Clinical and Urgent Colonoscopy Outcomes using the Pure-Vu® Cleansing System in Hospitalized Patients with Lower Gastrointestinal Bleeding: A Single-Center Prospective Pilot Study

BACKGROUND:

Acute lower gastrointestinal bleeding (LGIB), while generally defined as gastrointestinal bleeding distal to the ligament of Treitz, can be categorized into small bowel and colorectal bleeding, two sites with distinct presentations as well as diagnostic and management options (1). Acute LGIB secondary to a colorectal source usually presents with sudden onset hematochezia with or without acute blood loss anemia and hemodynamic instability, and usually leads to multiple invasive procedures and hospitalizations. It accounts for up to one-third of all hospitalizations related to GIB (2). The current guidelines recommend urgent colonoscopy to be performed within 8 to 24 hours of presentation and after adequate colon preparation to improve visualization and diagnostic/therapeutic yield (1). While studies looking at optimal timing of colonoscopy are limited for patients with acute LGIB, a study comparing 48 patients with diverticular bleeding who underwent colonoscopy after rapid polyethylene glycol (PEG) preparation and within 12 hours of presentation with endoscopic hemostasis compared to 73 controls without endoscopic hemostasis, found a significant improvement in outcomes in the group that underwent hemostasis, including bleeding (0% vs. 53%) and hospital length (median of 2 days vs. 5 days) (3). In another RCT of 100 patients presenting with LGIB, colonoscopy within 8 hours of presentation after rapid preparation lead to a more definite diagnosis compared to patients who underwent elective colonoscopy within 96 hours of presentation (4). Urgent colonoscopy however requires the rapid administration of a large volume bowel preparation over 3-4 hours until the rectal effluent is clear (1). Purge preparation can be challenging in critically ill patients and frequently requires the placement of a nasogastric tube for administration of the preparation which could place the patient at risk of aspiration, poor tolerance, and rarely, electrolyte imbalances (1). Moreover, bleeding can

subside while awaiting resuscitation and bowel preparation prior to endoscopic intervention, which could lead to a decreased diagnostic and therapeutic yield. The guidelines recommend against unprepped colonoscopy due to poor visualization and increased perforation risk (1). A pilot study looked at the effect of "hydroflush colonoscopy" in acute LGIB with minimally prepped colons (tap water enema without oral preparation). "Hydroflush colonoscopy" was defined as colonoscopy using a combination of a water jet pump irrigation and a mechanical endoscope suction device (BioVac direct suction device). Out of the 12 patients included, the cecum was reached 69% of the time and endoscopic visualization was found to be adequate to find the source of bleeding in all procedures (5). The Pure-Vu® System (Motus^{GI} Ltd.), a novel Food and Drug Administration (FDA) 510k cleared intra-procedural cleansing device, has been recently introduced. The Pure-Vu® System integrates with the colonoscope and generates a pulsed vortex mixture of water and air in order to remove debris and is active at the time of cleansing to evacuate colonic contents simultaneously (6). Its effectiveness has been studied in colonoscopies requiring minimal preparation regimens with excellent and safe results (7,8). A multicenter European feasibility study looked at 47 patients referred for colonoscopy who received a limited bowel preparation and found significant improvement in the proportion of patients with adequate preparation, with a median Boston bowel preparation score (BBPS) increased from 3[0-5] to 9 [8-9] (8). The REDUCE trial (9), another multicenter, single-arm study, was the first trial to study Pure-Vu® in the inpatient setting, which enrolled 95 hospitalized subjects. Adequate bowel preparation improved from 38% (95% CI 28,49) to 96% (CI 90-99) in the evaluated segments. The mean BBPS improved from 1.74 in the left colon, 1.74 in the transverse colon, 1.5 in the right colon to 2.89, 2.91 and 2.86 respectively ($p<0.001$) (9).

HYPOTHESIS:

The Pure-Vu® System can be effectively used as a cleansing device in patients admitted with acute LGIB to the intensive care unit and the regular nurse floor (RNF) bypassing the need to

administer an oral bowel preparation for adequate visualization and hence decreasing time to colonoscopy and improving diagnostic and therapeutic yield.

PRIMARY OUTCOME:

The primary outcome of the study will be the proportion of patients who achieve an adequate bowel preparation to identify bleeding lesions (i.e. BBPS≥ 2 in all 3 colonic segments, which will be determined by the endoscopist).

SECONDARY OUTCOMES:

Secondary outcome measures will include:

- Diagnostic yield defined as the identification of the source of bleed or adequate visibility to rule out a LGIB source
- Therapeutic yield defined as control of bleeding source through endoscopic interventions
- Re-bleeding rate defined as recurrent hematochezia/ bright red blood per rectum within 48 hours of the index colonoscopy with Pure-Vu® system
- Need for repeat colonoscopy within 48 hours of index colonoscopy using Pure-Vu® to control source of bleed
- Length of the procedure
- Endoscopist satisfaction
- Length of intensive care unit (ICU) stay (only applicable if subject had colonoscopy in the ICU)
- Length of hospital stay

METHODOLOGY:

Study Design:

This will be a single-center, single-arm feasibility study which will be conducted at our tertiary care center, Cleveland Clinic, Cleveland, Ohio, United States.

