Effectiveness of a Protocol-Based Team Approach to Peptic Ulcer Hemorrhage: A Prospective Randomized Trial

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A. Study Purpose and Rationale

Acute gastrointestinal hemorrhage represents a common and serious reason for hospitalization, and ranges in severity from minor isolated bleeding to extensive hemorrhage, shock, and even death. Gastrointestinal bleeding is commonly divided into upper and lower sources. Peptic ulcers are the most common cause of upper gastrointestinal bleeding, accounting for approximately 50% of cases'. Roughly, 80% of bleeding peptic ulcers stop spontaneously, but the overall mortality has remained at between 6% and 7% over the last three decades'.

Very few studies have attempted to elucidate a rigid protocol to manage acute peptic ulcer bleeding [1-11]. A retrospective study done by Stevens, et. al., has demonstrated that employing a rigid protocol to manage peptic ulcer bleeding can significantly reduce rebleeding rates, rates of surgery, total length of hospital stay, and total hospital charges. Compared with the control group, rebleeding was reduced from 31.1 % to 15.5%, the rate of patients going to surgery was reduced from 20% to 4.4%, the length of stay was reduced from 16.15 days to 9.37 days, and the total hospital charges were reduced from $76, 935 to $29, 9819. This study aims to evaluate this protocol-based multidisciplinary gastrointestinal rapid response team (GIRRT) for the management of peptic ulcer bleeding in a prospective, randomized trial.

Peptic ulcers can be categorized into five distinct appearances at endoscopy and are listed in order of lowest to highest risk of rebleeding and complications: clean base, flat spot, adherent clot, non-bleeding visible vessel, and active bleeding (both oozing and spurting),. Several studies have incorporated the appearance of ulcers along with other clinical information of patients (age, comorbidity, the presence or absence of shock) into scoring systems to predict clinical outcomes [1,4.16,11]. The Baylor bleeding score is one such scoring system that will be used in this study (table 1)[1]. Specifically, this scoring system encompasses a pre-endoscopy score which is based on patients' age and comorbidities, an endoscopy score based on the appearance and location of ulcers, and a post-endoscopy score which is the sum of the pre-endoscopy and endoscopy scores. Those patients with pre-endoscopy scores of less than 5 and post-endoscopy scores of less than [10] are considered low-risk, whereas patients with pre-endoscopy scores greater than 5 and post-endoscopy scores greater than are considered high risk and are more likely to rebleed. The Charlson comorbidity index will also be used in this study to risk stratify patients[1].

B. Study Design and Statistical Analysis

This will be a prospective, randomized study' Patients will be randomized to either the GIRRT or to the comparison group. Patients in the comparison group will be treated for peptic ulcer bleeding by gastroenterologists not associated with the GIRRT and not following the protocol. Randomization will be carried out by sealed envelope. Applying the equation,

plqi + + 2 (pi -P2)2 (pi-P2)

to the results of the rebleeding rate reduction in the study by Stevens et. al., approximately 130 patients will need to be randomized to each arm of the study. There will be no crossover between the two arms of the study. The data will be analyzed using multivariate and univariate logistic regression analysis.

The primary outcome measured will be rebleeding rates. Secondary outcomes will be the number of blood transfusions, the rate of patients requiring surgery to achieve hemostasis, length of stay, mean total hospital charges, and overall'mortality.

C. Study Subjects

All adult patients presenting with either hematemesis, melena, or both associated with one or more of the following: syncope, hypotension, (systolic blood pressure< 1 00mmHg), and orthostatic changes in pulse (>20 beats per minute) and blood pressure (>20mmHg) will be included in the study. Patients with variceal bleeding will be excluded from this study. Only those patients who do not have a regular physician will be included in this study, so as to avoid any potential bias from having treated a patient prior to enrollment.

D. Study Procedures

Upon presentation to Columbia Presbyterian Medical Center, each patient will be evaluated by the Gastroenterology (GI) fellow on-call. Once he or she has determined that eligibility criteria have been met, the GI fellow will pull a sealed envelope to randomize each patient to either the GIRRT or to a Gastroenterologist oncall, not associated with the GIRRT. Informed consent is obtained prior to all endoscopies, either from the patient or next of kin. Informed consent for participation in this study will be obtained from the patient only at the earliest possible time. For patients enrolled in the protocol-based GIRRT arm, endoscopy will be performed within 12 hours of presentation. Only those uclers with non-bleeding visible vessels or active bleeding will be treated. Treatment will consist of an injection of 1: 10, 000 epinephrine followed by therapy with a 10 Fr bipolar probe or 10 Fr heater probe until hemostasis is achieved and the vessel is flattened. Adherent clots, flat spots, and clean-based ulcers will not be treated. Those patients with active bleeding and nonbleeding ulcers with visible vessels will be admitted to the ICU for at least 24 hours. If there is no evidence of rebleeding, these patients will be further observed on the floor for another 24 hours and discharged if there are no complications. Those patients with clean-based ulcers, flat spots, or adherent clots will be observed on the floor for at least 24 hours and discharged if there is no rebleeding or other complications. After discharge, patients will be followed up at one week, one month, and three months, with a follow-Lip CBC at each interval. All patients will be maintained on proton-pump inhibitor therapy once oral intake is resumed.

