**PURLs Surveillance System**

**Family Physicians Inquiries Network**

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|  **Consider this strategy for upper GI bleeds. *J Fam Pract*. 2013;62:E6-E8.**  |

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| **Potential PURL Review Form: Randomized controlled trial** |

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| **SECTION 1: IDENTIFYING INFORMATION** |
| **1.** Citation  | Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med*. 2013;368:11-21. |
| **2.** Hypertext link to PDF of full article  | <http://www.nejm.org/doi/full/10.1056/NEJMoa1211801> |
| **3.** First date published study available to readers  | January 3, 2013 |
| **4.** PubMed ID  | 2381973 |
| **5.** Nominated By  | Jim Stevermer |
| **6.** Institutional Affiliation of Nominator  | University of Missouri |
| **7.** Date Nominated  | January 15, 2013 |
| **8.** Identified Through  | InfoPOEMs |
| **9.** PURLS Editor Reviewing Nominated Potential PURL | Kate Rowland |
| **10.** Nomination Decision Date  | January 24, 2013 |
| **11.** Potential PURL Review Form (PPRF) Type  | Randomized controlled trial |
| **12.** Other comments, materials or discussion  |   |
| **13.** Assigned Potential PURL Reviewer  | Kate Kirley |
| **14.** Reviewer Affiliation  | University of Chicago |
| **15.** Date Review Due  | February 14, 2013 |
| **16.** Abstract  | **BACKGROUND:**The hemoglobin threshold for transfusion of red cells in patients with acute gastrointestinal bleeding is controversial. We compared the efficacy and safety of a restrictive transfusion strategy with those of a liberal transfusion strategy.**METHODS:**We enrolled 921 patients with severe acute upper gastrointestinal bleeding and randomly assigned 461 of them to a restrictive strategy (transfusion when the hemoglobin level fell below 7 g per deciliter) and 460 to a liberal strategy (transfusion when the hemoglobin fell below 9 g per deciliter). Randomization was stratified according to the presence or absence of liver cirrhosis.**RESULTS:**A total of 225 patients assigned to the restrictive strategy (51%), as compared with 65 assigned to the liberal strategy (15%), did not receive transfusions (*P*<0.001). The probability of survival at 6 weeks was higher in the restrictive-strategy group than in the liberal-strategy group (95% vs. 91%; hazard ratio for death with restrictive strategy, 0.55; 95% confidence interval [CI], 0.33 to 0.92; *P*=0.02). Further bleeding occurred in 10% of the patients in the restrictive-strategy group as compared with 16% of the patients in the liberal-strategy group (*P*=0.01), and adverse events occurred in 40% as compared with 48% (*P*=0.02). The probability of survival was slightly higher with the restrictive strategy than with the liberal strategy in the subgroup of patients who had bleeding associated with a peptic ulcer (hazard ratio, 0.70; 95% CI, 0.26 to 1.25) and was significantly higher in the subgroup of patients with cirrhosis and Child-Pugh class A or B disease (hazard ratio, 0.30; 95% CI, 0.11 to 0.85), but not in those with cirrhosis and Child-Pugh class C disease (hazard ratio, 1.04; 95% CI, 0.45 to 2.37). Within the first 5 days, the portal-pressure gradient increased significantly in patients assigned to the liberal strategy (*P*=0.03) but not in those assigned to the restrictive strategy.**CONCLUSIONS:**As compared with a liberal transfusion strategy, a restrictive strategy significantly improved outcomes in patients with acute upper gastrointestinal bleeding. (Funded by Fundació Investigació Sant Pau; ClinicalTrials.gov number, NCT00414713.). |
| **sECTION 2: CRITICAL APPRAISAL OF VALIDITY** |
| **1.** Number of patients starting each arm of the study? | Restrictive: 461Liberal: 460 |
| **2.** Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc.)? | Presented to one hospital in Barcelona>18 years with upper gastrointestinal (GI) bleeding (hematemasis or melena)Excluded if declined transfusion, massive exsanguinating bleeding, acute coronary syndrome, symptomatic peripheral vasculopathy, stroke, transient ischemic attack, or transfusion within the previous 90 days; recent trauma or surgery, lower GI bleed, or very-low-risk bleeding |
| **3.** Intervention(s) being investigated? | Restrictive transfusion strategy (transfused for hemoglobin [Hgb] level <7 g/dL, target post-transfusion Hgb level of 7-9 g/dL) |
| **4.** Comparison treatment(s), placebo, or nothing? | Liberal transfusion strategy (transfused for Hgb <9 g/dL, target post-transfusion Hgb of 9-11 g/dL) |
| **5.** Length of follow-up? Note specified end points, eg, death, cure, etc. | 45 days |
| **6.** What outcome measures are used? List all that assess effectiveness. | Primary: rate of death from any cause within 45 daysSecondary: rate of further bleeding (repeat hematemesis or melena with hemodynamic instability or decrease in Hgb of 2 g/dL), rate of in-hospital complications (any "untoward events that necessitated active therapy or prolonged hospitalization") |
| **7.** What is the effect of the intervention(s)? Include absolute risk, relative risk, NNT, CI, p-values, etc. | Primary (mortality within 45 days): 5% (23 patients) restrictive vs 9% (41 patients) liberal; *P*=.02; hazard ratio (HR) 0.55; 95% CI, 0.33-0.92.Secondary:1. Rate of further bleeding: 10% restrictive vs 16% liberal; *P*=.01; HR 0.68; 95% CI, 0.47-0.982. Rate of in-hospital complications:* % receiving no transfusions: 51% restrictive vs 14% liberal; *P*<.001
* Violation of transfusion protocol: 9% restrictive v. 3% liberal, *P*<.001
* Length of stay: 9.6 days restrictive vs 11.5 days liberal; *P*=.01
 |
| **8.** What are the adverse effects of intervention compared with no intervention? | Overall complications: 40% (179 patients) restrictive vs 48% (214 patients) liberal; *P*=.02  |
| **9.** Study addresses an appropriate and clearly focused question - ***select one*** | Well covered |