Study Population:

Eligible patients will be hospitalized patients with acute LGIB undergoing urgent colonoscopy under monitored anesthesia care or conscious sedation.

Inclusion criteria:

1. Hospitalized patients in the ICU or the RNF with acute LGIB (defined as maroon-colored stool or bright red blood per rectum with suspicion of acute blood loss anemia, and hemodynamically stable and/or stabilized at the time of procedure. Hospitalized patients include:
    - Patients who develop LGIB while admitted for different reasons
    - Patients transferred from an outside hospital for further management of acute LGIB
    - Patients admitted through the emergency room for management of acute LGIB
2. ≥22 years old (age cleared by the FDA for device use)
3. Undergoing urgent colonoscopy under general anesthesia or conscious sedation

Exclusion criteria:

Patients will be excluded if:

1. Suspicion for bowel obstruction/ stricture
2. Toxic megacolon or severe colitis (determined by degree of colitis on imaging and clinical condition including pain, fevers, abdominal exam, elevated inflammatory markers)
3. Active Diverticulitis
4. Confirmed COVID-19 positive
5. Patients with no capacity and unable to provide informed consent

Variables to be collected and studied:

- Patients Characteristics and Demographics:

  Date of birth, gender, ethnicity, body mass index, American Society of Anesthesiologists classification, surgical history of the abdomen and pelvis.

- Admission Characteristics:

  Hospital (CCF) admission date and time, presenting GI Bleeding symptoms (maroon-colored stool, bright red blood per rectum, abdominal pain, etc.), Baseline labs (if available) and labs at the time of LGIB development (hemoglobin, INR, platelet count), last dose of anticoagulation at time of colonoscopy, blood product transfusion

- Procedure Characteristics:

  Date of colonoscopy procedure, type of scope used, type of oversleeve used, colonoscopy start time (scope in time), colonoscopy end time (scope out time), colonoscopy completion, reason for colonoscopy non-completion, segment reached if colonoscopy incomplete, desired segment if colonoscopy incomplete (ileum vs. cecum), cecal

intubation, time to cecal intubation, time for device assembly, sedation type, BBPS pre and post Pure-Vu® System, pathologies found and characteristics (including size, location, morphology, etc.), interventions performed and time spent on each intervention

- Follow up and Adverse event collection:

  Adverse event (AE) occurring at the time of the procedure will be documented in the AE form. A follow up visit or call will be conducted 24-48 hours after the procedure. The patient will be interviewed by one of the study co-investigators or coordinator and if an adverse event (AE) is reported, the AE form will be completed.

  Any adverse events related to the study will be immediately reported to the Institutional Review Board (IRB).

Definitions:

Boston bowel preparation score:

The BBPS is a well validated tool used to describe the adequacy of a bowel preparation. It is applied upon withdrawal and after thorough cleaning and suctioning of each of the left colon (rectum, sigmoid colon and descending colon), transverse colon (including hepatic and splenic flexures) and right colon (ascending colon and cecum). Each of the 3 segments is then given a score as follows:

- 0 = Unprepared colon segment with mucosa not visualized due to solid stool that cannot be cleared.
- 1 = Areas of colonic mucosa seen, but other areas of the colon segment not well seen due to staining, residual stool and/or opaque liquid (residual fluid/ stool covering more than one-third of a colonic segment).
- 2 = Minor amount of residual fluid content, small fragments of stool and/or opaque liquid, but mucosa of colon segment seen well (contents covering less than one-third of a segment's mucosal surface).
- 3 = Excellent visualization of the colonic mucosa with no residual fluid or stool fragments.

In our study, we will be measuring the BBPS in each colonic segment before and after washing with the Pure-Vu® System. Endoscopists will be required to spend at least 3 minutes washing in each segment before assigning it a BBPS score.

Withdrawal time:

Withdrawal time is defined as the amount spent examining the colonic mucosa as the scope is being withdrawn from the cecum to the anus.

Acute blood loss anemia

Acute blood loss anemia will be defined as at least 1 gram drop in hemoglobin when compared to baseline.

Urgent colonoscopy

Urgent colonoscopy will be defined as colonoscopy performed within 24 hours of presentation

Study Procedures:

Identification of participants:

Patients admitted to CCF intensive care unit or RNF, with acute LGIB will have their chart reviewed by one of the study members to ensure eligibility and eligible patients will be invited to participate in the study. The patient will be introduced to the study and provided with the study information. Consent will be obtained from the patient the day of the procedure prior to any study activities. As previously mentioned, patients unable to provide informed consent will be excluded from the study.