Patients randomized to the non-protocol, non-GIRRT arm will be followed by the GI fellow under the supervision of the attending gastroenterologist not associated with the GIRRT. All aspects of endoscopic therapy, hospital disposition (ie. ICU vs. floor admission) will be determined by this attending gastroenterologist according to his or her clinical judgement.

Table I
Baylor Bleeding Scoring System
Pre-endoscopy s ore (PES) Endoscopy score (ES)
Assigned Age Number of Illness Site Stigmata
Score Illnesses Severity
<10
0 0
1 30-49 1 or 2 clot
2 50-59 -
3 60-69 - vessel
4 - 3 or 4 chronic posterior
5 >70 >5 acute Active bleed
Post-Endoscopy Score (POES) PES + ES

E. Confidentiality of Study Data

All study data will be separately coded using data collection sheets. Hospital unit numbers, social security numbers, subject initials, phone numbers and addresses will not be used in the final coding mechanism.

F. Potential Risks

There will be no added risk to patients in the study group as compared with those in the comparison group. There are inherent risks to endoscopy that are equal in both groups. These are perforation, bleeding, or infection.

G. Potential Benefits

The potential benefits of being in the protocol, GIRRT arm of the study are twofold. First, there is a potentially immediate benefit to the patient, as more aggressive therapy is aimed at higher risk cases, and more conservative therapy is aimed at high risk cases. This approach will better risk stratify patients, and avoid unnecessary

procedures. Second, there is a potential benefit to society, in that overall length of stay and cost are reduced in the GIRRT arm of the study. Patients are able to return to work sooner and safer, and'the overall burden on the health insurance infrastructure is lessened.

H. Alternative Therapies

Alternative therapies in the treatment of peptic ulcer bleeding are surgery and arterial embolization. Surgery consultation is obtained on all patients evaluated by the GIRRT. If endoscopic therapy fails to stop peptic ulcer bleeding, or if there is a complication such as perforation, patients are then taken to surgery to treat the bleeding and/or perforation. Usual procedures in the operation room are duodenal oversew (if the ulcer is duodenal and has eroded in the gastroduodenal artery), partial gastrectomy with either a Billroth I or 11 anastomosis, or a pyloroplasty with vagotomy. The relative advantage of surgery is that treatment is usually final with effective hemostasis, however the drawbacks of surgery are several, including the use of general anesthesia, hemodynamic stresses that may not be well-tolerated by more decompensated patients, and a potentially complicated post-operative course.

Arterial embolization is another alternative for the management of peptic ulcer disease. Performed by interventional radiologists, this relatively new procedure allows visualization of the culprit vessel through contrast fluoroscopy and embolization of this vessel using gelfbarn sponges. This procedure is relatively safe, however, is not first line therapy because of the limited access to the angiography suit during non-business hours and weekends and holidays. There is also a contrast-dye load that may not be tolerated by those patients with renal insufficiency.

I. Compensation to Subjects

There will be no compensation offered to study subjects.

J. Costs to Subjects

Subjects will incur no additional costs as a result of participating in the study.

K. Minors as Research Subjects

No minors will be used in this study.

L. Radiation or Radioactive Substances

No radiation or radioactive substances will be used.

Consent Form
Columbia Presbyterian Medical Center Consent to Participate in a Research Study

The purpose of this consent form is to provide you with the information you need to consider in deciding whether to participate in this research study.

Study Title: Effectiveness of a Protocol-Based Team Approach to Peptic Ulcer Hemorrhage.

Study Purpose

The purpose of this study is to evaluate whether using a specialized, protocol-based gastrointestinal rapid response team in the treatment of peptic ulcers will result in better outcomes for you, the patient in terms of decreasing rebleeding rates, the rates of going to surgery, reducing the length of stay in the hospital, and reducing overall hospital charges. You qualify as a possible participant because you have suffered a gastrointestinal bleed as a result of a peptic ulcer.