| **10.** Random allocation to comparison groups | Well covered |
| **11.** Concealed allocation to comparison groups | Well covered |
| **12.** Subjects and investigators kept “blind” to comparison group allocation | Not applicableComments: No blinding, not really possible |
| **13.** Comparison groups are similar at the start of the trial | Adequately addressedComments: Clinically similar, although they didn’t address whether demographics are similar |
| **14.** Were there any differences between the groups/arms of the study other than the intervention under investigation? If yes, please indicate whether the differences are a potential source of bias. | Poorly addressed Comments: They explained that all patients underwent esophagogastroduodenoscopy (EGD) near the beginning of the study and may have been treated with various modalities during the procedure, but they did not report the numbers of these procedures. If the restrictive or liberal group received significantly more procedures during their initial EGD, that may affect later outcomes. |
| **15.** Were all relevant outcomes measured in a standardized, valid, and reliable way? | Well covered  |
| **16.** Are patient-oriented outcomes included? If yes, what are they? | Yes, death and complications |
| **17.** What percent dropped out, and were lost to follow up? Could this bias the results? How? | 17 patients were withdrawn from the restrictive group, 15 patients from the liberal group. See the answer to 18 below. |
| **18.** Was there an intention-to-treat analysis? If not, could this bias the results? How? | They called the analysis intention to treat, although they did not include 9 patients who withdrew from the study or who had major protocol violations in the analysis. It is not clear which treatment group these excluded patients were from, but there is potential for bias of results given the low overall rate of outcomes. |
| **19.** If a multi-site study, are results comparable for all sites? | N/A |
| **20.** Is the funding for the trial a potential source of bias? If yes, what measures were taken to insure scientific integrity? | No |
| **21.** To which patients might the findings apply? Include patients in the study and other patients to whom the findings may be generalized. | Adults with upper GI bleeding that is not severe or very mild who do not have coronary artery disease or peripheral vascular disease |
| **22.** In what care settings might the findings apply, or not apply? | Medical care setting (hospital) |
| **23.** To which clinicians or policy makers might the findings be relevant? | Family physicians practicing inpatient medicine |
| **SECTION 3: REVIEW OF SECONDARY LITERATURE** |
| **1.** DynaMed excerpts |   |
| **2.** DynaMed citation/access date | Acute upper gastrointestinal bleeding. In: DynaMed [database online]. Available at: www.DynamicMedical.com. Last updated February 11, 2013. Accessed February 12, 2013. |
| **3.** Bottom line recommendation or summary of evidence from DynaMed(1-2 sentences) | Use Hgb 7 g/dL as threshold for transfusion. |
| **4.** UpToDate excerpts |   |
| **5.** UpToDate citation/access date | Saltzman JR. Approach to acute upper gastrointestinal bleeding in adults. In: Basow DS, ed. UpToDate [database online]. Waltham, Mass: UpToDate; 2013. Available at: http://www.uptodate.com. Last updated January 11, 2013. Accessed February 12, 2013. |
| **6.** Bottom line recommendation or summary of evidence from UpToDate(1-2 sentences) | Use threshold Hgb of 7 g/dL to transfuse most patients with acute upper GI bleed. |
| **7.** PEPID PCP excerpts[www.pepidonline.com](http://www.pepidonline.com)username: fpinauthorpw: pepidpcp | Fluid/blood treatment• (5-20 cc/kg) NS bolus wide open• Reassess after bolus infused, may repeat if needed• If poor clinical picture / severely anemic, transfuse  |
| **8.** PEPID citation/access data | GI bleed: approach and resuscitation. In: PEPID [database online]. Available at: http://www.pepidonline.com. Accessed February 12, 2013. |
| **9.** PEPID content updating | 1. Do you recommend that PEPID get updated on this topic?Yes, there is important evidence or recommendations that are missingIf yes, which PEPID Topic, Title(s):GI bleed: approach and resuscitation |
| **SECTION 4: CONCLUSIONS** |
| **1.** **Validity:** How well does the study minimize sources of internal bias and maximize internal validity? Give one number on a scale of 1 to 7 (1=extremely well; 4=neutral; 7=extremely poorly) | 3  |
| **2.** If 4.1 was coded as 4, 5, 6, or 7, please describe the potential bias and how it could affect the study results. Specifically, what is the likely direction in which potential sources of internal bias might affect the results? | It would be helpful to know whether the rates of procedures during the initial EGD varied between the 2 groups, and also to know if the rates of patients who withdrew by choice or due to major protocol violations differed in the 2 groups. |
| **3. Relevance:** Are the results of this study generalizable to and relevant to the health care needs of patients cared for by “full scope” family physicians? Give one number on a scale of 1 to 7 (1=extremely well; 4=neutral; 7=extremely poorly) | 1  |
| **4.** If 4.3 was coded as 4, 5, 6, or 7,please provide an explanation. |   |
| **5. Practice-changing potential:** If the findings of the study are both valid and relevant, does the practice that would be based on these findings represent a change from current practice? Give one number on a scale of 1 to 7 (1=definitely a change from current practice; 4=uncertain; 7=definitely not a change from current practice) | 5  |
| **6.** If 4.5 was coded as 1, 2, 3, or 4, please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit. | Current recommendations seem to go along with the 7 g/dL threshold, although I'm not clear if this is widely practiced. |
| 1. **Applicability to a Family Medical Care Setting:**