Bowel preparation:

Enrolled patients will not receive any oral bowel preparation but will receive 2 tap water enemas approximately 30-60 minutes prior to the procedure, 15-20 minutes apart. Patients will be required to be *Nulla per Os* for at least 4 hours prior to the procedure to decrease aspiration risk with sedation.

Anesthesia and Colonoscopy:

Patients will receive general anesthesia by the ICU or anesthesia team, or, conscious sedation (usually a combination of Fentanyl and Midazolam) by the endoscopist. The choice of sedation will be determined by the primary team, anesthesiologist and/or endoscopist.

Colonoscopies will be performed using Olympus CF-HQ190L and PCF-H190L colonoscopes. The choice of an adult or pediatric colonoscope will be left to the endoscopist's discretion. Each procedure will be performed by a senior gastroenterology fellow under the supervision of a gastroenterology attending. The endoscopy cart nurses will be trained to set up and trouble shoot the Pure-Vu® System. The gastroenterology fellow and attending will receive instructions and training of device use prior to use.

Cleansing success will be attained if a BBPS of ≥2 is achieved in all segments. Pre and post cleansing photo-documentation will be obtained as well photo-documentation of any bleeding lesion.

A colonoscopy using the Pure-Vu® System will be considered complete if the cecum is reached or bleeding site is found distal to the cecum. A colonoscopy will be considered "incomplete" if the endoscopist elects to stop the procedure for patient safety (patient intolerability, or hemodynamic instability) or technical difficulties. If the endoscopist cannot reach the cecum with Pure-Vu® due to technical difficulties, the endoscopist has an option to use a naked scope to attempt to complete the procedure. If the procedure is incomplete the patient will then undergo standard of care bowel preparation and standard colonoscopy. This will include having the patient consume a bowel preparation at least 4 hours prior to standard of care colonoscopy.

After the procedure, a follow up visit or call will be conducted to check in on the patient's wellbeing. If an adverse event is reported, the adverse event form will be completed and submitted to the IRB.

Database:

This study will utilize IBM Clinical Connect as the electronic data capture (EDC) system which is a web-based platform maintained by IBM's Standard Operating Procedures. The IBM System has been fully validated according to 21 CRF Part 11 and predicate rules, using a risk-based validation model. IBM is hosted in a SAS-70 Type II certified datacenter located in Raleigh, NC.

Data Processing:

Data will be entered into the database by trained study team members. Any data queries will be resolved and entered into the database. Only Research Coordinators or PIs trained to the use of the database will have access for data entry.

The investigators shall ensure the accuracy, completeness, legibility and timelines of the data reported into the database. Data reported shall be supported by the source documents with any discrepancies being explained. If an item is not available or is not applicable, this fact should be indicated; no space is to be left blank.

Case Report Form:

The Case Report Form (CRF) will be filled up by one of the study team members. The CRF will include questions noted under methodology- variable to be collected and studied.

Post procedure endoscopist/nursing staff satisfaction survey:

Immediately following the procedure, endoscopists (Fellow and attending) and nursing staff will be required to complete the following questions at the time of colonoscopy report completion

- On a scale from 1 to 5, 1 being very unsatisfied and 5 being very satisfied:

For the endoscopist(s): "Did this device enable you to have a successful and satisfactory exam?"

For the nursing staff(s): "Were you satisfied with the loading and unloading process of this device?"

Adverse Events Form:

If an adverse event occurred in the procedure or reported during the follow up visit or call, one of the study team members will be responsible to fill out an adverse events form.

All adverse events will be immediately reported to the Institutional Review Board.

Data monitoring:

Data will be collected from the electronic medical record and managed using an IBM platform built by Motus and the Cleveland Clinic team.

Data collection forms including the case report forms, pre and post-procedure patient surveys, post-procedure endoscopist and nursing staff satisfaction surveys, adverse event forms will be completed as described above. The study coordinator will enter the data into the IBM platform. The data collection forms and questionnaires will be stored safely with the study coordinator in the DDSI department.

Sample size calculation:

This is a pilot study of 20 patients who will undergo urgent colonoscopy using the Pure-Vu® System for acute LGIB in the intensive care unit or the GI endoscopy suite. Interim analysis will occur after the first 10 patients are enrolled.

BUDGET

The study will be funded by Motus^{GI} Ltd. The company will cover the costs of all the Pure-Vu® System devices used. They will provide free training (on-site if allowed) and virtually to all providers who will be performing colonoscopies using the Pure-Vu® System. In addition they will cover administrative costs, IRB review costs, regulatory documentation for the duration of the

study, close out, project manager and statistics costs, and subject fee (please see budget form attached). In addition, in the rare instance that the initial colonoscopy could not be performed using the Pure-vu device, the sponsor has agreed to pay for the cost of the second colonoscopy performed in the traditional method without the use of the Pure-vu device. All other standard of care costs, including the index colonoscopy procedure (at the time of Pure-Vu® System device is used) will be charged to the patient and/or insurer.

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