeding  Thromboembolism  Mortality | **OR 1.65 (1.04-2.62)**  **OR 0.34 (0.18-0.65)**  **OR 0.50 (0.42-0.60)** |
| ***Cohort study comparing resumption of DOAC to warfarin resumption in GIB*** | | | | | |
| *Tapaskar N et al* | | Retrospective insurance claims cohort of pts with GIB on warfarin (n=1872) or DOACs (n=1219). Resumption of warfarin vs. DOAC and risks of recurrent bleeding and thromboembolism | ***Risk of recurrent GIB***  Resumption of warfarin  Resumption of DOAC  Resumption of Rivarox  ***Risk of thromboembolism***  *Resumption of warfarin*  *Resumption of DOAC* | | **HR 2.12 (1.43-3.14)**  HR 1.43 (0.81-2.52)  **HR 2.73 (1.43-5.20)**  **0.61 (0.39-0.96)**  **0.52 (0.28-0.98)** |
| ***Cohort Studies with data specific to LGIB*** | | | | | |
| *Sostres C et al* | | Retrospective cohort of patients with LGIB (n=407), subgroup analysis on resuming anticoagulants | | Resuming anticoagulants vs. not  Ischemic events  Recurrent GIB  Death | 0.53 (0.18-1.60)  1.46 (0.35-6.12)  **0.33 (0.15-0.75)** |
| *Vajravelu R et al* | | Insurance database of 14,925 with initial CDB. HRs for recurrent CDB a/w anticoagulants, and risks of anticoagulant d/c and CVA measured | | Risks of second CDB  Risks of ischemic CVA with anticoagulation discontinuation | ND with use of DOACs or warfarin  **HR 1.93 (1.17-3.19)** |
| *Oakland K et al* | | Retrospective multicenter cohort of 2528 pts with LGIB, of whom 334 were on anticoag (n=232 on warfarn, n=102 on DOAC). Risk factors compared to unexposed patients | | Risks of recurrent bleeding  Mortality | ND with DOAC or warfarin  ND with DOAC or warfarin |
| *Aoki T et al* | | Retrospective cohort of 342 pts with LGIB, of whom 25 on warfarin | | Risks of rebleeding (warfarin use vs. not)  Risks of death (warfarin use vs. not) | ND with warfarin  P<.01 (warfarin risk factor for mortality in LGIB |
| *Sato Y et al* | | Retrospective cohort of n=519 with LGIB, n=48 on warfarin, and n=26 on DOAC | | Risks of late rebleeding with use of warfarin or DOAC | ND |

1. Bingzheng X et al. The effects of anticoagulant therapy re-initiation after gastrointestinal bleeding: A systematic review and meta-analysis. J Clin Pharm Ther 2021
2. Chai-Adisaksopha C et al. Thromboembolic events, recurrent bleeding and mortality after resuming anticoagulant following gastrointestinal bleeding. A meta-analysis. Thromb Haemost 2015; 114: 819-25
3. Little D, Chai-Adisaksopha C, Hillis C et al. Resumption of anticoagulant therapy after anticoagulant-related gastrointestinal bleeding: A systematic review and meta-analysis. Thromb Res 2019; 175: 102–109
4. Tapaskar N, Pang A, Werner DA et al. Resuming anticoagulation following hospitalization for gastrointestinal bleeding is associated with reduced thromboembolic events and improved mortality: Results from a systematic review and meta-analysis. Dig Dis Sci 2021; 66: 554–566
5. Tapaskar N et al. Restarting Warfarin vs Direct Oral Anticoagulants After Major Gastrointestinal Bleeding and Associated Outcomes in Atrial Fibrillation: A Cohort Study. Clin Gastroenterol Hepatol 2020
6. Sostres C, Marcen B, Laredo V et al. Risk of rebleeding, vascular events and death after gastrointestinal bleeding in anticoagulant and/or antiplatelet users. Aliment Pharmacol Ther 2019
7. Vajravelu R et al. Incidence, risk factors, and clinical effects of recurrent diverticular hemorrhage: a large cohort study Gastroenterology 2018
8. Oakland K et al. Rebleeding and mortality after lower gastrointestinal bleeding in patients taking antiplatelets or anticoagulants Clin Gastroenterol Hepatol 2019
9. Aoki T et al. Recurrence and mortality among patients hospitalized for acute lower gastrointestinal bleeding. Clin Gastroenterol Hepatol 2015
10. Sato Y et al. Risk Factors for Late Rebleeding of Colonic Diverticular Bleeding in Elderly Individuals. J Anus Rectum Colon 2021; 5(2): 148-157.