Is the change in practice recommendation something that could be done in a medical care setting by a family physician (office, hospital, nursing home, etc), such as a prescribing a medication, vitamin or herbal remedy; performing or ordering a diagnostic test; performing or referring for a procedure; advising, educating or counseling a patient; or creating a system for implementing an intervention? Give one number on a scale of 1 to 7 (1=definitely could be done in a medical care setting; 4=uncertain; 7=definitely could not be done in a medical care setting) | 1  |
| **8.** If you coded 4.7 as a 4, 5, 6 or 7, please explain.  |   |
| **9. Immediacy of Implementation:** Are there major barriers to immediate implementation? Would the cost or the potential for reimbursement prohibit implementation in most family medicine practices? Are there regulatory issues that prohibit implementation? Is the service, device, drug or other essentials available on the market?Give one number on a scale of 1 to 7 (1=definitely could be immediately applied; 4=uncertain; 7=definitely could not be immediately applied) | 1  |
| **10.** If you coded 4.9 as 4, 5, 6, or 7, please explain why. |   |
| **11. Clinical meaningful outcomes or patient-oriented outcomes:** Are the outcomes measured in the study clinically meaningful or patient oriented? Give one number on a scale of 1 to 7 (1=definitely clinically meaningful or patient oriented; 4=uncertain; 7=definitely not clinically meaningful or patient oriented) | 1  |
| **12.** If you coded 4.11 as a 4, 5, 6, or 7 please explain why. |   |
| **13.** In your opinion, is this a Pending PURL? Give one number on a scale of 1 to 7(1=definitely a Pending PURL; 4=uncertain; 7=definitely not a Pending PURL)Criteria for a Pending PURL:* Valid: Strong internal scientific validity; the findings appears to be true.
* Relevant: Relevant to the practice of family medicine
* Practice changing: There is a specific identifiable new practice recommendation that is applicable to what family physicians do in medical care settings and seems different than current practice.
* Applicability in medical setting:
* Immediacy of implementation
 | 5  |
| **14.** Comments on your response in 4.13 | Unless others feel that current guidelines to transfuse at 7 g/dL are not being widely followed, then this fails on practice change. |