Study Procedures

If you decide to participate, you will undergo upper endoscopy. A tube with a video camera and other channels used for washing and cautery is inserted into your mouth and into your esophagus and stomach. You will be given adequate amounts of sedation during the procedure so that there is minimum discomfort. During the procedure, ethanol injection and electrocautery may be used to stop the bleeding. Biopsies of your intestine, stomach, or esophagus may be taken during the procedure.

You will be assigned by chance to either a bleeding team which will follow a protocol throughout your hospitalization or a non-bleeding team gastroenterologist, who will not use this protocol. After you are discharged from the hospital, follow-up visits will be scheduled after I week, I month, and 33 months. Approximately I teaspoon of blood will be collected at those times to check your blood counts.

This study will take place on the inpatient floors of the Milstein Pavilion, the PH 12 Center Endo scopy'Suite, and the outpatient Vanderbilt Clinic, I 01h floor.

Duration of participation will depend on the length of stay in the hospital. Once you are discharged, the outpatient appointments will take approximately 30 minutes each.

Study Risks

Your participation in this study involves the following risks. There are risks of the endoscopy itself which is shared in both groups of the study. These are infection, bleeding, and perforation, and are exceedingly rare. There is a risk that the bleeding team group may not be as effective as standard treatment, but there is also a risk that the nonbleeding team treatment may not be as effective as that of the bleeding team. Your condition may worsen as a result of these uncertainties.

Study Benefits

You may or may not benefit personally from this study. Benefits to you may include earlier and safer discharge, more aggressive or conservative therapy depending on the situation, which may reduce further complications. Benefits to society may include reduced length of stay for patients, thus allowing them to return to their families and jobs earlier, thus minimizing disruptions in everyday life. Reduced hospital costs may put less of a burden on insurance companies, which may, in turn reduce premiums. The reduced hospital costs may also put less burden on Medicare and Medicaid, which may translate into reduced income taxes.

Alternatives

Endoscopy is the first-line therapy for the diagnosis and treatment of peptic ulcers. However, alternatives exist if this first-line therapy fails to stop the bleeding. Surgery is an alternative that involves going to the operating room. The type of operation is at the discretion of the surgeon, but these usually involve making an incision into your abdomen and having part of your stomach removed.

Arterial embolization is another alternative procedure. If endoscopy fails to stop the bleeding, the interventional radiologists can selectively embolize the blood vessel that is bleeding. This procedure is less invasive and safer than surgery, but may not be suitable for patients with kidney. problems. Another disadvantage of this procedure is that bleeding may continue, in which case surgery is the remaining option.

Costs There will be no costs to you.

Compensation

You will receive no compensation for participation in this study.

Compensation for Injury

If you should require medical care (as determined by the medical staff) due to a researchrelated injury, the study sponsor (Division of Gastroenterology) will cover the cost of such medical care. Such reimbursement may extend only to that portion of the medical bills which are not covered by your medical or hospital insurance.

Confidentiality

Any information obtained during this study and identified with you will remain confidential. A separate coding mechanism will be used for study purposes. Hospital unit numbers, social security numbers, birthdates, addresses, names, initials, telephone numbers will not be included in this coding system.

Participation is Voluntary

Your participation in this study is completely voluntary. You can refuse to participate, or withdraw from the study at any time, and such a decision will not affect your medical care at Columbia-Presbyterian Medical Center, now or in the future. Signing this form does not waive your legal rights.

There will be no consequences from withdrawing from this study. Any new findings which may affect your willingness to continue in the study will be communicated to you.

Questions

If you have any questions, please ask, and we will do our best to answer them. If you have additional questions in the future, you can reach Dr. E. Shin at (212) 305-2913. If you have any questions on your rights as a research subject, you can call the Institutional Review Board at (212) 305-5883 for information.

Statement of Consent

I have discussed this study with Dr. E. Shin and/or colleagues to my satisfaction. I understand that my participation is voluntary and that I can withdraw from the study at any time without prejudice. I have read the above and agree to enter this research study. Signing this form does not waive any of my legal rights.

I have been informed that if I believe that I have sustained injury as a result of participating in a research study, I may contact the principal investigator, Dr. P. Stevens at (212) 305-2341, or the Institutional Review Board at (212) 305-5883, so that I can review the matter and identify the medical resources which may be available to me.

I understand that:

a) The Presbyterian Hospital will furnish emergency medical care determined to be necessary by the medical staff of this hospital;

b) I will be responsible for the cost of such care, either personally or through my medical insurance or other form of medical coverage;

c) No monetary compensation for wages lost as a result of injury will be paid to me by the Columbia-Presbyterian Medical Center, and;

d) I will receive a copy of this consent form.

Signatures:

Participant Date

Investigator Eliciting Consent Date

M. References

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